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Disclaimer:

Mind and Art (ORP-01)

Zahra Niknam

Recent research on music and brain function has suggested that the temporal pattern structure in music and rhythm can enhance cognitive functions.

To further elucidate this question specifically for memory, these are primary goals of this talk:

Declare mysterious mechanisms of memory formation at first, and then, different kinds of memory (declarative and non-declarative) with special attention to "episodic memory" from neuroscience, physics and literature point of view.

The last part returns back to how Art, preferably Music can augment and trigger different aspects of memory in MS patients.

Keywords: memory, cognition, Multiple Sclerosis, Art, Music

MS Prodrome; Is it a fact? (ORP-02)

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Multiple sclerosis (MS) is a partially heritable immune-mediated inflammatory demyelinating, and neurodegenerative disease affecting the CNS, with genetic and environmental factors contributing to disease development.

A prodrome is an early set of signs and symptoms, often non-specific, that indicates the onset of a disease before more classic symptoms occur. Prodromal stages are well recognized in some neurological and immune-mediated diseases such as Parkinson disease, Alzheimer, Schizophrenia, type 1 diabetes mellitus and rheumatoid arthritis.

During the past decade, studies have been published that indicate the existence of a prodrome in multiple sclerosis. Emerging evidence suggests that there is a prodromal period in MS that is measurable as an increase in healthcare use in the years preceding MS onset or diagnosis. Also, it evidenced by increased physician encounters for a diverse range of diagnoses and increased prescription medication use. The symptoms shown to occur 5–10 years before MS symptom onset in people who are subsequently diagnosed with MS. Many of the MS prodromal features characterized thus far are non-specific and are common in the general population (e.g. fatigue, anxiety, depression, migraine and lower cognitive performance ,…); no single feature alone is sufficient to identify an individual with prodromal MS. Biomarkers may increase specificity and accuracy for detecting individuals in the MS prodromal phase, but are yet to be discovered or formally validated.

Identification of individuals in the MS prodromal phase should be based on a combination of clinical features, genetic and environmental factors and magnetic resonance imaging (MRI) and/or laboratory biomarkers. Brain MRI abnormalities are sometimes detected by chance in the white matter in people with no typical symptoms of MS, and these findings are referred to as RIS. RIS may be a prodromal neuroimaging correlate. The next steps would be to combine prodromal symptoms, individual characteristics (Age, sex, comorbidities, …) and biomarkers to develop diagnostic criteria for the MS prodrome, which would allow for early identification and provides opportunity for early management and possibly even prevention of MS in the future.

Keywords: Multiple sclerosis (MS), MS Prodrome Criteria, Prevention, Biomarkers

A narrative review on the dietary interventions in multiple sclerosis (ORP-03)

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Currently, multiple sclerosis (MS) lacks a definitive treatment, emphasizing the need for research that prioritizes the investigation of modifiable environmental risk factors such as diet associated with MS development or the manifestation of its symptoms. Therefore, we designed a narrative review to investigate the role of dietary interventions on multiple sclerosis symptoms.

Swank is one of the oldest dietary interventions in MS. In 1948, swank started utilizing low fat diet, supplemented by cod liver oil. After 34 years follow-up, the survival rate was higher in swank diet group and patients were still ambulatory and otherwise healthy.

Modified Paleo diet (Wahl's protocol), recommends green leafy and sulfur-rich vegetables, as well as intensely colored fruits and vegetables, encourage to eat omega-3 sources, animal and plant protein, nutritional yeast, plant based milk, and kelp and spirulina, and excludes gluten, dairy and eggs. A 12-month multimodal intervention of it resulted in improvement in anxiety, depression, cognitive function and executive function (self-reported).

Sand et al in 2019 investigated the effects of modified Mediterranean dietary program in MS patients in a 6 months intervention. They reported the significantly improvement in fatigue score.

Ketogenic diet is a high fat and low carbohydrate diet. Benton et al, in 2019 investigated the effects of 6-month intervention of modified Atkins diet as a type of ketogenic diet (KDMAD) in MS patients. No subject experienced worsening disease on diet. Body mass index and total fat mass decreased. Fatigue and depression improved and leptin declined after 3 month.

Data on the effects of dietary interventions in MS is limited and the available studies are not methodologically strong. Based on the beneficial effects of some investigated diet and modifiable characteristics of diet, it seems to there is a need for more investigation with better methodology to prove the effects of each dietary patterns.

Keywords: Diet, Multiple sclerosis, Clinical trial, Intervention

The importance of vestibular evaluation and rehabilitation in improving the balance in MS patients (ORP-04)

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About two-thirds of MS patients report problems with balance or coordination in their daily lives. The prevalence of vestibular symptoms in MS patients is about 49-59%. Balance disorders can be seen even in the early stages of MS. The fear of falling due to balance disorder and its consequences significantly limits the quality of life in these patients and leads to a decrease in their activity level, productivity and social withdrawal. Timely identification of balance and vestibular disorders in MS patients is important because it leads to the adoption of appropriate drug treatments or appropriate rehabilitation strategies to minimize disability. The input and integration of three visual, vestibular and somatosensory senses are used to stimulate balance reflexes and maintain balance in static and moving conditions. Balance and vestibular disorders are usually associated with eye movement disorders, which can cause vertigo. Therefore, it is important to examine eye movements in vestibular disorders. Classification of eye movement disorder often leads to the identification of the neural structures involved. An increase in the amount of eye movement disorder leads to an increase in the disability of a person with MS and an increase in the EDSS score. Oculomotor tests such as saccade and smooth pursuit have a high diagnostic value in examining brainstem and cerebellar circuits. The VOR reflex can also be impaired following damage to the central part of the vestibular system. Also, vestibular evoked potentials can be a good tool for predicting and diagnosing brainstem involvement in MS patients, despite the correlation with MRI results. Static Posturography evaluation can also quantify balance disorders in MS patients. Adding static Posturography as an objective functional test to the assessment of EDSS in the early stages of MS is significant. In general, the results of balance evaluation tests show that these tests, along with clinical and MRI evaluations, are a good tool for diagnosing and following the treatment and rehabilitation process of MS patients. Due to the high prevalence of vestibular symptoms in patients with MS, it is better to implement vestibular system rehabilitation programs alongside the usual rehabilitation program for patients. Vestibular rehabilitation protocol with emphasis on gaze and postural stability. Improvement of VOR function leads to reduction of imbalance symptoms. Visual stability exercises, static and dynamic balance exercises, walking in different postures, and walking exercises with changes in visual inputs can effectively improve vestibular function in MS.

Keywords: vestibular evaluation, vestibular rehabilitation, MS

Physical disability assessment: EDSS calculation (ORP-05)

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The course of disease in more than >80% of patients with multiple sclerosis is relapsing remitting.in natural course of disease after 10-15 years, about sixty percent of patients experience a gradual decline in their neurological examination (secondar progressive MS, SPMS). In about 15% of patients have progressive disease from onset (primary progressive MS, PPMS).

In recent decades, many drugs are introduced for treatment MS. The primary aim of these drugs is to control relapse and progression in patients with MS. So, it is essential to design instrument for assessment the neurological function in these patients and evaluate the efficacy of the specific drugs.

Unfortunately, in many centers, the progress of the disease is detected with a delay and the golden time for treatment escalating is lost. One of the causes of this situation is the lack of familiarity of clinicians with tools for progression investigation.

Different type of scales has been designed to evaluate and measure neurological function in these patients. The described impairment in different parts of neurological system such as motor, sensory, cerebellar, autonomic and visual systems. Also, these tools have been used in different clinical trials.

The most popular and widely used instrument is the Expanded Disability Status Scale (EDSS) of Kurtzke. The EDSS is a physician-administered assessment scale investigating the functional systems of the central nervous system. This instrument is used to find progression and neurological deterioration in patients with MS. It consists of ordinal rating system ranging from 0 (normal neurological status) to 10 (death due to MS) in 0.5 increments interval (when reaching EDSS 1). The lower scale values of the EDSS measure impairments based on the neurological examination, while the upper range of the scale (> EDSS 6) measures handicaps of patients with MS. The determination of EDSS 4 – 6 is heavily dependent on aspects of walking ability.

Keywords: Multiple sclerosis, EDSS

Horizons of MS therapy: during 30 years (ORP-06)

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Before developing the first disease modifying therapy for MS, the therapeutic goals only had been focused on treatment of some symptoms or maximum targeting the immune systems by old immunosuperssor drugs with unknown efficacy.30 years ago,in 1993 the first disease-modifying therapy for relapsing multiple sclerosis was approved for use in the United States and soon thereafter across the globe. Since then the field of MS therapeutics, and studies of immunopathogenesis and genetics, have advanced our understanding of the disease and raised the hope of better addressing the next challenges of, better relapse control, treating progressive disease, enhancing repair of the damaged nervous system and, hopefully, of a cure. Thirty years into the MS treatment era, the field continues to debate fundamental aspects of MS, and there exists a widening chasm between the triumphs in relapsing disease and the desolation of MS progression, which remains the principal unmet need. In the panel, "New therapeutics horizons of MS', we outline lessons learned from the first era of great therapeutic development,adderessing on new MS drug targets, The role of new DMDs and future of the treatment. We then discuss the situation of old and new therapeutics and also the role of MS specialist in the optimized treatment decision making, as we look to the future of MS research

Keywords: Multiple sclerosis;, Future of MS,MS therapeutics targets disease course; disease-modifying therapy

Women and Multiple Sclerosis (ORP-07)

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MS is a female predominant disease. Multiple aspects of MS are influenced by sex-based differences. Women with MS were less likely to have a live birth, more likely to have a diagnosis of infertility, and less likely to receive infertility treatments compared with women without MS. Among women who received oral or injectable infertility treatments, LBRs for those with and without MS did not significantly differ.Several studies have showen an increased risk of relapse after IVF,especially with GnRH agonists stimulation protocol ,however 3 recent studieswith higher sample sizes and based on current therapeutics did not find any increase(3 mo after vs.3 mo .before).

Most contraceptive methods appear effective and safe for women with MS. LARC methods (long-acting reversible contraceptive) (intrauterine devices, implantable rods, tubal sterilization, hormonal contraceptives, and barrier methods) may be particularly appropriate in female patients because, once positioned, they do not require proactive user compliance .According to the WHO, UK MEC and US MEC, progestin-only and combined hormonal contraceptives are not recommended for patients with prolonged immobility, because of increased risk of venous thromboembolism and concerns about decreased bone mineral density.

Although MS onset typically occurs during reproductive age, women with MS will reach menopause during follow-up. For this reason, it is important to know the influence of menopause on MS and vice versa. The age at reaching natural menopause does not seem to be modified due to MS. Retrospective observational studies suggest an additive effect of menopause and some MS symptoms, especially in the genitourinary and affective domains. The effect of menopause on disability accumulation seems more controversial.

HRT, when used within the 'therapeutic window of opportunity', may be protective against cognitive impairment.

The current findings suggest that HRT is not harmful in women with MS.

Keywords: Multiple sclerosis, Women

Clinical Outcome and Volumetric MRI Assessment of Brain and Cervical Spinal Cord Area in Secondary Progressive Multiple Sclerosis Patients Treated with Rituximab: one-year follow-up (ORP-08)

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Background: Rituximab, a monoclonal antibody that targets and eliminates CD20+ B cells, has shown effectiveness in decreasing disease activity in patients with multiple sclerosis (pwMS). This study aimed to investigate disability, motor function, and volumetric magnetic resonance imaging (MRI) changes after one-year rituximab administration in secondary progressive MS (SPMS) patients.

Methods: This longitudinal prospective study was conducted from January 2019 to October 2020 on SPMS patients undertreatment with rituximab at the Kashani MS Clinic in Isfahan, Iran. Expanded Disability Status Scale (EDSS), timed 25- feet walk test (T25-FW), and 9-hole Peg test (9-HPT) were utilized to evaluate the disability status. All patients underwent disability assessment tests and brain MRI at the baseline and after one-year rituximab treatment. MRI measurements such as lesion load, cortical atrophy, and spinal cord atrophy at C2-C3 levels were assessed with the Siemens 1.5-tesla Avanto MRI machine. The Spearman correlation was performed to determine the association between disabilities and volumetric MRI factors.

Results: 31 pwMS were included (39.9±6.9 years, 64.5% females). PwMS receiving rituximab experienced stable MRI volumetric parameters, disability, and motor function. Deep white matter lesion volume was increased during follow-up (0.26±0.19 at baseline to 0.38±0.29 one year later). The mean EDSS, T25-FW, and 9-HPT did not change significantly after treatment with rituximab within 12 months ($p > 0.05$). Significant correlations were found between the white, gray matter volumes and the 9-HPT test of the left and right hand at follow-up ($p < 0.05$), as well as the T25-FW and the C1-C2 cross-sectional area at baseline ($r=-0.444$, $p=0.016$).

Conclusion: As a result of the administration of rituximab, disability, brain atrophy, cervical spinal cord area, and lesion load did not change significantly during 12 months in SPMS. The role of rituximab in SPMS management needs further research with longer follow-up.

Keywords: Secondary Progressive Multiple Sclerosis, Rituximab, Magnetic Resonance Imaging, Disability

The role of Artificial Intelligence in cognitive impairment assessment by MRI in people with MS (Iranian Research) (ORP-09)

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Artificial intelligence (AI) is increasingly gaining attention in the field of medicine, particularly in the context of neurological diseases such as multiple sclerosis (MS). AI methods have proven effective in organizing, analyzing, and extracting valuable insights from complex and extensive datasets encompassing clinical records and medical images. This capability has facilitated the identification of subtle markers of disease, leading to enhanced early diagnosis and a deeper understanding of disease variability and progression.

Consequently, healthcare professionals can optimize treatment strategies, ultimately enhancing the quality of life for people with MS (PwMS). Cognitive impairment (CI) is a common occurrence among PwMS and is associated with an elevated risk of disease progression. Magnetic resonance imaging (MRI) is widely considered the gold standard for diagnosing MS. Numerous studies have utilized various MRI types, including functional MRI (fMRI) and diffusion tensor imaging (DTI), as inputs for AI models. Research indicates that integration of demographic information, clinical data, and results of Brief International Cognitive Assessment for MS (BICAMS) and Paced Auditory Serial Addition Test (PASAT) with medical images yields promising performance. In our study, with the aim of presenting a structured overview of relevant research based on AI applications, we organized them into three categories: "utilizing AI algorithms in statistical methodologies", "employing AI for analyzing or segmenting brain imaging results", and "developing novel AI-based methods for evaluating specific cognitive phenomena". In the realm of "Utilizing AI techniques in statistical methodologies", researchers concentrate on applying AI algorithms, such as diverse regression models, to explore the relationships among clinical variables. In a study aimed at discerning the relationship between cognitive measures and the thalamus in fingolimod-treated relapsing-remitting MS (RRMS) patients and healthy controls using ultra-high-field MRI, they employed a mixed-effects linear model. This model was utilized to investigate the relationship between MRI parameters—such as thalamic volume, thalamic myelin density, thalamic axon density—and neuropsychological test performance over time, providing an example within this category. In the domain of "utilizing AI for analyzing brain imaging results", AI models, particularly deep learning (DL) models, assume a crucial role in segmenting and analyzing brain imaging results, helping to offer a comprehensive evaluation of cognitive impairment in MS. Various models, including convolutional neural networks and other emerging DL-based models, are utilized for tasks ranging from assessing specific cognitive phenomena to studying brain networks and analyzing MR images. These models excel in discerning intricate patterns and structures within medical images, facilitating automated and accurate identification of lesions and other pertinent features in MRI scans. Researchers in the category of "developing innovative AI-based methods for evaluating specific cognitive phenomena", propose a novel approach for the early diagnosis of cognitive impairment. The method utilizes a machine learning (ML) system with feature selection to analyze cognitive task-related fMRI data and graph-theoretical measures. Central to this approach is a linear support vector machine (SVM) classifier, a widely used AI-based supervised ML technique in neuroimaging applications. AI plays a crucial role by enabling the system to effectively classify MS and healthy subjects. The SVM classifier leverages AI's capability to discern patterns and relationships within the data, contributing to the automation of the diagnosis process. Overall, AI empowers the study by enhancing accuracy through automated data analysis and pattern recognition. Examining all pertinent studies reveals that AI methodologies have the potential to help in CI assessment among PwMS. As a result, further research efforts can propel and sustain advancements in this field.

Keywords: Artificial Intelligence, Machine learning, Multiple Sclerosis, Cognition, Cognitive Impairment, Magnetic Resonance Imaging

Definition and treatment of the multiple sclerosis relapse (ORP-10)

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Definition of MS relapse

Multiple sclerosis (MS) relapse is defined as a new neurological deficit in any system, with objective findings, Developing acutely or sub-acutely, with a duration of at least 24 hours, with or without recovery, in the absence of fever or infection. Relapses could be associated with Systemic infections, Stress, Postpartum period, and assisted reproductive technique (ART).

Due to the relationship between viral or bacterial infections and relapses, preventive vaccination is reasonable and recommended.

Pseudo-relapse is similar to symptoms in the presence of fever, heat exposure, infection, menstrual period, and stress. Affects the same body part as in the previous relapse, although symptoms may not be as intense. It should be considered when patients report symptoms similar to past MS relapses.

Importance of relapse treatment

Treatment of MS relapses helps to shorten the duration of relapses and lessen the disability. Residual deficits may persist after MS relapse and contribute to the stepwise progression of disability.

Clinical points

Evaluate patients with possible MS relapse within 1 week (or 5 working days) of the onset,

Rule out pseudo-exacerbation; (clinical and laboratory signs of infection, exposure to high temperature).

No need to stop DMDs during relapse treatment.

Good clinical response may be achieved 2-3 weeks after treatment.

Mild MS attack may not require immediate treatment,

Moderate to severe relapses with disabling symptoms should be treated.

Starting treatment as early as possible (within 1 week) is best.

Relapse treatment can be successful as late as 1 to 2 months after relapse.

MRI is not indicated for MS relapse diagnosis, as it is a clinical diagnosis. However, an MRI may be done for a different reason; such as to assess the adequacy of the current disease-modifying therapy. If MS relapse is confirmed, treatment should be started as soon as possible.

Treatment

The FDA approval for MS relapse is IV methylprednisolone. High-dose steroid treatment was defined as at least 500 mg methylprednisolone or equivalent. As usual, 1 gram per day for 3-5 days is considered. Oral prednisone tapering should be noted on an individual basis. However, some data suggest no additional benefit for oral taper. lack of improvement by 2 weeks as an indication for additional treatment. In patients not respond to initial treatment, especially clinical worsening following first-line treatment, the second line of treatment is followed. Plasma exchange, every other day for up to 5 to 10 exchanges is the best-supported option as second-line therapy.

Keywords: Multiple sclerosis, relapse, attack, methylprednisolone

Patients Monitoring During Treatment With Injectable DMDs (INF and GA) (ORP-11)

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IFN-β :

All interferons are approved for the treatment of RRMS, moreover Betaferon and Avonex are also approved for the treatment of clinical isolated syndrome (CIS) and Betaferon for the treatment of active secondary progressive MS (SPMS) as well (EMA website). Long-term data regarding safety and efficacy show.

IFN-β was first approved for MS in the in 1993.

There are three different products available:

IFN-β-1b preparations (Betaseron®, Extavia®) that are administered s.c. every other day

IFN-β-1a preparations that are either administered s.c. (Rebif®) three times weekly

intramuscularly (i.m.) (Avonex®) once a week.

The mechanism of action by which interferon be mediates its beneficial effects in multiple sclerosis

(MS) treatment is only partly resolved, and likely multifactorial and complex:

1-shift expression of cytokines from a pro-inflammatory cytokine profile towards an anti-inflammatory

cytokine profile.

2-reduce inflammatory cell populations in the central nervous system (CNS) by preventing cellmigration across the blood brain barrier.

3- may stimulate neuronal growth.

Side effects:

1-injection site reactions and necrosis

2-allergic reactions

3-flu like symptoms

4-transient deterioration of neurologic symptoms

5-mood disorder and depression.

6-hematologic abnormalities

7-hepatic injuries

8-thyroid autoimmunity and hypothyroidism

9-Menstrual disorders:Menstrual disorders, such as breakthrough bleeding or spotting

10-Other rare potential side effects. Capillary leak syndrome, TTP–like syndrome, anaphylactic shock, psoriasis

Monitoring:

liver enzymes measurement at 1, 3, and 6 months and then every 6 months after initiating therapy. The dose needs to be reduced if the liver enzymes are found tobe five times greater than baseline.

Interferon b needs to be discontinued if liver enzymes do not normalize with dose reduction, but a full dose can be re-implemented if enzymes normalize.

Blood cell count should be done 1,3,6 months after iniatiation of treatment and then every 6 months.

Thyroid testing should be performed initially and afterwards only in the case of abnormalities every 6 months and when clinical signs of hypo- or hyperthyroidism are obvious.

GLATIRAMER ACETATE:

Glatiramer acetate is one of the first generation DMTs approved by the FDA for management of

RRMS.

There are two doses that are currently approved by the FDA:

20mg subcutaneously (s.c.) daily

40mg s.c. 3 times a week.

Mechanism of action : is still not fully understood.Although glatiramer acetate itself does not cross the blood brain barrier, it shifts the pro-inflammatory T helper type 1 (interleukin-2, interleukin-12, IFNg, tumor necrosis factor) cytokine profile to anti-inflammatory T helper type 2 (interleukin-4,interleukin-5, interleukin-10, transforming growth factor-b) cytokine profile, leading to down re some neuro-protective action by increasing the production of brain derived neurotrophic factor (BDNF)

Side effects:

The most common side effect reported is injection site reaction.

Only 5% of patients discontinued glatiramer acetate because of injection site reaction, urticaria, flushing, chest pain, palpitation, anxiety, and throat constriction

Reports of liver injury by GA has been documented.

Most of the side effects from glatiramer acetate were self-limited.

Rare side effects:

Drug-induced liver injury by glatiramer acetate leading to liver transplant: A case report

Normocomplementemic urticarial vasculitis.

central retinal vein occlusion

Calcinosis Cutis Associated With Subcutaneous Glatiramer Acetate

Monitoring: No laboratory monitoring is required during GA therapy.

Keywords: Multiple sclerosis, DMD

Everything we need to know about vaccination in MS (ORP-12)

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With the approval of novel disease -modifying therapies (DMTs) ,in last decades, new approaches have been developed for treatment of multiple sclerosis.

These newly approved drugs are either immunomodulatory or immunosuppresor , and concern about their side effects , especially infections ,increased.

Therefore, it is noteworthy to consider infection-related complications in MS patients before or during DMTs usage.

For this reason , proper evaluation of immunization status of patient regardless of initial therapeutic plans is mandatory.

Vaccination should be performed in the early stages of the disease to prevent future delays in the

initiation of immunosuppressive drugs ,because ,live vaccines are generally contraindicated during treatment with these drugs.

Another point which could be considered is the appropriate intervals between vaccination and DMT ,which vary with different treatments and vaccines.

European consensus on vaccination in multiple sclerosis proposes the best vaccination strategy according to current evidence and expert knowledge

In this topic ,we review the EAN guideline and some other points about vaccination in patient with multiple sclerosis.

Keywords: Multiple sclerosis, Vaccination

Typical MRI lesions of multiple sclerosis in the brain and spinal cord (ORP-13)

Zahra Hamed

Multiple sclerosis is the most prevalent chronic demyelinating autoimmune disease that affects the central nervous system (CNS). It can be effectively managed with a favorable prognosis when promptly and accurately diagnosed and treated. Among the array of diagnostic tools, magnetic resonance imaging (MRI) stands out as the foremost paraclinical resource, playing a pivotal role in diagnosis, treatment monitoring, and prognosis assessment in multiple sclerosis patients. Proficiency in recognizing the distinctive features of typical multiple sclerosis lesions in the brain and spinal cord necessitates a comprehensive understanding of the underlying pathological factors. This knowledge is fundamental for achieving a precise diagnosis in suspected cases and mitigating the risk of misdiagnosis. This article will review the attributes and characteristics of typical multiple sclerosis lesions and important red flags and delving into the key indicators within imaging.

Keywords: multiple sclerosis, MRI, typical lesions

Advanced imaging for multiple sclerosis (ORP-14)

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This study focuses on the use of advanced imaging techniques for the assessment of multiple sclerosis (MS). The objective is to explore the potential of these imaging modalities in providing valuable insights into the pathophysiology and characterization of MS lesions.

One such technique, quantitative susceptibility mapping (QSM), allows for the classification of white matter (WM) lesions into different types based on their QSM characteristics. QSM demonstrates high accuracy in identifying fully remyelinated areas, chronic inactive lesions, and chronic active/smoldering lesions.

Magnetization Transfer MRI (MTR) is another imaging method that reveals markedly decreased MTR values in areas associated with severe tissue loss, indicating demyelination and axonal loss in MS patients.

The T1w/T2w ratio is a measure used to assess demyelination, inflammation, axonal damage, and other pathological changes. A lower T1w/T2w ratio is indicative of demyelination or inflammation, while a higher ratio suggests iron accumulation, microglia activation, and astrogliosis.

Neurite Orientation Dispersion and Density Imaging (NODDI) is an advanced diffusion-weighted imaging model utilized to evaluate WM microstructure. This technique provides valuable information about the integrity and orientation of neurites in MS lesions.

Additionally, the study explores the potential of PET-based biomarkers such as glucose metabolism or amyloid deposition in MS research.

Overall, these advanced imaging techniques offer promising tools for the assessment and characterization of MS lesions. They provide valuable insights into the underlying pathophysiology and can aid in the development of targeted treatment strategies for individuals with MS. Further research and validation are necessary to fully establish the clinical utility of these imaging modalities in routine MS care.

Keywords: MRI, Multiple sclerosis

Diagnostic approach to autoimmune encephalitis (ORP-15)

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Autoimmune encephalitis is the commonest form of non_infectious encephalitis. It occurs secondary to three groups autoantibodies targeting neural epitopes like: neuronal cell surface proteins (e.g., as NMDAR, LGI1, and CASPR2, GABABR and AMPAR, Synaptic antigens: GAD65 and also amphiphysin , intracellular antigens (onconeural antigens such as anti-Hu, ant-Ri, and anti-Ma which is mostly related with the presence of an underlying malignancy. The diagnosis can be challenging. Consequently, clinical algorithm was developed in 2016 to find patients with rapidly progressive autoimmune encephalitis (<3 months) who need immediate treatment. Possible Diagnosis can be carried out when all of the three requirements of mentioned criteria are satisfied, after that clinical and paraclinical assessments (MRI, electroencephalography, or Cerebrospinal fluid (csf) analysis for pleocytosis and auto antibodies) are finally led to the diagnosis. Note that for significant number of patients with suspected autoimmune encephalitis, despite strong evidence of an immune-mediated disorder (e.g. compatible brain MRI, inflammatory CSF profile), no autoantibody can be found. Moreover immediate treatment avoiding to wait for antibody results can be led to good outcomes, seronegative autoimmune encephalitis criteria was explained. In this article, we review these criteria and clinical and Para clinical diagnostic approach to seronegative and seropositive autoimmune encephalitis.

Keywords: Autoimmune encephalitis, Autoantibody ,MRI ,CSF

Femoral head AVN concept and treatments (ORP-16)

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Avascular necrosis(AVN), which is known as osteonecrosis, ischemic bone necrosis, or aseptic necrosis, is a condition that results in the destruction of bone cells.

This ischemic disease, which more commonly has an effect on the femoral head and hip joint, is more prevalent in middle age

and the elderly, but it is estimated that in the future, it will involve all ages. Furthermore, the conquering population in this disease is females.

Femoral head AVN is caused by a disruption in the femoral head blood flow and is popularly known as the blackening of the femoral head or hip joint(3). The alterations in the blood supply may fall out following a trauma or due to a non-traumatic event. Hip dislocation, fracture of the Femoral neck and related surgical procedures, alcohol abuse, and corticosteroid therapy frequently lead to AVN development.

Several studies show that the most common cause of AVN is corticosteroid use.

Corticosteroids as rescue drugs in treating the bulk of autoimmune diseases like MS and Behchet, pulmonary diseases like asthma, and recent covid 19 patients are the most suspected cause of this disease.

Femoral head AVN Signs and symptoms are Increasing pain and stiff joints, Limited range of motion, Limping, and Difficulty climbing stairs, standing, or walking.

Diagnosis of AVN can be established based on history, physical examinations, and radiographic evaluations. In the primitive phases, bone scintigraphy and MRI are the favored indicative implements. X-ray findings of AVN in the early periods normally look regular.

Spontaneous regression of avascular necrosis is rare, and there is no agreement on the AVN therapy up to now. Non-surgical techniques are devoted to patients in the early phase of the disease and are composed of pharmacologic and physical therapy. Operation is highly recommended for patients with advanced disease.

Total Hip Arthroplasty as a prosperous surgery is the choice of treatment for patients with intolerant symptoms and high-stage involvement of the hip joint.

Keywords: AVN, osteonecrosis

Brain Stimulation for Cognitive impairment in Multiple Sclerosis (ORP-17)

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Cognitive impairment is a common feature in patients with multiple sclerosis (MS) and can significantly impact their quality of life. Non-invasive brain stimulation techniques, such as transcranial direct current stimulation (tDCS) and repetitive transcranial magnetic stimulation (rTMS), have emerged as potential treatment options for cognitive impairment in MS. This abstract provides an overview of the use of tDCS and rTMS in the treatment of cognitive impairment in MS, based on the available literature.

Several studies have investigated the feasibility and efficacy of tDCS in patients with MS. developed a remotely supervised tDCS protocol (RS-tDCS) that allows participants to complete daily sessions from home while being supervised by a study technician. This protocol has shown feasibility and tolerability in patients with MS. Additionally, RS-tDCS paired with cognitive training (CT) has demonstrated preliminary efficacy in improving fatigue and cognitive processing speed in patients with MS. These findings suggest that tDCS, particularly when combined with CT, may have potential benefits for cognitive impairment in MS.

Similarly, rTMS has been explored as a potential treatment for cognitive impairment in MS. In a meta-analysis by , the therapeutic effects of rTMS on core symptoms of MS were summarized. Although the specific effects on cognitive impairment were not highlighted, the study provides evidence of the potential benefits of rTMS in MS. Furthermore, studies have shown positive effects of rTMS combined with physical or cognitive training on motor and cognitive impairments in patients with Parkinson's disease. These findings suggest that rTMS, in combination with other interventions, may have a positive impact on cognitive function in MS.

It is important to note that cognitive impairment in MS is a complex and multifaceted condition, and the underlying mechanisms are not fully understood. Multiple cognitive domains, including information processing speed, attention, memory, and executive function, can be affected. The severity and type of cognitive impairment can vary among individuals and disease stages. Therefore, the treatment of cognitive impairment in MS requires a personalized approach, taking into account the specific cognitive deficits and individual needs of each patient.

In conclusion, tDCS and rTMS have shown promise as potential treatments for cognitive impairment in patients with MS. The use of RS-tDCS and CT has demonstrated feasibility and preliminary efficacy in improving cognitive function and reducing fatigue in MS. Additionally, rTMS, in combination with other interventions, has shown positive effects on motor and cognitive impairments in related neurological conditions. However, further research is needed to optimize stimulation protocols, determine the long-term effects, and establish the therapeutic efficacy of tDCS and rTMS in the treatment of cognitive impairment in MS.

Keywords: Cognitive, Multiple sclerosis, Brain Stimulation

MS and cognition: review of clinical, neuro-radiological features, and treatment (ORP-18)

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Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS) that damages the brain and spinal cord via various pathophysiological mechanisms. Although cognitive impairment (CI) is a common symptom in MS, it is usually disregarded in clinical evaluations. Cognitive impairment (CI) can present in all stages of multiple sclerosis and affects 40–60% of patients. All cognitive domains may be impaired in MS, but information processing speed (IPS), working memory, and learning memory are the most affected cognitive domains.

The Minimal Assessment of Cognitive Function in Multiple Sclerosis (MACFIMS) is currently the gold standard for the cognitive assessment of MS patients. The Symbol Digit Modalities Test (SDMT) showed higher sensitivity for cognitive dysfunction in MS and is now widely acknowledged as the gold standard for a quick cognitive screening.However, the test is not specific and is limited to processing speed assessment, overlooking other relevant cognitive domains such as learning and memory (see cognitive profile section).

MRI assessment in cognitive impairment: Subsequent attempts to visualize more subtle damage, by use of more advanced MRI techniques, such as magnetisation transfer, diffusion tensor imaging, and T1 relaxometry, indicated widespread damage to brain tissue that appeared normal on conventional T1-weighted or T2-weighted MRI. Other improvements in MRI technology included double inversion recovery, providing visualisation of cortical lesions, which were robustly correlated with cognitive decline. Network functional MRI studies indicate that cognitive decline is explained by an accruing destabilization of the brain network physiology.

Treatment of cognitive impairment: Disease-modifying treatments (DMTs) effects on cognitive impairment are mostly unknown. Despite the widespread use of different DMTs in MS, there is no consensus as to which therapy effectively improves cognitive impairment, one of the most frequent and debilitating symptoms of the disease.Currently, no clinical guidelines exist on whether cognitive impairment or its longitudinal progression presents the need in its own right for changing the DMT.

Keywords: Cognition, Multiple sclerosis, DMT

Comorbidity in patients with MS (ORP-19)

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Numerous comorbidities are common in patients with multiple sclerosis (PwMS). Comorbidity is one of the important concern of clinicians because can obscure or delay MS diagnosis, and can affect the disease course. Therefore, notice to comorbidities is important for improving the quality of life and optimizing treatment.

Depression, anxiety, cardiovascular disease, epilepsy, metabolic disease, autoimmune diseases, and sleep disorder are the most common comorbidities in PwMS.

Cardiovascular disorder such as abnormalities in blood pressure, heart rate, heart rhythm, and left ventricular systolic function are common in PwMS and have been reported as the second or third most common cause of death in these patients.

There is evidence that vascular risk factors and vascular comorbidities are associated with faster progression of disability, including both physical and cognitive. In addition, comorbid metabolic conditions, such as diabetes, hypertension, and hyperlipidemia, are typically elevated in the MS population and are co-occur with cardiovascular disease. The elevated prevalence of metabolic disorders, may worsen disease in PwMS, but the frequency of metabolic comorbidities in PwMS is still not fully understood..

The most common Psychiatric problem in PwMS are depression and anxiety and bipolar disorders that are associated with fatigue and reduced Quality of Life(QoL) and may impact on adherence to DMT. Early recognition and manage of psychiatric disorder could help to determine optimal treatment, ensuring better long-term outcomes.

RLS an irresistible urge to move the legs is more frequent in PwMS than general population, and can disturb sleep and QoL. The mechanism of RLS in MS is not fully understood, but may involve aberrant signaling in the dopaminergic system caused by demyelinating or neurodegenerative damage to the diencephalon-spinal tract.

MS has common risk factors and immunopathologic mechanisms with other autoimmune diseases (AID). Common coexist AID with MS include psoriasis, asthma, type 1 diabetes autoimmune thyroiditis, celiac disease, Sjogren's syndrome, inflammatory bowel disease (IBD), rheumatoid arthritis, systemic lupus erythematosus, and atopic dermatitis.

Early diagnosis and management of Comorbidities is important because some of them have an adverse influence on outcome.

Various comorbidities were associated with disability and clinical features of disease progression in PwMS: RLS with faster clinical progression, migraine with a more symptomatic course of disease, hypertension with structural brain changes, asthma and rheumatoid arthritis with more relapse in PwMS.

Furthermore, it is important to notice that DMT use may also increase the risk of comorbidity in PwMS. Triflunamide may increase blood pressure and there are some report that showed an increased prevalence of cardiovascular risk factors, including elevated diastolic blood pressure and plasma glucose, and altered lipid profiles in patients that use interferon beta and glatiramer acetate. Alemtuzumam may cause an increased risk of autoimmune diseases and malignancy.

One of the important issue is treatment approach in PwMS with coexisting autoimmune disorders. DMF is effective in treatment of psoriasis and MS. On the other hand, anti TNF monoclonal antibodies including Adalimumab, infliximab that have approved for several autoimmune diseases including psoriasis, RA, and IBD can promoting or exacerbating MS, therefore, should not be used in MS patients.

Natalizumab is effective in treatment of IBD and MS but due to the risk of PML, long time use of this drug is limited. Anatalizumab monotherapy is a valid option for patients with highly active RRMS and IBD. Ozanimod has recently been approved for both RRMS and IBD.

Therefore, improved understanding of the effects of comorbidity on safety, the effectiveness of DMT, and potential interactions between DMT use and comorbidity in PwMS is necessary. Ndeed, comorbidities must be continually monitored due to possible effect on MS progression, and potentially forecasting exacerbations.

Keywords: Comorbidity, Multiple sclerosis

Review of McDonald criteria (ORP-20)

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Diagnostic criteria in MS facilitate a rapid diagnosis of CIS or relapsing-remitting MS (RRMS) in patients who present with typical demyelinating syndromes.

Previous criteria, including the Poser criteria, focused exclusively on clinical symptoms and signs. The emergence of the McDonald criteria in 2001 marked a new era in the diagnosis of MS where paraclinical criteria were incorporated so that the hallmark features of dissemination in space and dissemination in time could be met using a combination of clinical and MRI features

The McDonald criteria have since undergone numerous revisions (2005, 2010, and most recently 2017). The latest revisions of the McDonald criteria have the benefit of higher sensitivity but also have a slight decrease in specificity compared with previous iterations

Current MS diagnostic criteria facilitate the early diagnosis of MS in people presenting with typical clinical syndromes, allowing for the initiation of DMT in appropriate patients. However, the diagnosis can be challenging for several reasons, and diagnostic criteria should be used cautiously in patients presenting with atypical syndromes and those in special populations in whom the criteria have not yet been adequately validated. Clinical judgment and existing paraclinical tools are useful in minimizing misdiagnosis and facilitating an accurate diagnosis of MS.

Keywords: Multiple sclerosis, diagnosis

Defining seizure type and frequency, and analyzing MRI and EEG findings in MS populations of Khorasan. A cross-sectional study (ORP-21)

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Introduction: Seizures have been recognized to occur in multiple sclerosis since early descriptions of the disease. The goal of this study is to evaluate type of seizures, and also EEG and MRI findings in patients of Khorasan Razavi MS society in a cross_sectional study

Material and Method: 812 patients with MS were evaluated and followed up for one year in terms of seizure attacks. Patients who had seizure before and during this period, were assessed clinically and paraclinically based on MRI and EEG. And final data were analyzed with SPSS.

Findings: 13 patients of all cases (1.6%) experienced seizure; which 3 of them were excluded because of unwillingness to cooperate. Thus seizure type of 10 patients was assessed. All of them experienced generalized seizure. MS type was RRMS in 9 patients (90%) and PPMS in 1(10%) of them. EEG pattern showed background slowing in 6 cases (60%) and epileptiform discharges in 6 cases (60%). MRI pathologies included cortical atrophy in 9 patients (90%), subcortical and juxtacortical high t2 lesions in all patients. There was not significant relation between years of illness and intensity of MRI lesions (p value>0/05). A significant relation between EEG background slowing and intensity of subcortical and juxtacortical lesions (p value<0/015(was seen. And also a significant relation

between epileptiform discharges in EEG and severity of cortical atrophy(p value<0/036).

Conclusion: the prevalence of seizure in MS population was 1/6% (n=13). Despite finding some correlations between lesions in MRI and EEG, yet can not find a charactristic pattern of seizure in MS.

Keywords: Multiple sclerosis, Seizure, epilepsy

Diagnosis of myelin oligodendrocyte glycoprotein antibody-associated disease: International MOGAD Panel proposed criteria (ORP-22)

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Patients with Myelin Oligodendrocyte Glycoprotein (MOG)-IgG present with isolated optic neuritis or transverse myelitis, acute disseminated encephalomyelitis (ADEM), brainstem or cerebellar features, or cerebral cortical encephalitis. Unlike Multiple Sclerosis (MS) and AQP4-IgG-seropositive Neuromyelitis Optica Spectrum Disorders (NMOSD), in which multiple clinical attacks characterize relapsing forms of disease, individuals with MOG antibody-associated disease (MOGAD) can have either a monophasic or relapsing course. Studies from multiple countries support MOGAD as a global disease affecting people of all ages. MOGAD incidence is 1·6–3·4 per million people per year, and prevalence is estimated at 20 per million (95% CI11–34). Optic neuritis is by far the most common onset feature, particularly among adults, while Acute Encephalomyelitis (ADEM) with or without concomitant optic nerve involvement is the typical first manifestation in children, particularly before the age of 11 years. Transverse myelitis is another common presentation. Less common presentations include cerebral cortical encephalitis (often with seizures), brainstem and cerebellar demyelinating attacks, tumefactive brain lesions, cerebral monofocal and polyfocal CNS deficits associated with demyelinating lesions, cranial neuropathies, and progressive white matter damage (leukodystrophy-like pattern). In contrast to AQP4-IgG-seropositive NMOSD and MS, no marked sex or racial predominance has emerged in populations with MOGAD. A panel strongly endorses serum testing for patients with suspected MOGAD using cell-based assays that use full-length human MOG to detect MOG-IgG. MOG-IgG are IgG1, and the panel recommends testing with IgG-Fc, an IgG1 secondary antibody, or an IgG (heavy and light) secondary antibody if externally validated in-house assays are used. Fixed cell-based assays are a reasonable alternative when live cell-based assay testing is unavailable, with the caveat that sensitivity and specificity of fixed cell based assays are lower than cell-based assays. However, antibody titers are often not consistently provided by testing centers and reproducibility between testing centers has not been systematically investigated for commercial cell-based assays. ELISA is not recommended for MOG-IgG measurement owing to low sensitivity and specificity. The panel proposes criteria for clear positive and low positive fixed and live cell-based assay results. For live assays, they recommend that clear positives are defined as at least two doubling dilutions above the assay cutoff, or above the assay-specific titers cutoff, or flow-cytometry ratio cutoff. Fixed assays are considered clear positive by titers greater than or equal to 1:100. Fixed or live assay results are considered to be low positives if in the low range of the individual live assay or if titers are at least 1:10 and less than 1:100 for fixed cell-based assays. Patients with one of the core clinical attack types and clear positive MOG-IgG test results in serum measured by fixed or live cell-based assay can be diagnosed with MOGAD. Patients with low positive serum MOG-IgG titres measured by fixed or live cell based assay, patients with serum results reported as positive on fixed cell-based assay without titer, or seronegative patients with clear positive CSF MOG-IgG test results who present with one of the core clinical attack types (Optic neuritis, Myelitis, ADEM, Cerebral monofocal or polyfocal deficits, Brainstem or cerebellar deficits, Cerebral cortical encephalitis often with seizures) are also required to have at least one of the supporting clinical or MRI features (Optic neuritis with Bilateral simultaneous clinical involvement, Longitudinal optic nerve involvement (> 50% length of the optic nerve), Perineural optic sheath enhancement, Optic disc oedema or Myelitis with Longitudinally extension,Central cord lesion or H-sign, Conus lesion or Brain, brainstem, or cerebral syndrome with Multiple ill-defined T2 hyperintense lesions in supratentorial and often infratentorial white matter, Deep grey matter involvement, Ill-defined T2-hyperintensity involving pons, middle cerebellar peduncle, or medulla, Cortical lesion with or without lesional and overlying meningeal enhancement) to be diagnosed with MOGAD. Patients should be diagnosed with MOGAD only after other diagnoses that better explain their features have been excluded.

Conclusions: These proposed criteria rest on the presence of MOG-IgG as a fundamental inclusion criterion, accompanied by clinical presentations identified as being associated with MOG-IgG. For future research will be the validation of these proposed criteria in prospective pediatric and adult cohorts of patients with acquired CNS inflammatory demyelination.

Keywords: MOGAD, Diagnosis

Patients monitoring during treatment with Dimethyl fumarate (ORP-23)

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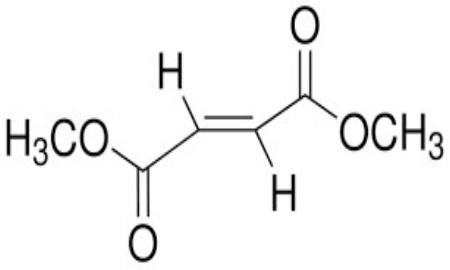
Dimethyl Fumarate (DMF) is a methyl ester of fumaric acid (chemical formula C6H8O4) that is hydrolyzed in the small intestine to the active metabolite monomethyl fumarate, approved for the treatment of RMS, and moderate to severe Psoriasis.



In addition to relative frequencies, we also examined the absolute numbers of the various cell types over time. As expected, DMF led to a decrease in total leukocyte and lymphocyte counts, with a strong reduction in CD4 and CD8 T cell, B cells also decreased, while NK cells and monocytes were minimally affected.

Dimethyl fumarate may cause serious side effects, including allergic reaction. PML, which is a rare Brain infection that usually leads to death or severe disability. JCV test or if clinically suspected (Brain MRI with DWI sequence). Among over 500000 cases exposed to DMF 11-13 cases of PML have been confirmed.

What labs to monitor with DMF?

Obtain a CBC-diff, including lymphocyte count, before initiating treatment with DMF, 6 months after starting treatment, and then every 6 to 12 months thereafter, and as clinically indicated, consider interruption of DMF in patients with absolute lymphocyte counts less than 500 per/ml persisting for more than 6months.

Does it necessary to measure CD4 and CD8 T cells or B cells marker for monitoring of DMF, as we do testing CD19, CD20 for monitoring of Rituximab?

In conclusion, both B cell and T cell compartments undergo a drastic decrease of mature populations under DMF treatment.

Independent cohorts and serum neuro-filament confirm a DMF/ associated immune phenotype. Serum neuro-filament light chain (NFL) is a blood biomarker in MS specific for neuro-axonal damage (axon and myelin) in MS. Less caused by inflammatory activity or chronic neurodegeneration.

Clinically and radiologically active patients were identified by both high (NFL) and the predictive population fraction.

Increased serum NFL reflects acute disease activity (relapse associated worsening) and also PIRA (progression independent of relapse activity).

Combined measurement of NFL in blood as a biomarker of axonal damage and cellular composition as a marker of inflammatory activity will allow discrimination of the different disease aspects and guide therapeutic strategies (DMF).

How do patients with MS should be monitored?

MRI, which can reveal areas of MS lesions, on your Brain, Cervical and Thoracic cord with and without Gd every 6-12months, a contrast material to highlight new or active lesions.

How long DMF can be taken?

DMF can be taken for as long as it continues to have clinical benefit and you are not experiencing intolerable or severe side effects. Your disease is not progressing significantly. You are not developing any new T2 or Gd lesions or existing lesions are not enlarging. You are not having an increase in relapse. Your Brain is not atrophying at a faster than normal rate. You have not experienced a prolonged reduction in Lymphocyte numbers.

A recent European review of safety data identified 11 cases of PML with lymphopenia associated with DMF treatment, including 3 cases with mild lymphopenia (lymphocyte counts defined as absolute lymphocyte counts between 800/dl and lower limit of normal).

Keywords: Dimethyl fumarate, Multiple sclerosis

Patient monitoring during treatment with natalizumab (ORP-24)

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Natalizumab (Tysabri), a recombinant humanized monoclonal antibody selective for α4- integrin, is indicated for CIS, RRMS and active SPMS in adults. Baseline and routine evaluation of patients who receive natalizumab is essential because of the association of natalizumab with progressive multifocal leukoencephalopathy (PML), an opportunistic infection caused by the JC virus.

Three major factors have been associated with increased risk of the development of PML in MS patients treated with netalizumab. (1) The presence of JCV antibodies (2) prior immunosuppression and (3) duration of therapy especially beyond 2 years. Patients who have all three of these risk factors should be closely monitored clinically and radiologically for potential sign and symptoms of PML during natalizumab treatment and for 6 months post treatment.

It is recommended to monitor JCV serostatus and anti JCV antibody index level in all patients being assessed for natalizumab treatment before initiating treatment (or around the time of, in highly active disease) and in the regular intervals during natalizumab therapy.

Also, MRI monitoring should be performed regularly for early detection of PML in a pre-symptomatic state and in the context of new neurological symptoms or unexpected clinical worsening. Howevere, extended interval dosing (EID) of natalizumab treatment (Q6 weeks) has been shown comparable efficacy as the standard interval dosing (Q 4 weeks), with minimizing the risk of PML.

In general, an individualized approach to patient selection and subsequent monitoring of natalizumab treatment outcomes and risk factors for PML is key to optimizing the benefit-risk ratio of this highly efficacy therapy for RRMS.

Keywords: Natalizumab, PML, MS

New Technological Approach to Physical Therapy in Patients with Multiple Sclerosis (ORP-25)

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Multiple sclerosis (MS) is a chronic and inflammatory disease of the brain and spinal cord characterized by focal demyelination and axon destruction. MS causes many symptoms such as motor, sensory, visual, and autonomic disorders, and also impairs physical and cognitive functions. Balance problems and limited gait cause fear of falling and decreased multitasking performance. Physiotherapy is one of the most important treatment options and frequently used for managing symptoms in patients with MS. It is critical that rehabilitative interventions should comprehensively manage and control abovementioned symptoms in the patients with MS. New technological based approach has provided new possibilities for neurorehabilitation. Along with technological developments, the multiple symptoms in MS can be managed. Here, the clinical goal is to reach an important principle of neurorehabilitation and motor learning, the "concept of practice". The concept of practice is known as a critical principle in neurorehabilitation that should contain three main characteristics modified in MS, including 'optimal intensity', 'optimal repetition' and 'task specific'. Technology-based rehabilitation, as a sensory-motor-cognitive network, provides multisensory feedback and allows therapist to control quantitatively and adjust the therapeutic parameters such as duration, intensity and frequency in a planned manner. It also allows to create a motivational context to transform the patients from a passive element to an active participant in compliance with the treatment regimen. Therefore, new technological approach provides various advantages in patients with MS with providing goal-specific training based on motor learning principles, and enabling objective evaluation of functional performance.

Keywords: Multiple sclerosis, Technology, Practice, Rehabilitation, Physiotherapy, Technological-based approach

EEG Patterns in MS related epilepsy

A literature Review (ORP-26)

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Introduction: EEG abnormalities show variability in time and space and a low degree of specificity in patients with multiple sclerosis. However, in some cases, EEG abnormalities may provide additional information about the extent and severity of the disease. In addition to detecting the electro clinical particularities of epileptic seizures; video-EEG and activation techniques such as hyperventilation, photic stimulation, and sleep deprivation) are important tools in detecting the abnormalities of EEG.

Methods and Materials: This study was carried out in literature in the period of 2012-2023 in the most important online databases (PubMed, Embase and Google Scholar). For this purpose, the following terms were used: 'Multiple sclerosis', 'seizure', 'epilepsy', 'convulsion', 'Electroencephalogram', 'EEG patterns and MS related epilepsy.

Results: EEG abnormalities in MS patients depended on location of the lesions, the duration, and the stage of the disease, its progression and EDSS. Patients with MS and epilepsy had significantly lower posterior dominant rhythm (PDR) frequency and amplitude compared with controls, with 34% having a PDR frequency of <8.5 Hz. Frequent abnormalities consist of diffuse asynchronous theta activity, slow rhythmic synchronous activity, and occasionally, mainly during chronic-progressive disease evolution, low voltage, occasionally, slow focal waves or localized EEG suppression may be found. These abnormalities are about 20-60% according to previous studies. However, the interictal epileptiform activity appears to be quite rare. In table 1, the

most relevant EEG patterns found in patients with MS with epilepsy is summarized.

First author	Study design	Relevant findings related to EEG pathological patterns	(Refs.)
Salim A, 2021	50 patients with MS with epilepsyvs. 50 controls	Lower posterior dominant rhythm (PDR) frequency and amplitude; PDR frequency of less than 8.5 Hz in 34% of cases	(106)
Dagiasi I, 2018	Multicenter retrospective study 62 patients with MS	Focal slowing in 40% of cases; epileptiform changes in 38% of cases	(52)
Viveiros C, 2010	Case series 160 patients with MS (5 with concomitant epilepsy)	Focal slowing; isolated or grouped diffuse theta waves; EEG anomalies located predominantly bilateral frontal-temporal	(43)
Moreau T, 1998	402 patients with MS (17 with concomitant epilepsy)	Focal spikes; focal slowing; periodic lateralized epileptiform discharges (PLEDs);	(104)

MS, multiple sclerosis; EEG, electroencephalogram; PDR, posterior dominant rhythm; PLED, periodic lateralized epileptiform discharge.

Discussion: Seizures are not a common symptom of MS. The cumulative incidence of epilepsy was 3.5% for patients with MS, compared with 1.4% for the control group. EEG abnormalities is more common in MS-related epilepsy than MS without seizures. EEG abnormalities in MS patients may include changes in the frequency and amplitude of the tracing, as well as abnormal patterns of activity in certain areas of the brain. Most of MS patients showed normal EEG. Abnormal patterns were detected in patients with active MS or in advanced stages of the disease and potential result of the variable degree of cortical atrophy. Several studies have commented on EEG abnormalities in MS patients with seizures. Interpretation of these studies is difficult, as the timing of EEG in relation to seizure and in relation to the onset of epilepsy varies both within and among studies. In general, these studies identified EEG abnormalities in most patients with seizures. However, no available data support whether similar abnormalities in EEG would be present in MS patients without a history of seizures. These studies have important methodological differences that could easily account for the different frequencies of epileptiform EEG findings that they report. Periodic Lateralized Epileptiform Discharges (PLEDs) are seen in a variety of disorders, including in association with MS exacerbations. These have been associated with clinical manifestations of altered consciousness or prolonged aphasia, resulting from prolonged complex and simple partial status epilepticus and with focal motor seizures followed by secondarily generalized seizures.

Conclusion: Generalization from the available data is limited to the statement that most patients do have abnormalities identified on EEG and no single EEG abnormality has been identified that would suggest MS as the etiology for epilepsy in the absence of clinical or radiological evidence that suggests the disease.

Keywords: Multiple Sclerosis, Electroencephalogram, EEG Pattern, Seizure, epilepsy

Epidemiological view of national MS registry in Iran (NMSRI) (ORP-27)

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Background: Implementing a nationwide MS registry system of Iran (NMSRI) established in 2018 by the MS research center of Tehran for improving quality of care in MS patients.

Objectives/Aims: The aim of study is to the epidemiological view of MS in different provinces and ethnicities in Iran, effect of patients' disability, socio-economic status, disease risk factors and enlighten the use of pharmacological treatments and their side effects.

Method: The population-base study consisted of all MS patients in the NMSRI who were registrars from 18 provinces of Iran including 24 medical universities, up to September, 2023. All cases were diagnosed by neurologists. Information on baseline characteristics, MS type, Expanded Disability Status Scale (EDSS), familial MS and prescribed disease-modifying treatment (DMT) were extracted. Diagnostic delay was defined as the time lag between disease onset and final diagnosis of MS. Totally, 26344 cases were enrolled with mean age of 36.71 years.

Results: The majority 19947 (75.72%) were female. The mean age at the MS symptoms was 29.33 years and the mean age at diagnosis MS was 30.37 years. Diagnosis delay was under one year in most cases. The diagnostic interval of 41.6% of patients was less than one month and 14.8% of them had one month time to diagnosis. The patients with age of onset below 18 years (mean±SD=21.19±46.79, P<0.001) and the patients diagnosed after the age of 50 years (41.06±68.51, P<0.001) had longer time to diagnosis. The mean±SD diagnostic interval for males (14.15±34.32) was more than females (13.18±31.75, P=0.029). The patients with primary progressive MS had the longest time to diagnosis (23.65±42.13) and relapsing-remitting type had the shortest time (11.72±29.38, P value<0.001).

Almost 14.5% of patients reported a family history of MS. The most common type of MS in patients was relapsing remitting MS 15491 (58.8%) and secondary progressive 2564 (9.73%) respectively. The mean EDDS of patients was 2.19 and EDSS score was significantly higher in woman with pregnancy history (P = 0.02) or abortion history (P = 0.04). The most commonly used drugs is Avonex/Cynnovex/Actovex in 6259 (23.76%) and Rituximab among 4495 (17.06%) cases, respectively.

Conclusion: The NMSRI could help in understanding the current situation of disease and improve the quality of care and conducting research projects on a wide international, national or regional scale. The observed epidemiology of MS in Iran could help in understanding the current approach among Iranian neurologists and improve the quality of care delivered to MS patients by appropriate policy making.

Keywords: registry, Multiple sclerosis

Autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy diagnosis and management: A case report study (ORP-28)

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Background: Autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy is a new autoimmune disease of CNS, that can be associated with other autoimmune disease, also about 20% of them are related to neoplasms. This disease is usually single-episode and is resolved with a course of corticosteroids. But in recurrent cases, maintenance treatment is required, in which case the choice of treatment is challenging, especially if there is another autoimmune disease at the same time.

Case presentation: Here, a 37-year-old man is introduced who suffered from hallucinations and visual and auditory hallucinations along with a convulsion, followed by ataxia and headache. On examination, the patient had vitiligo lesions that had not been treated before. In the patient's MRI, typical GFAP astrocytopathy lesions were seen, and due to a period of recurrence of symptoms after initial treatment with corticosteroid pulse, the patient was treated with plasmapheresis and then rituximab.

Discussion: Considering that the patient's symptoms were initially purely psychiatric and he had a history of substance abuse, the diagnosis is at risk of misdiagnosis and the lack of diagnostic criteria for this disease makes the diagnosis more difficult. This patient had another treatment challenge due to the simultaneous presence of another autoimmune disease and the recurrence of symptoms after a course of treatment. Anyway, according to the experience of using anti-CD20 in similar autoimmune diseases, it seems reasonable to use rituximab in this patient.

Conclusion: Due to the rarity and novelty of this disease and the smaller number of patients who relapse, fewer studies have been published in this field, and choosing the appropriate treatment for these patients requires more and more detailed studies.

Keywords: white matter lesion, anti-CD20, autoimmune disease, encephalitis, GFAP astrocytopathy

Gut-Brain axis and MS: Is this true? (ORP-29)

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Multiple sclerosis (MS) is an autoimmune disease of central nervous system (CNS), that is associated with demyelination and axonal damage, mainly affect young people, the main cause of disease remained undetermined, but probably a number of etiologic and epidemiologic factors are involved. The gut-brain axis is communication pathway for exchange of information between the microbiota of gastrointestinal tract and nervous system or a link between the external environment and the CNS and may be have important role in pathogenesis of MS. The intestinal barrier and gut microbiota are main parts that any change or disruption of them (dysbiosis) lead release cytokines and other immune cells which may be associated with CNS autoimmune disease such as MS. The enteric nervous system is connected to the CNS through the parasympathetic (via the vagus nerve) and sympathetic (via the paravertebral ganglia) nervous systems. Probiotic supplementation, which can be used for treat gastrointestinal dysbiosis, calm down the immune system, have beneficial effects on serum levels of some factors associated with systemic inflammation and will be a promising strategy for prevention and treatment of MS.

Keywords: gut-brain axis; multiple sclerosis

Multiple sclerosis and viral hepatitis (ORP-30)

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Hepatitis B virus (HBV) can reactivate in patients after infection. This is because the HBV cccDNA integrates into the patient's hepatocyte DNA. Reactivation occurs in the setting of a decreased host immune system or the occurrence of harmful HBV mutations. Multiple Sclerosis (MS) patients who receive "Disease Modifying Drugs" (DMDs) are at risk of HBV reactivation. Justified screening for HBV before starting immunotherapy is a lifesaving situation in this special group of individuals. The triple panel is a valuable method for primary screening. However, HBV viral load measurement is

used when previous immunosuppression is a concern. It seems to be a reasonable approach to use prophylaxis in high risk patients for HBV reactivation while using potent immunosuppressive DMDs in MS patients. High risk groups include: cancer chemotherapy, organ transplant, B cell–depleting agents (Rituximab), Anti-TNF agents, monoclonal immune-modulators, use of 10mg of Prednisolone daily for 4 weeks. Occult HBV infection is defined when the HBs Ag is negative and anti-HB core IgG is positive with repeatedly detectable HBV DNA. Occult HBV should receive prophylaxis during Rituximab therapy and at least 18 months afterwards. It is recommended to identify the early markers of HBV reactivation and apply prompt treatment to reduce the risk of fatal liver failure. Reactivation is diagnosed if there is at least a 2-log increase in HBV DNA compared to the baseline level, or HBV DNA at least a 3-log in patients with previously undetectable HBV DNA, or HBV DNA at least a 4-log if the baseline level is unavailable.

Keywords: Multiple sclerosis, viral hepatitis

Lower urinary tract dysfunction in Multiple Sclerosis, Updates (ORP-31)

Shekoofeh Alaie

MS is a leading cause of LUT dysfunction in neurological i patients and LUT symptoms are reported in an average 8 yrs after the diagnosis of MS.

LUT dysfunction is simply and traditionally divided into Storage failure , emptying failure and combination of these two. Today ICS classification is based on UDS characteristics measured for both storage and emptying phases.

The management of LUT dysfunction is highly personalized and focuses, primarily, on the improvement of patients' symptoms and QoL and secondarily, on the preservation of the upper urinary tract and avoidance of urological complications (e.g., urinary tract infections, bladder stones, and renal impairment .

First-line treatments include fluid management, pelvic floor muscle training (PFMT), and medical therapies (e.g., antimuscarinic agents alone or in combination with B3 receptor agonists).

second-line treatments include BTX-A injections, intravesical therapies, invasive and non-invasive neuromodulation, and catheterization. Surgery may be indicated in select cases.

First-line management can be initiated in neurological practice, but early referral to a urology service should be considered in certain situations, specially if red flags are present.

Keywords: Multiple sclerosis, Lower urinary tract dysfunction

Sleep Disturbances and Disease Characteristics of Patients with Multiple Sclerosis in Iran: A Cross-sectional Study (ORP-32)

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Background: Sleep disorders are more prevalent in people with multiple sclerosis (pwMS) than in the general population. This study aimed to examine the clinical and sociodemographic factors contributing to sleep disorders in pwMS.

Method: The participants in this cross-sectional study were pwMS from the Isfahan Province in Iran. Sleep disorders were assessed using the Insomnia Severity Index (ISI), International Restless Legs Syndrome Study Group (IRLSSG), Berlin, and STOP-Bang questionnaires. A logistic regression model was applied to determine the accuracy of independent factors in predicting sleep impairment. A multivariate logistic regression analysis was conducted to examine the impact of multiple sclerosis (MS) types on sleep disorder severity predictability by independent variables.

Result: A total of 796 pwMS were included in the current study, 693 with relapsing-remitting MS and 103 with secondary-progressive MS. Rest leg syndrome (RLS) and insomnia disorders were not present in 48.1% and 50.5% of the pwMS, respectively. According to STOP-Bang and Berlin, 87.3% and 88.4% of patients had a low-severity risk for obstructive sleep apnea (OSA), respectively. The logistic regression showed that age, gender, and Expanded Disability Status Scale (EDSS) were associated with the risk of OSA ($p < 0.05$). RLS severity was also correlated with age and EDSS ($p < 0.05$). The association between sleep disorder severity and independent variables was not affected by MS type in multivariate logistic regression.

Conclusion: In this study, we found that sleep disorders such as RLS, insomnia, and OSA are common among pwMS in Iran. Sociodemographic factors, as well as disease characteristics, can have an impact on sleep disorders among pwMS.

Keywords: Multiple sclerosis, Sleep, Rest leg syndrome, Obstructive sleep apnea, Insomnia, Iran

Effect of eight weeks respiratory muscle training on respiratory capacity, functional capacity and quality of life on subjects with mild to moderate relapsing-remitting multiple sclerosis (ORP-33)

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Background: Multiple Sclerosis (MS) is a chronic inflammatory disease of the nervous system leading to muscle weakness, including the respiratory muscles that cause pulmonary complications, impair functional capacity, increased fatigue, and as a result decreases the quality of life.

Aim: The purpose of the present study is to examine the influence of 8 weeks of respiratory muscle training (RMT) on pulmonary function and respiratory muscle strength in MS patients.

Methods: The present study was a single-blind, randomized controlled trial that was conducted on 36 (27 Female, 9 Male) relapsing-remitting MS patients who were definitively diagnosed by a neurologist and randomly were divided into intervention and control groups. Both groups were educated on lifestyle modification with an emphasis on regular physical activity. In addition, the intervention group was prescribed eight weeks of respiratory muscle training with a threshold resistance device, daily, twice a day for three sets of 15 repetitions per set. Maximal expiratory pressure (PImax), maximal expiratory pressure (PEmax), spirometric indices, functional tests (six-minute walk test, timed up and go test), fatigue questionnaire, and questionnaire of quality of life were assessed before and after trials.

Results: A total of 36 patients (75% female; mean age 38.00(8.86) years; BMI 26.56(2.64) kg/m2) were included in the study. The strength of inspiratory and expiratory muscles, respiratory function, fatigue, and quality of life were significantly improved in the intervention group ($p<0.005$). In addition, there was a significant improvement in the rate of fatigue and quality of life in all their dimensions ($p<0.005$). Only in the six-minute walk test, no significant improvement was seen in the intervention group compared to the control group ($p = 0.262$).

Conclusion: Findings could help therapists to provide MS patients with more effective respiratory muscle training protocols to maximize the benefits of rehabilitation.

Keywords: quality of life, Multiple sclerosis, muscle training

Multiple sclerosis and legal medicine (ORP-34)

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Multiple sclerosis is an auto-immune disorder that harms a person's central nervous system. Thus, multiple sclerosis can cause bladder or bowel incontinence, vision disturbances, muscle weakness and spasm, mood disturbances, and loss of mobility. The symptoms of multiple sclerosis are similar to the symptoms of other diseases, however, and there is no test that can definitively diagnose a person with multiple sclerosis. Thus, when a patient presents with symptoms that may be caused by multiple sclerosis, this symptoms may be due to diseases other than multiple sclerosis or vice versa .

Diagnosing multiple sclerosis as early as possible is essential to providing treatment appropriate to lessen the effects of the disease. The failure to diagnose or wrong diagnose multiple sclerosis in a timely manner can lead to a progression, resulting in nerve damage that causes significant impairment.

When physician failed to diagnose in a timely manner or misdiagnose multiple sclerosis, which delayed treatment and caused patient,s condition to permanently damage vision, memory, mobility, or brain functioning, it may constitute medical negligence. Similarly, if a treating physician selected or administered the wrong medication or otherwise prescribed the wrong type of therapeutic intervention for specific form of MS, she or he may have cause for legal action. These are just a few of the many ways in which MS can be mishandled, an all too frequent occurrence in the healthcare field. Common examples of medical malpractice include:

A failure to diagnose or a misdiagnosis

Unnecessary surgery or surgical error, such as operating on the wrong body part

Prescribing improper medication

Ignoring or misreading test results

Failing to order necessary tests

We present some cases that refer to legal medicine and discussion about causes that leading to refferal judicial proceeding

Keywords: multiple sclerosis, Legal medicine, misdiagnosis

Optic neuritis and autoimmune optic neuropathies (ORP-35)

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Optic neuritis(ON) is an inflammatory involvement of the optic nerve that is commonly indicative of autoimmune neurological disorders including Multiple Sclerosis (MS), Myelin-Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD), and Neuromyelitis- Optica Spectrum Disorder (NMOSD). Access to several serological markers makes a diversity of autoimmune optic neuropathies and can now be used to diagnose disorders that are distinct from MS-associated ON.

Epidemiological studies determine that in White ethnic origin people, MS accounts for about 50–80% of ON cases, and around 30% remain idiopathic. Due to NMOSD and MOGAD are more frequent causes of ON in the Asian population, with NMOSD accounting for 3·4–43·5% and MOGAD for 10·2–27·6% of ON cases. Other autoimmune optic neuropathies, such GFAP-associated meningoencephalomyelitis and CRMP5-IgG-associated autoimmunity are other less frequent etiologies. In this lecture, we will determine ON and other autoimmune neuropathies.

MS: The ON in MS is usually unilateral, with painful eye-movement, dyschromatopsia, contrast sensitivity loss, and visual field loss are common in MS-associated-ON. The pattern of visual field loss was quite variable, with central defects more common than peripheral defects. It's not often sever with good recovery.

Atypical ON: Childhood or elderly onset, severe vision loss, prominent optic disc edema, poor visual recovery, recurrence after steroid treatment, and steroid dependence are features that point to atypical ON, prompting serologic testing for NMOSD and MOGAD. Less frequent causes are CRION, GFAP, and CRMP5.

NMOSD: NMOSD-associated ON accounts for around 3% of ON in studies related to white patients, but is up to tenfold in blacks and Asians. It often involves long segments of the optic nerve on MRI and commonly involves the optic chiasm. Around 30% of patients becoming legal blind, and nearly 70% in patients with recurrent ON attacks.

MOGAD: Optic disc edema is present in a majority (~80%) of the cases, which can be severe and associated with peripapillary hemorrhage. Radiographically, long segments of optic nerve enhancement with perineural enhancement.

CRION: A steroid responsive but steroid-dependent idiopathic ON. It can affects any age, sex, and ethnicity, although it most frequently affects young to middle-aged women. CRION can cause bilateral vision loss, either simultaneous or sequential. CRION is both rare and a diagnosis of exclusion, and requires negative testing for autoimmune disease, sarcoidosis, MS, NMOSD, MOGAD, as well as other causes of optic neuropathy.

GFAP: Coexisting immune system stimulation is common, including infection, autoimmune disease, and malignancy. No known ethnicity or sex bias, but typically affects middle-aged adults. The optic neuropathy is typically painless, bilateral, and associated with optic disc edema. Visual acuity is usually preserved, with a HCVA of 20/30 or better. There may be accompanying verities and venular leakage on fluorescein angiography. Optic nerve enhancement is typically –but not always- absent.

CRMP5: Up to 20% of CRMP5-IgG-associated paraneoplastic syndromes are associated with an optic neuropathy, which is usually painless, subacute, bilateral, and associated with optic disc edema and nerve fiber layer hemorrhages, although the optic nerve is typically non-enhancing on MRI. Nystagmus, diplopia, and opsoclonus have also been reported in association with CRMP5-IgG autoimmunity. The clinical triad of papillitis, vitritis, and retinopathy although helpful in diagnosis but is not always present.

Keywords: Optic neuritis, Multiple sclerosis, autoimmune optic neuropathies

Treatment approach in Autoimmune encephalitis (ORP-36)

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Autoimmune encephalitis is a type of brain inflammation caused by a dysregulation of immune system against some antigens in the central nervous system. It comprises a heterogeneous group of disorders that have some recognized or nonrecognised symptoms.

These conditions often show cognitive, seizure (i.e. encephalopathy)and movement disorder phenotypes.

Early diagnosis and treatment improve patient outcomes,and may decresed morbidity and mortality of these disorders

We should maintain a high-level of suspicion for autoimmune encephalitis and consideration of empiric immunotherapy once infectious causes are excluded.we divied the treatment in

3 categories include first line and second line and treatment of patients refractory to pervious approach.

Here we summarise the step by step treatment approach for common subtypes of these disorders and present a review from near 45 articles to clear the more acceptable management of all of these disorder when we suspect to these disorder. We focus on practical aspects of autoimmune encephalitis treatment.

Keywords: Autoimmune encephalitis, Management, Treatment

Effect of dynamic neuromuscular stabilization on fatigue and spasticity in people with multiple sclerosis: a randomized controlled trial (ORP-37)

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Objective: To compare the effects of core stabilization (CS) and dynamic neuromuscular stabilization (DNS) on fatigue and spasticity in People with Multiple Sclerosis (PWMS).

Design: Two-group randomized controlled trial.

Setting: general community and referral center.

Participants: A total of 66 PWMS, between 30 and 60 years old, and an expanded disability status scale (EDSS) between 2 and 6, participated in this study.

Interventions: Participants were randomly assigned to CS (n = 33) and DNS (n = 33) groups. Both groups received a total of 24 sessions of CS or DNS exercises, 60 minutes per session, three times a week during the 8 weeks.

Outcome measures: Fatigue was measured as the primary outcome measure. Spasticity was measured as a secondary outcome.

Results: The DNS group had significant improvement in The five-item Modified Fatigue Impact Scale (MFIS-5) and Multiple Sclerosis Spasticity Scale 88 (MSSS88) in PWMS compared with the CS group, ($P < 0.0001$) after 8 weeks of intervention and 18 weeks of follow-up. Significant improvements were seen in all outcome measures in both groups after 8 weeks of intervention.

Conclusion: This is the first clinical evidence to support the importance of DNS exercise in reducing fatigue and spasticity in PWMS. This study provides clinical evidence that DNS may be more effective for PWMS than CS.

Keywords: fatigue, Multiple sclerosis, Clinical trial, dynamic neuromuscular stabilization

MS Variants (ORP-38)

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In this lecture, multiple sclerosis variants will be discussed, which include Solitary Sclerosis, Schilder's disease, Baló's concentric sclerosis, Marburg variant of multiple sclerosis.

Solitary sclerosis: Solitary Sclerosis (SS) is a progressive disorder caused by an isolated CNS demyelinating lesion, which may be located in different areas, including the spinal cord, the brainstem, or the cerebral hemispheres.

Although the patients with this disease do not meet the criteria for MS, in 13% of cases, one of their first-degree relatives suffers from MS, and in 50% of cases, there is an evidence of inflammation in the cerebrospinal fluid. In addition, conventional drugs used for MS, whether immunomodulatory or immunosuppressive, were shown to have no effect on the progressive course of this disease.

Some cases with different manifestations have been reported. For example, Sahraian, et al. in their study reported a 24-year-old patient who was initially presented with diplopia, which healed completely. The patient had only one lesion in the pontomedullary region; however, she has then developed a progressive course of quadriparesis and became completely incapacitated within 6 years.

When a patient with solitary sclerosis proceeds to fulfill the minimum MRI requirement for an MS, the diagnosis of single-attack MS may be used. If solitary sclerosis leads to a progressive phase, it is described as progressive solitary sclerosis.

Schilder's disease: Schilder's disease, also known as myelinoclastic diffuse sclerosis, is a rare and aggressive variant of multiple sclerosis that was first described in 1912 by Austrian physician, Paul Schilder. The original case involved a teenage girl who died after several months of progressive neurologic deficits and signs of increased intracranial pressure. Over the years more cases were added to the literature, mostly describing children and adolescents with large bilateral demyelinating cerebral lesions with some degree of corticosteroid responsiveness. An additional frequent feature is its monophasic disease course.

Baló's concentric sclerosis: Baló's concentric sclerosis (BCS) is a rare demyelinating disorder of the central nervous system (CNS) characterized by concentric layers of demyelination as

detected by MRI or histopathology, and named after the Hungarian pathologist József Baló (1895-1979).

BCS is often regarded as a rare variant of multiple sclerosis (MS). While there are indeed similarities in terms of clinical presentation, BCS differs in several aspects from typical MS: lesion morphology (onion-like configuration characterized by concentric, alternating layers of demyelinated and myelinated tissue), lesion size (high frequency of large or 'tumefactive' lesions), and disease course (often monophasic and self-limiting rather than relapsing-remitting) and disease severity (not uncommonly fatal at first occurrence). This suggests that BCS and MS may be distinct disorders.

Marburg's variant of multiple sclerosis: is a malignant form of MS that evolves rapidly leading to death or severe disability. Otto Marburg first described this severe form of MS in 1906,

Patients usually present with focal neurological deficits or seizures. They often show acute neurological deterioration and succumbs to death in few weeks to months due to brainstem involvement.

The Marburg variant of multiple sclerosis which accounts for <4% of the total incidence of MS cases mostly affects children and young. It is a fulminant form of MS, featuring an acute onset of severe neurological deficits often resulting in death within weeks to months .Histology usually shows extensive demyelination as well as necrosis, which often involves vital areas like the brainstem. Synonyms for Marburg MS, which is the most aggressive variant of the disease, include malign, acute fulminant, acute malignant, and rapidly progressive MS. Its most important differential diagnoses are acute disseminated encephalomyelitis, Balo's concentric sclerosis, and Schilder's diffuse sclerosis.

Keywords: Solitary Sclerosis, Schilder's disease, Baló's concentric sclerosis, Marburg variant of multiple sclerosis

Multiple sclerosis, infectious and Gastrointestinal complications (ORP-39)

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Multiple sclerosis (MS) primarily affects the central nervous system, but it can have secondary effects on other parts of the body, including the gastrointestinal (GI) system. These effects can include both infectious and non-infectious complications. It's important to note that each individual's experience with MS can vary, so it's always best to consult with the healthcare provider for personalized advice.

When it comes to infectious complications in MS, individuals may have a higher risk of certain infections due to immune system dysfunction. (1,2)Common infections in MS can include urinary tract infections (UTIs), respiratory infections, and skin infections. On the other hand, DMTs affect the immune system in particular ways leading to immune suppression and cause infection. We discuss the interpretation of some lab data relevant to MS medications.

In terms of gastrointestinal complications, individuals with MS can experience a range of symptoms related to digestion and bowel function mainly due to side effects of their DMTs. Also, some gastrointestinal infections may limit the use of DMTs.

Managing these gastrointestinal complications and infectious risks in MS involves a combination of lifestyle modifications, medications, and supportive care.

Keywords: Multiple sclerosis, Gastrointestinal

Multiple sclerosis, Pregnancy, Breastfeeding (ORP-40)

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Multiple sclerosis (MS) is a chronic autoimmune disease that affects the central nervous system. It affects mainly people between 20 to 40. it's crucial to have open and ongoing discussions with your patients If they are living with MS and planning to become pregnant or if they are already pregnant, and provide personalized guidance and recommendations based on patient-specific health conditions and circumstances.

Pregnancy itself does not increase the risk of developing multiple sclerosis, nor does MS adversely affect the ability to conceive. In fact, research suggests that pregnancy can have a protective effect on the progression of MS symptoms. Many women with MS experience a decrease in disease activity during pregnancy, particularly in the later stages.

However, it's important to note that every person's experience with MS is unique, and the impact of pregnancy on MS can vary significantly from person to person. It's not uncommon for some women to experience a temporary worsening of symptoms during the postpartum period, commonly referred to as a "relapse."

When it comes to breastfeeding, it is generally considered safe for women with MS to breastfeed their babies. Breastfeeding has numerous benefits for both the baby and the mother, and in most cases, it does not impact the course of MS.

However, certain medications used to manage MS symptoms may affect breastfeeding. Some disease-modifying therapies (DMTs) are not recommended while breastfeeding due to

limited safety data. the healthcare provider can guide patients on the best approach, considering factors such as the severity of MS, the specific medication, and the potential benefits and risks for both mother and baby.

It is crucial to communicate plans for pregnancy and breastfeeding with healthcare providers early on. They can assess overall health, review medication regimens, and develop a management plan that allows patients to have a safe and healthy pregnancy while effectively managing their MS symptoms.

Apart from medical considerations, it's also important to prioritize self-care during pregnancy and while breastfeeding. This includes getting enough rest, eating a healthy diet, engaging in moderate exercise as recommended by healthcare providers, and managing stress levels. Support from loved ones and connecting with local or online communities of women with MS can also provide emotional support and helpful tips during this special time.

Keywords: Breastfeeding, Multiple sclerosis, Pregnancy

Patients monitoring during treatment with Teriflunamide (ORP-41)

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These treatments may be used as sequential monotherapies or for escalation or induction strategies based on the efficacy and safety measures showed significant reductions in disability progression, relapse rates,and magnetic resonance imaging measures of disease activity. In keeping with this primary MoA, teriflunomide acts to impair the proliferation of activated T and B cells, and reduces their ability to participate in a potentially damaging immune attack on the CNS.

We found that older adults with MS who switched to teriflunomid from other DMTs exhibited significantly reduced ARR after 2 years. Patients with severe renal impairment undergoing dialysis were not evaluated. Teriflunomide is contraindicated in this population dosage adjustment is necessary for patients with mild and moderate hepatic impairment. Teriflunomide is contraindicated in patients with severe hepatic impairment .Elevations of liver enzymes have been observed in patients receiving teriflunomide . These elevations occurred mostly within the first 6 months of treatment. Liver enzymes should be assessed before initiation of teriflunomide therapy - every two weeks during the first 6 months of treatment, and every 8 weeks thereafter or as indicated by clinical signs and symptoms such as unexplained nausea, vomiting, abdominal pain, fatigue, anorexia, or jaundice and/or dark urine. For ALT (SGPT) elevations between 2- and 3-fold the upper limit of normal, monitoring must be performed weekly Mild increases in transaminase, ALT below or equal to 3-fold ULN were more frequently seen in teriflunomide-treated groups as compared to placebo. The frequency of elevations above 3-fold ULN and higher was balanced across treatment groups. These elevations in transaminase occurred mostly within the first 6 months of treatment and were reversible after treatment cessation. The recovery time varied between months and years.

Elevation of blood pressure may occur during treatment with teriflunomide. Blood pressure must be checked before the start of teriflunomide treatment and periodically thereafter. ILD and worsening of pre-existing ILD have been reported during treatment with leflunomide, the parent compound of teriflunomide. Alopecia was reported as hair thinning, decreased hair density, hair loss, associated or not with hair texture change. Overall, teriflunomide therapy does not seem to have a clinically relevant impact on vaccine response .

There are limited amount of data from the use of teriflunomide in pregnant women. Studies in animals have shown reproductive toxicity . Teriflunomide may cause serious birth defects when administered during pregnancy. Teriflunomide is contraindicated in pregnancy.

Teriflunomide is found in semen. The manufacturer recommends that males and their partners should use reliable contraception during therapy. The rapid elimination procedure should be used in males who are planning to conceive.

Keywords: teriflunamide- multiple sclerosis - disease-modifying therapies

The Role of Advanced MRI Techniques and Artificial Intelligence-based Methods In Diagnosis of Multiple Sclerosis (ORP-42)

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MS is a common condition that affects the central nervous system, causing inflammation and damage to the spinal cord and brain. MRI is an important tool for assessing neurological diseases, and AI algorithms have improved the accuracy of lesion detection in MR images. The AIR Recon DL is a new deep learning-based MRI reconstruction pipeline that

produces high-resolution images, allowing for better detection of small lesions in difficult areas of the brain. Quantitative Susceptibility Mapping (QSM) is an advanced MRI technique that is more sensitive to MS-related tissue changes, such as iron accumulation and demyelination. Diffusion Tensor Imaging (DTI) is another powerful technique that can assess microstructural changes in white matter, potentially predicting the development of acute MS lesions. Chemical Exchange Saturation Transfer (CEST) MRI is a novel pulse sequence that can detect biomolecules altered in MS that may not be visible on conventional MRI. Recent advancements in CEST MRI allow for monitoring of protein and glutamate content in MS patients. Magnetic Resonance Fingerprinting (MRF) is a new approach to quantitative MRI that can measure multiple tissue properties in a single acquisition, allowing for more objective diagnosis and comparison of scans taken at different times and locations. The ability to quantitatively evaluate MRF-derived relaxometry has been helpful in characterizing chronic demyelinating lesions. Overall, The aim of this study is to review the advanced MRI techniques and artificial intelligence-based methods in the diagnosis of Multiple Sclerosis.

Keywords: Artificial Intelligence, Multiple sclerosis

How to estimate the Multiple Sclerosis Functional Composite (MSFC) in patients with multiple sclerosis? (ORP-43)

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A proper clinical evaluation of patients with Multiple Sclerosis (MS) is of great importance to detect disability progression. The EDSS is one of the first standardized tools in the assessment of MS-related disability, which is still the most frequently used scale in clinical trials. However, it has been criticized for having some limitations, which mainly include the subjective nature of the neurological examination and the insufficient assessment of some functional arears such as cognitive function. The MS Functional Composite (MSFC) was developed following a task force set up by the US National Multiple Sclerosis Society specifically to address the limitations of the EDSS. The MSFC is a three-part, standardized, quantitative, assessment instrument that measures arm, leg, and cognitive function with the 9-Hole Peg Test (arm/hand dexterity), the Timed 25-Foot Walk (leg function), and the Paced Auditory Serial Addition Test (3-second version, PASAT3; cognition). The interpretation of the MSFC is still difficult and unfamiliar for physicians and needs practice effects with the PASAT. Moreover, variations in the reference populations used to calculate Z-scores, and the lack of an accepted definition of a clinically meaningful change are considered as other limitations in clinical practice.

Keywords: Multiple sclerosis functional composite, MSFC, progression

Update on inflammation, neurodegeneration and immunoregulation in MS (ORP-44)

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Multiple sclerosis (MS) is an inflammatory, demyelinating, and neurodegenerative disease of the central nervous system (CNS) of uncertain etiology. There is consensus that a dysregulated immune system plays a critical role in the pathogenesis of MS.

MS is characterized by immune dysregulation, which results in the infiltration of the CNS by immune cells, triggering demyelination, axonal damage, and neurodegeneration. There have been tremendous advances in the neuroimmunology of MS over the past five decades, which have led to improved diagnosis and therapy in the clinic. Not surprisingly given the incredible complexity of both the nervous and immune systems, our understanding of the basic biology of the disease is very incomplete.

In this article, we review the main immunological mechanisms involved in MS pathogenesis and Updates on inflammation, neurodegeneration, and immunoregulation in MS.

Keywords: Multiple sclerosis, Neuroinflammation, Immunopathophysiology, Neurodegeneration

Treatment escalation vs early high efficacy treatment in multiple sclerosis (cons and pros) (ORP-45)

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Early highly active treatment (HAT) vs. escalation treatment (ET) in multiple sclerosis (MS) is a topic of debate and research in the field of neurology. MS is a chronic inflammatory disease of the central nervous system that causes

demyelination, axonal damage, and neurodegeneration. The goal of treatment is to reduce the frequency and severity of relapses, prevent or delay disability progression, and preserve brain tissue and function.

HAT is an approach that uses the most effective disease-modifying therapies (DMTs) as first-line treatment for patients with high disease activity or aggressive MS, while ET is an approach that starts with less potent DMTs and escalates to more potent ones if the disease progresses. HAT aims to prevent or delay irreversible disability and brain atrophy by reducing inflammation and relapses, while ET may expose patients to prolonged periods of suboptimal treatment and worsening disease. HAT may also have advantages in terms of cost-effectiveness, quality of life, and patient satisfaction.

However, HAT is not without challenges and limitations. HAT may have higher risks and side effects than ET, such as infections, malignancies, or infusion reactions. HAT may also face barriers and uncertainties regarding availability, accessibility, affordability, patient preferences, and long-term data. Moreover, there is no clear consensus on the definition and criteria of high disease activity or aggressive MS, nor the optimal choice and duration of DMTs for HAT.

Therefore, more research and evidence are needed to compare the efficacy and safety of HAT versus ET in MS and to identify the best candidates and strategies for HAT. Several ongoing clinical trials and observational studies are addressing these questions, such as the DELIVER-MS, TREAT-MS, and OPTIMISE-MS trials. These studies will provide valuable insights and guidance for clinicians and patients to make informed decisions about the optimal treatment approach for MS.

Keywords: Multiple sclerosis, DMT

Nutritional recommendations in multiple sclerosis patients: a narrative review (ORP-46)

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Studies show that nutritional factors have an effect on both the incidence and symptoms as well as progression of multiple sclerosis (MS). We reviewed nutritional recommendations in MS. Unfortunately; there is currently no proven beneficial diet for MS patients. However, having a healthy diet to get adequate amount of nutrients and weight control can be beneficial for MS patients. Diets characterized by elevated consumption of fruits, vegetables, whole grains, and lean sources of protein, while concurrently restricting intake of processed foods, sugar, and saturated fats, demonstrate advantageous due to their antioxidative and anti-inflammatory properties.

Fortunately, in most MS patients, the disease is mild and moderate. However, in the advanced stages of the disease, there is a possibility of needing nutritional support, and the progress of the disease is associated with dysphagia, so it is necessary to adjust the consistency of food, transfer from solid food to puree, and concentrate liquids. Neurogenic bowel in these patients or drug side effects can lead to constipation or diarrhea, so the prevalence of constipation in these patients is high and its control is recommended through consumption of fluids, fibers and increased physical activity. Neurogenic bladder is also common in MS patients, which leads to frequent urination, urinary incontinence and urinary infection. Therefore, distribution of liquid consumption during waking hours and minimizing liquid consumption before going to sleep can minimize problems and complications.

The expansion of following the western dietary pattern (food pattern including high amounts of animal fat, red meat, fried foods, sweetened and high sugar drinks, high salt amounts) and its subsequent results such as obesity is one of the risk factors for MS, and following A healthy non-western diet can help control MS.

The Mediterranean dietary pattern is known as an anti-inflammatory pattern. The beneficial effects of this diet are related to the presence of large amounts of polyphenols, flavonoids and tannins. Due to the inflammatory nature of MS, this diet has been of great interest. Several studies have shown the role of following this diet in reducing the risk of MS. A pilot RCT study showed the role of following a Mediterranean dietary pattern on reducing fatigue, disease symptoms and EDSS in MS patients. Another cohort study has also shown its role in less disability in MS patients .

Keywords: Diet, Recommendation, Multiple sclerosis

Ophthalmology in multiple sclerosis (ORP-47)

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A vision problem is one of the most common symptoms of multiple sclerosis (MS) people.

In this lecture, I am going to talk about the role of the ophthalmologist in evaluating vision problems in MS patients. The vision problems were categorized into two main fields: blurred vision and diplopia.

Blurred vision:

a. Refractive Errors: There are several reasons for this complaint. MS patients like other people might have refractive errors and need a glasses prescription. There are also other reasons such as corneal irregularities or corneal problems such as keratoconus.

b. Cataract: MS patients usually have been treated with corticosteroids and this might cause cataracts even in young people.

c. Uveitis: Uveitis is an intraocular inflammation involving the uveal tract, retina, or vitreous body which appears unusually in MS. The association between MS and uveitis is unclear. In patients with MS, the frequency of uveitis ranges from 0.4 to 26.9%.

d. Optic neuritis: One study showed that optic neuritis is the first symptom of MS in about 15–20% of people with MS.

e. Other optic neuropathies: Ischemic optic neuropathies, peri-optic neuritis, optic nerve tumors, and hereditary optic neuropathies such as LHON.

f. Retinopathies: Several diseases such as macular edema, and retinal vasculopathy (as BRVO) should be considered in MS people.

g. Damage to the Visual Pathways in the brain: Due to space-occupying lesions or plaques.

h. Papilledema: Idiopathic intracranial hypertension (IIH) is a disorder related to high pressure in the brain and may occur in MS people.

Diplopia:

a. INO: Internuclear ophthalmoplegia or ophthalmoparesis (INO) is a common presentation of MS and is an ocular movement disorder that presents as an inability to perform conjugate lateral gaze and ophthalmoplegia.

b. Sixth nerve palsy

c. Third nerve palsy

d. Fourth nerve palsy

Oscillopsia: Due to nystagmus

Keywords: MS, Optic neuropathies, Uveitis, Diplopia

Paroxysmal Events in Multiple Sclerosis (MS); Pseudoathetosis as a Presenting Symptom of MS (ORP-48)

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Introduction: Movement disorders like tremor, myoclonus, paroxysmal hemi facial, paroxysmal dystonia, tonic spasms and pseudoathetosis can be caused by demyelinating lesions in spinal multiple sclerosis (MS), patient may present with acute proprioceptive sensory impairment and pseudoathetosis in limbs. Pseudoathetosis or piano playing movements of hands consisting of involuntary slow writing movements of fingers caused by a failure of joint position sense (proprioception) and indication disruption of the proprioceptive pathway form nerve to parietal cortex.

Pseudoathesois as presenting symptom of MS

A 38- year- old female present with acute proprioceptive sensory impairment and pseudo athetosis in the four limbs- particularly in the fingers of both hands, she had great difficulty in buttoning, unbuttoning, using chop sticks and writing. In neurologic exam she has profound loss of position and vibration sensation in all limbs, especially in both hands, pseudoathetoid movements was observed in the outstretched hands and extended fingers, and other neurologic exams were insignificant. In T2- weight MRI with GAD spinal cord reveal an active lesion in the posterior columns of cervical cord at the C3 vertebral level which was responsible for pseudoathetiod movements. Flair brain MRI shows multiple plaques in white matter periventricular and juxta cortical area.

Conclusion: Pseudoathetoid movements is a rare presentation of MS and is caused by loss of proprioception due to plaques in posterior column of spinal cord.

Keywords: Pseudoathetosis, Multiple sclerosis

Patient Monitoring during Treatment with Ocrelizumab and Rituximab (ORP-49)

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Monoclonal antibodies that target CD20 expressing B cells represent an important new treatment option for patients with multiple sclerosis (MS). This therapy may be associated with an increased risk of adverse effects which are reviewed in this study.

The generally favorable safety profile of anti-CD20 therapies may be due to several factors. First, although B cell depletion from the circulation is nearly complete, only 2% of the body's

total lymphocyte pool exists in peripheral blood, and depletion of the body's major stores of B cells in lymphoid organs is only partial. Early B cell precursors and late-stage plasma cells are both CD20-negative and unaffected by treatment, meaning that immune reconstitution by stem cells and pre-existing humoral immunity mediated by long-lived plasma cells are both preserved.

The most important adverse effects are Infusion Related Reactions (IRR), infections, PML, Immune mediated colitis and malignancy.

Infusion reactions are frequent and include: itchy skin, rash, hives, tiredness, coughing or wheezing, trouble breathing, throat irritation or pain, feeling faint, fever, redness on face (flushing), nausea, headache, swelling of the throat, dizziness, fatigue and fast heartbeat. Reduction of these IRR is possible with using premedication with methylprednisolone (100 mg IV) 30 minutes prior to each infusion, and an antihistamine (e g, diphenhydramine) 30 to 60 minutes prior each infusion; may also consider premedication with acetaminophen. Further reductions in IRR frequency can be obtained instructing patients to increase hydration from one day before the infusion and to take cetirizine 10 mg on the night before and morning of the infusion.

Infections are the other concern in this type of treatment. The most common infections are Herpes infections, upper respiratory tract infections, lower respiratory tract infection, hepatitis B virus (HBV) reactivation, weakened immune system and Progressive Multifocal Leukoencephalopathy (PML). Prior to initiating therapy, screening all patients for hepatitis B virus (HBsAg and anti-HBc measurements), and screening for latent infections (eg, hepatitis, tuberculosis) in high-risk populations or in countries with a high tuberculosis burden are recommended.

Treatment with anti-CD20-mAb results in a decrease in total immunoglobulins, mainly driven by reduction in IgM. Monitoring of quantitative serum immunoglobulins during treatment, especially in patients with opportunistic or recurrent infections and after discontinuation of therapy until B-cell repletion is recommended.

A review of post marketing cases identified 38 cases consistent with inflammatory, non-ischemic, and non-infectious colitis in association with ocrelizumab. This case series highlights ocrelizumab induced immune-mediated colitis that can be clinically severe and potentially life-threatening. Attention to gastrointestinal symptoms during treatment is crusial.

There was a small but concerning imbalance in the number of malignancies, and breast cancer in particular, in MS patients who received ocrelizumab in the phase 3 trials. The total numbers of patients with breast or other cancers in the ocrelizumab-treated populations were not higher than epidemiological expectations. The incidence of cancer has fallen during the subsequent open-label extension studies. There are no official recommendations for increased malignancy surveillance screening in patients receiving ocrelizumab. Rituximab, after 20 years and > 4.8 million total infusions, has also not been associated with any increased risk of malignancy. Age-appropriate cancer screening guidelines should be followed.

Keywords: Ocrelizumab, Rituximab, Multiple sclerosis

Current Updates on the Use of Probiotics as a New Treatment Option for Multiple Sclerosis (ORP-50)

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Multiple sclerosis (MS) is a chronic inflammatory disease that affects the central nervous system and causes nerve demyelination. Although the precise cause of MS is unknown, controlling the immune system and obstructing inflammatory pathways may help manage and treat the condition. According to studies, probiotics can change the gut microbiome, which affects and improves the immune system and immune responses in MS patients. According to research, the imbalance of microbes in the digestive system has a significant impact on autoimmune diseases like MS and disorders of the central nervous system (CNS), such as Alzheimer's, Parkinson's, and autism. MS is an autoimmune disease that damages the myelin in the CNS, and the gut-brain axis serves as a two-way channel for communication between gut microorganisms and the CNS. Immune cell and cytokine production that results from disruptions in the gut microbiome affect the blood-brain barrier and gut permeability. Recent animal studies reveal a strong connection between gut microbiota and MS onset and severity. In addition to altering short-chain fatty acid levels and inflammatory cytokines, changes in the gut can also impact the metabolites that cause neuroinflammation and myelin loss. Probiotics have been shown through in-vivo and in-vitro research to alter the immune system, potentially curing MS. In addition, the mechanisms of unaltered probiotics are often unclear, limiting their usefulness for detailed mechanistic studies. Synthetic biology offers the capability to create probiotics specifically designed for immune modulation with well-defined mechanisms of action. A recent investigation involved the engineering of synthetic probiotics to influence this pathway in MS therapies. Consequently, directing interventions toward a pathway in intestinal dendritic cells emerges as a promising

therapeutic strategy for modifying CNS autoimmunity. The potential to utilize living cells as a body medicine source holds tremendous promise for developing more personalized and precise therapies.

Keywords: Multiple sclerosis; Probiotics; gut brain axis; microbiota

Management of seizure in patients with multiple sclerosis (ORP-51)

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In a systematic review, the authors concluded that the incidence of seizures was 2.3%, while its prevalence was 3.1% in patients with multiple sclerosis (MS). In a study from Iran, 3.2% of the patients with MS experienced seizures. Occurrence of an epileptic seizure in a patient with MS may complicate the management process of the patient. Questions, that may arise include “how should we approach the patient”, “how should we treat the patient”, “how should we modify the patient’s MS treatment strategy”, etc. During this talk, I will try to provide answers to the frequently asked questions about the management of seizures in patients with MS considering the best available scientific evidence.

Keywords: seizure; multiple sclerosis; consensus; management

The role of stereotacic biopsy in atypical brain lesions (ORP-52)

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Many cases of abnormal brain masses may refer for stereotaxic biopsy (Strotaxic: It is a type of surgery that with the help of special and accurate tools, certain points of the brain are identified and by making a small cut in the scalp and creating a hole in the skull and dura, and with minimal damage to the brain tissue, it will be possible to reach that point and perform the desired actions as obtain tissue sample, thalamotomy ,pallidotomy, brachytherapy , electrode placement…). Among these lesions we can mention "MS" plaques, infectious lesions, granulomatous masses, ischemic lesions, vasculopathies, neoplastic tumors…Brain masses can be detected and differentiated with different modalities of "MRI", "MRS" and "MR perfusion" with a high percentage, and biopsy is not necessary for many of them. On the other hand, in some cases as possible diagnoses, the patient has been treated for a long time, but since there is no certain response from the treatment obtained, they are referred to have a pathology sample for a definitive diagnosis. Several cases in this regard have been biopsied by me, some of which confirmed the initial diagnosis, and some were contrary to the initial opinion. Plaques suspected of "MS Plaques " which are observed in "MRI", according to clinical signs and symptoms and the course of the disease and non-invasive paraclinical examinations, including "VEP","MRS" and "MR perfusion" can be recognized and differentiated with a high percentage, and the biopsy of MS Plaques are an invasive and unnecessary procedure, which may aggravated complications, and on the other hand, the result of the pathology, except in acute phases cases where macrophages and reactive cells are observed, due to the lack of access to specific and special "myelin" staining, is uncertain and it will be controversial. Nevertheless, sometimes the plaques are very large and even in acute phases cases, due to the high metabolism of the area, MRS may falsely suggest neoplasia, because increased choline level, and in these cases, they are referred for biopsy for definitive diagnosis.

During 33 years in four hospitals (Shohada,Tehran,Arad,Mehrad) By three Stereotaxic systems I have done over than 7000 brain lesions biopsies and Some of the most interesting brain lesions are introduced and discussed in this presentation with clinical description and imaging and pathology reports.

Keywords: stereotacic biopsy, Multiple sclerosis, lesions

Relationship between severity of symptoms of sleep disorders and information processing speed in people with multiple sclerosis (ORP-53)

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Objectives: It is estimated that up to 65% of pwMS (people with multiple sclerosis) experience varying degrees of cognitive impairment, the most commonly affected domain being information processing speed (IPS). As sleep disturbance is a predictor of detriments in IPS, we aimed to study the association between severity of restless leg syndrome (RLS) and obstructive sleep apnea (OSA) symptoms with IPS in pwMS using a language and education independent tool.

Methods: In a cross-sectional study, we enrolled pwMS referred to multiple sclerosis comprehensive center of Kashani hospital in Isfahan, Iran. We used Berlin and STOP-Bang questionnaires for assessing OSA symptom severity. The International Restless Legs Syndrome Study Group scale was utilized for determining presence and severity of symptoms of restless leg syndrome. We used Integrated Cognitive Assessment (ICA) test assess visual processing speed.

Results: We included 211 pwMS, with a mean age of 36.88±8.76 (82.9% female). There were significant association between RLS symptoms severity and ICA index (p=0.00), but there is no association between ICA index and OSA symptom severity using STOP-Bang scale (ICA index of 0.61±0.14 and 0.60±0.08 in low and high-risk pwMS respectively; p=0.897) and Berlin scale (ICA index of 0.61±0.14 and 0.59±0.15 in low and high-risk pwMS, respectively; p=0.384).

Conclusion: We found that the severity of RLS in patients with MS can worsen information processing speed, but sleep apnea did not show any effect on this domain of cognitive dysfunction.

Keywords: Multiple sclerosis; cognitive dysfunction; information processing speed; obstructive sleep apnea; restless leg syndrome

System biology review of multiple sclerosis and discovery of drug targets (ORP-54)

Ali Alizadeh Amiri

Summary

Multiple sclerosis (MS) is a chronic autoimmune disorder characterized by inflammatory-demyelinating events in the central nervous system. will be The aim of this study is to identify the genes and metabolic pathways effective in the disease using microarray data and to create gene interaction networks. The results of this study lead to the identification of the signaling pathway of TLRs, which are vital components of innate immunity and are used to identify and remove pathogen-associated molecular patterns (PAMPs) from bacteria, viruses and other pathogenic agents. Typical PAMPs are nucleic acids, including viral RNA and DNA. This issue indicates the microbial factors in the pathogenesis of the disease. MSRV (multiple sclerosis-associated retrovirus) belongs to the HERV-W family of human endogenous retroviruses. A protein derived from MSRV has been found in most patients with multiple sclerosis (MS). This protein (Env-ms) has pro-inflammatory properties for various types of immune cells and therefore could play a role in the pathogenesis of MS by promoting the leukocyte diapadesis observed in the central nervous system of patients. TLRs are also effective in directly regulating the activation and survival of T cells, and the imbalance of regulatory T cells in MS is one of the main symptoms of the disease at the molecular level. Considering that MSRV is a HERV, it can be hoped that CRISPR technology will eliminate the pathogen. On the other hand, TLRs, with emphasis on TLR4, as a molecule that initiates inflammation after encountering Env-ms and is responsible for disrupting the balance of T cells, is a potential therapeutic target.

Method: In this study, differential analysis of gene expression using GEO database data was used. The keyword used to search is Multiple Sclerosis. The number of reported studies based on Dataset and Supplementary file & CEL and Homo Sapience filters, 2434 cases were obtained, after reviewing the first 40 studies, 36 cases with Accession: GSE37750 were selected for expression analysis. The study conducted in GSE37750 on 9 multiple sclerosis patients with samples before and after treatment with IFN beta (2 samples for each patient, a total of 18 samples) and 8 healthy controls in this study included 26 samples. The analysis was done by R software by creating two groups, Normal and MS, respectively, with 4 healthy samples and 4 patient samples with the condition before treatment with IFN beta. The data obtained from the analysis included 50,000 items, which were reduced to 2927 items with Excel software based on Pvalue 0.06 and saved in a new sheet with the name SIGDegs. The SIGDegs data was also stored in two tables larger than 0.6 with the name OVER and the number of data 1052 and smaller than -0.6 with the name Under and the number of data 1064 in a new sheet based on the value of LogFc. Over genes network obtained from STRING database using Cytoscape software based on Degree, Betweenness, Closeness filter and number of 100 genes were determined as HUB genes of the network. The Hubs of Over gene network obtained from the STRING database was sorted by Degree, Betweenness, Closeness using Gephi software, and the modules and clusters of the network were calculated and determined using Modularity Analysis. Hubs of over genes cluster obtained from Gephi was checked by Enrichr server and Pathways tab. The obtained results indicate that the excessive activity of the TLR signaling pathway disrupts the balance of immune cells effective in inflammation th1, th2, th17 and causes autoimmune effects of which MS is one of them.

Results: The data obtained from the study using the system biology method validates the results obtained from other studies. Excessive activity of Toll-like receptor signaling pathway can indicate the presence of a pathogen. According to the results obtained from [1], we show that Env-ms can stimulate several inflammatory parameters in an in vitro

human BBB model, the HCMEC/D3 brain endothelial cell line. Furthermore, using a silencing approach with siRNAs, we show that Env-ms is recognized through Toll-like receptor 4, an innate immune pattern recognition receptor found in endothelial cells. We also show using functional methods that treatment of brain endothelial cells with Env-ms significantly stimulates the adhesion and migration of activated immune cells across the endothelial cell monolayer. These findings support the hypothesis that MSRV may play a role in the pathogenesis of MS or at least in maintaining an inflammatory condition, thus fueling the autoimmune disorder. MSRV can also play a role in other chronic inflammatory diseases. Interestingly, the proinflammatory and immunopathogenic effects of MSRV are achieved by its envelope protein (Env-ms) through the activation of Toll-like receptor (TLR) 4 and its receptor CD14. These results lead to the targeting of genome editing with the approach of removing MSRV genes by CRISPR technology. TLR4 could also be considered as a drug target as (2) loss of TLR4 in CD4+ T cells alone almost completely abrogates disease symptoms, mainly through reduction of Th17 and, to a lesser extent, Th1.

Keywords: System biology, Multiple sclerosis, Drug target

Spinal cord MRI in multiple sclerosis; diagnostic, prognostic and clinical value (ORP-55)

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Introduction: Multiple sclerosis (MS) is a chronic neurological condition characterized pathologically by axonal loss, demyelination, inflammation, and gliosis. Magnetic resonance imaging (MRI) has had a major impact on diagnosing MS, understanding the condition, and monitoring the effects of treatments. Recently, spinal cord MRI has received increased attention. Advanced techniques have been used to image the spinal cord, particularly the cervical cord, and measure quantitative parameters such as T1 relaxation time, magnetization transfer ratio, and diffusivity. These metrics show central nervous system abnormalities in MS patients and various correlations with disability and might reflect specific pathological processes.

CONVENTIONAL SPINAL CORD MRI:

Lesion detection;

- T2-Weighted Sequences for Spinal Cord Lesion Detection

- Additional MRI Sequences for Spinal Cord Lesion Detection;

Standard T2-weighted FSE sequences with the goal of improving SC lesion detection

Short tau inversion recovery (STIR) is a fat suppression technique

Gradient echo (GRE) sequences are another possible complementary sequence to core T2-weighted, FSE sequences.

Phase-sensitive inversion recovery (PSTI-IR or PSIR), PSIR enabled superior lesion demarcation and localization.

RECOMMENDED STANDARDIZED SPINAL CORD MRI PROTOCOL IN MULTIPLE SCLEROSIS

CLINICAL USEFULNESS OF SPINAL CORD MRI IN MULTIPLE SCLEROSIS: DIAGNOSIS AND PREDICTION

THE CLINICORADIOLOGIC PARADOX

ADVANCED QUANTITATIVE SPINAL CORD MRI TECHNIQUES:

STRUCTURAL TECHNIQUES;

Spinal Cord Atrophy; SC Atrophy: Gray Matter

Magnetization Transfer Imaging

Diffusion Tensor Imaging

Ultra–High-Field MRI

FUNCTIONAL IMAGING;

Functional MRI

Magnetic Resonance Spectroscopy

Conclusions: Imaging the SC in MS has significant value, both in clinical and investigational settings. Conventional MRI techniques have been used predominately to evaluate SC lesions, and newer sequences have improved the ability to detect SC lesions. Conventional MRI of the SC is routinely used in clinical practice, because it has both diagnostic and prognostic usefulness. A number of advanced quantitative SC MRI measures that assess both the structural and functional integrity of the SC have been evaluated in investigational settings. These techniques include measures of SC atrophy, DTI, MTI, UHF MRI, fMRI, and MR spectroscopy.

Keywords: Multiple sclerosis , MRI , Cervical MRI

Neuromyelitis Optica Spectrum Disorders (NMOSD); Diagnostic criteria (ORP-56)

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Neuromyelitis optica spectrum disorders (NMOSD) is an autoimmune astrocytopathy. The term NMOSD is used as an umbrella term that refers to Aquaporin-4 (IgG) positive NMO and some closely related clinical syndromes without AQP4-IgG. Core clinical features of the disease are optic neuritis acute myelitis, area postrema syndrome (episode of unexplained hiccups or nausea and vomiting), acute brainstem syndrome, Symptomatic narcolepsy or acute diencephalic clinical syndrome (with NMOSD-typical diencephalic MRI lesions), symptomatic cerebral syndrome (with NMOSD-typical brain lesions).

Diagnostic criteria: For an IgG-positive situation, one clinical core presentation is enough to diagnose. However, in seronegative patients At least 2 core clinical characteristics and meeting all of the following requirements are mandatory:

a. At least 1 core clinical must be optic neuritis, acute myelitis with long-extending transverse myelitis (LETM), or area postrema syndrome.

b. Dissemination in space (2 or more different core clinical characteristics).

c. Fulfillment of additional MRI requirements.

Additional MRI requirements include normal findings or only nonspecific white matter lesions in brain MRI or T2 lesion or gad enhancing lesion extending over 1/2 optic nerve or involving optic chiasm in orbital MRI. Also, Intramedullary MRI lesions extending over 3 contiguous segments or 3 contiguous segments of focal spinal cord atrophy in patients with complaints compatible with acute myelitis. Associated dorsal medulla or area postrema lesions in area postrema syndrome and associated peri-ependymal brainstem lesions in acute brainstem syndrome should be documented.

Red flags: Clinical or Laboratory findings which are atypical for NMOSD diagnosis are Progressive overall clinical course, atypical time to attack nadir (less than 4 hours), continual worsening for more than four weeks from attack onset, partial transverse myelitis, especialy not associated with LETM, presence of CSF oligoclonal bands. In MRI, Imaging features suggestive of MS or other than MS and NMOSD (lesions with persistent [3 months] gad enhancement) are atypical for NMOSD.

Keywords: Neuromyelitis optica spectrum disorders, NMOSD, criteria, diagnosis

Optic neuritis updates (ORP-57)

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The optic nerve is a relatively small structure, with a total length of 50 mm, but there are numerous causes of optic nerve disorders, including: inflammation, tumours, vascular disorders, metabolic diseases, infections, drugs, systemic diseases, genetic diseases, and trauma .

Optic neuritis (ON) is the most common cause of optic nerve involvement in young adults and occure as a demyelinating disorder of central nervous system. The estimated incidence of ON is 1.5–5.1 cases per 100,000 person-years, which are predominantly typical ON (i.e., idiopathic or associated with multiple sclerosis (MS). Our understanding of the significance of optic neuritis has changed over the recent years. It was considered as a presentation of multiple sclerosis for decades, however Multiple sclerosis is the most common demyelinating disease associated with optic neuritis , it is important to differentiate from other auto immune processes such as NMOSD , MOGAD , GFAP-IgG-associated optic neuropathy, CRMP5-IgG-associated optic neuropathy . CRION is another idiopathic optic neuritis and is both rare and a diagnosis of exclusion.

It is important to differentiate typical from atypical ON because the prognosis and treatment differ among these etiologies. Features that should raise concern for atypical ON are as below :

Childhood or elderly onset,

Severe vision loss,

Prominent optic disc edema,

Poor visual recovery,

Recurrence after steroid treatment,

Steroid dependence

Presentation of Acute Optic Neuritis, Treatment Considerations for Acute or Recurrent Optic Neuritis, Workup Considerations for Acute or Recurrent Optic Neuritis (Diagnosis of optic neuritis and autoimmune optic neuropathies) will be discussed.

Keywords: Optic neuritis, Acute Optic Neuritis

A middle-aged woman with history of Multiple sclerosis presented with sub-acute encephalopathy (ORP-58)

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Introduction: The correct diagnostic approach and paying attention to clinical and imaging red flags for multiple sclerosis are necessary to evaluate patients suspected for MS attack due to the wide range of its differential diagnoses.

Case presentation: Our patient is a 58-year-old woman known case of MS since 13 years ago, who was diagnosed with right optic neuritis in 2010 and typical demyelinating lesions in brain and cervical MRI. There was a history of advanced MS in her sister. The patient was first treated with Cinnovex, and following clinical & imaging disease activity, her treatment was escalated to Rituximab from 2019.

She was referred to MS clinic because of sub-acute progressive headache, nausea and vomiting, followed by imbalance, cognitive problem & drowsiness from 1 month before. The patient was not febrile during this period. On admission disorientation, bilateral papilledema, decreased gag reflex, asymmetric quadriparesis (Left>Right), spasticity & hyperreflexia was noted & she was unable to walk.

Considering the progressive encephalopathy and history of Anti CD20 treatment, imaging was performed for the patient with high suspicion for superimposed infection or neoplastic lesions. Brain MRI showed extensive confluent abnormal white matter signal intensity in both centrum semiovale crossing splenium of the corpus callosum with extension to midbrain & right side of pons (more dominant on right side), with mild mass effect & midline shift. Also, patchy enhancement & diffusion restriction was evident at parts of lesions. Regarding atypical clinical & imaging features for demyelinating attack, deep and periventricular location of the lesions, atypical patchy enhancement and spreading through the splenium of corpus callosum, diagnostic biopsy was performed. Pathology & IHC assessment confirmed high grade B cell lymphoproliferative disorder consistent with diffuse large B cell lymphoma.

Clinical Lesson: Superimposed infection or neoplastic comorbidity should be considered in any MS patient under treatment who presents with clinical and/or MRI red flags. This is especially true in patients who receive potent DMTs.

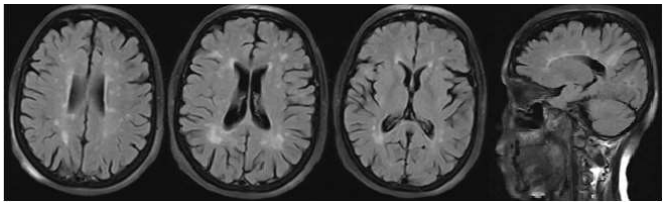

Figure 1: The patient's previous typical MS lesions (2017)

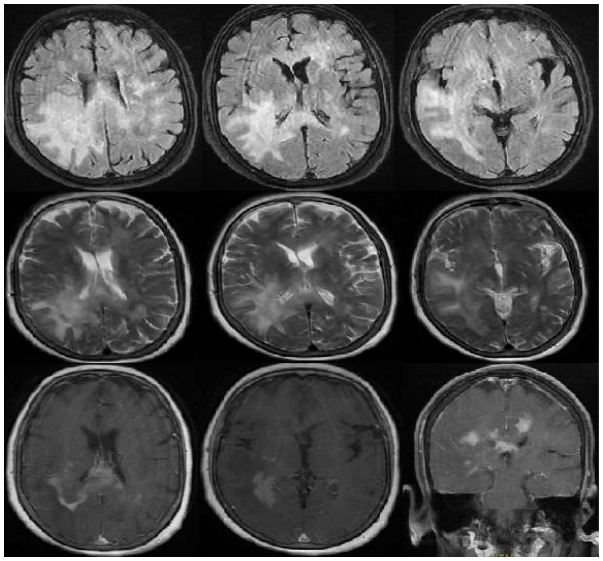

Figure 2: Atypical lesions in recent Brain MRI; diffuse large B cell lymphoma was confirmed.

Keywords: multiple sclerosis, encephalopathy

Reduction in Circulating Vitamin D Binding Protein in Patients with Multiple sclerosis (ORP-59)

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Background: In this study, we aimed to determine the risk association between vitamin D binding protein (VDBP) polymorphism in patients with multiple sclerosis (MS) in a MS biobank and the difference in VDBP serum levels in MS patients who were recently diagnosed.

Method: The current case-control study was performed on 296 MS patients and 313 controls. Thereafter, two common missense VDBP polymorphisms, named rs7041and rs4588, were evaluated in all the participants. Serum levels of vitamin D and vitamin D binding protein were assessed in 77 MS patients who were diagnosed since one year ago and in 67 healthy people who were matched in terms of age and sex.

Result: The frequency distributions of VDBP genotypes and alleles of SNP rs7041 and rs4588 were observed to be similar in both the MS and control groups ($p>0.05$). The VDBP haplotypes, as Gc2/Gc2, Gc1/Gc1, and Gc1/Gc2, were found to be similar in the MS and control groups ($p>0.05$).

In subgroup analysis, circulating VDBP was lower in MS patients (Ln-VDBP (µgr/ml): 3.64±0.91 vs. 5.31±0.77, $p=0.0001$) even after adjusting for vitamin D levels, body mass index, and taking vitamin D supplement. There was no

significant association between VDBP haplotypes and vitamin D levels in the two groups.

Conclusion: The present study suggested an association between lower levels of circulating VDBP and multiple sclerosis in newly diagnosed patients. However, the VDBP causative role in the development of MS is still unclear, so it needs more studies.

Keywords: Multiple sclerosis, Vitamin D binding protein, vitamin D, bioavailability of vitamin D

Multiple Sclerosis (MS) and Legal Medical Doctrines (ORP-60)

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In Iran, every year, several cases of patients with multiple sclerosis (MS) are referred to the legal medicine organization for many cases, which, according to the type of file and the request of the judge, about the severity of the disease, the time of its onset, timely diagnosis, and the use of appropriate of the planned treatment by the attending physician and, other cases should be issued an expert opinion. Therefore, the purpose of this study is to review several cases of patients' medical malpractice and Intolerance of Punishment imprisonment, or non-imprisonment referred to the legal medicine organization to present legal processes for MS medical malpractice complaints on one hand and to present indicators for determining the intolerance of punishment imprisonment, or non-imprisonment on the other hand, that will increase the awareness of the medical community and also reduce malpractice in the process of diagnosis and treatment.

Keywords: Multiple Sclerosis, Legal Medicine, Medical Malpractice, Intolerance of Punishment

MS and Environmental Factors (ORP-61)

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Introduction: Multiple sclerosis (MS) is a potentially disabling acquired demyelinating disease of central nervous system. We do not know for certain what causes multiple sclerosis. Scientists believe that a combination of factors trigger the disease. Studies support the opinion that MS is caused when people with the right combination of genes are exposed to some trigger in the environment.

At present it has shown that environmental factors play a significant role in your susceptibility to MS. For people with the 'right' genetic background – those predisposed to developing MS because of a strong family genetic tendency – certain environmental factors increase the risk of developing MS. it is felt that genes contribute 25% to your overall MS risk, while environment makes up 75%. Your genes are not your fate. The important risk factors include:

Age. (MS can occur at any age, but onset usually occurs around 20 and 40 years of age), sex, family history, fertain infections, race, climate,

Vitamin D (having low levels of vitamin D and low exposure to sunlight is associated with a greater risk of MS), high cow's milk consumption, high body-mass index during adolescence, smoking (including passive smoking), high saturated fat diet and stress. Not need to say that most of these risk factors are modifiable.

Keywords: Multiple Sclerosis, Environmental factors, Modifiable

Care ethics and empathic Practices in dealing with MS Patients (ORP-62)

Hanieh Zaer Rezaei

Empathy is often mistaken for pity and sympathy. In practice, when, instead of empathising, sympathising is bold, connections are broken, and a person finds a sense of sacrifice and uncontrollability, rather than hope and motivation.

In sympathy, our compassion makes the patient feel poor and see himself as a victim of compulsive conditions. The result of this compassionate model will be hopelessness, frustration, depression, and abandonment of treatment. When I feel sympathy, I actually expose myself to the same pain that afflicted the patient. His pain hurts me, and I react to his pain with my judgements and my mental outlook. I am standing besides him and suffering with him.

But in empathy, I try to figure out what he wants and what he needs. With me, I put a light on my hand, I walk next to him, I listen, I explore, and I try to see his problem and know the point of his pain. Without judgement and without entering my own thoughts. Empathy does not end here. I sit next to my patient, listen to his feelings and emotions, to understand his needs and help him to improve his condition as much as I can.

It has principles and guidelines: The first step is listening. We listen to him so that we can see his perspective. To find out what his perceptions of illness and concerns are, how much information is right or wrong about illness? We go ahead with

him and explore and try to empty our minds from all judgements and labels and accept him and his view as he is.

The next step is to encourage him to recognise and name his feelings. Fear, anger, disappointment, loneliness, shame, and... There are feelings that our patients are likely to experience in these circumstances, and we encourage them to talk about them.

We're not going to show him that the disease isn't as big as he thinks. We're not going to tell him that it might be worse than this or that there are more dangerous diseases than his. We are not going to tell him that life is beautiful; see its beauty and enjoy it. All of these phrases make patients feel incomprehensible.

I'm going to tell him that, it's quite natural that you're experiencing those feelings. It's great that you're here now because we're a professional team that stands by you, and you aren't alone, you are in the right place. These words make people feel connected and belonging. Social support and, social interest and trust are three key factors in human resilience and we raise them with empathy. Although some people are more empathic, fortunately, empathy is a skill. To be empathic, we need to practice listening well, and looking non-judgmentally, and raising our emotional awareness.

Keywords: ethic, Multiple sclerosis

The effects of crocin on inflammatory biomarkers and mental health in patients with multiple sclerosis: a randomized, double-blinded clinical trial (ORP-63)

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Introduction: Multiple sclerosis (MS) is a demyelinating disease that affects the central nervous system and is one of the leading causes of disability in young adults. It causes a wide range of psychiatric symptoms such as depression and anxiety. Considering the antioxidant effects of saffron and its role in preventing neuronal analysis and improving psychiatric symptoms such as depression, we investigated the effect of crocin, a saffron bioactive compound, on oxidative stress and inflammatory biomarkers, and mental health in patients with MS.

Materials and Methods: Patients with MS were randomized into two groups taking either 15 mg crocin tablets twice a day (n = 25; 30 mg/day) or placebo tablets (n = 25) for 8 weeks. Depression and anxiety questionnaires were recorded and fasting blood samples were collected at baseline and at week 8 following the intervention.

Results: The results showed no significant differences between crocin and placebo groups for depression and anxiety. Within-group comparisons, however showed that crocin significantly lowers anxiety in patinets with MS. Biochemical analyses revealed that crocin significantly decreases serum high-sensitivity C-reactive protein (hs-CRP), a main biomarker of inflammation, as compared to the placebo group (P=0.018). However, there was no significant difference between the two groups in terms of the effect on serum malondialdehyde (MDA) and nitric oxide (NO) after 8 weeks of intervention (both $P \geq 0.42$).

Conclusion: Our findings suggest that crocin supplementation for 8 week may not be effective in improving depression and anxiety in patients with MS. However, crocin supplement showed promise in attenuating inflammation evidenced by reducing hs-CRP in patients with MS. Future clinical studies with higher doses and long-term supplementation with crocin are recommended to assess the effects of crocin on inflammatory biomarkers and mental health of patients with MS.

Keywords: multiple sclerosis, crocin, saffron, inflammatory biomarkers, mental health, depression, anxiety.

Consent for publication

This manuscript has been approved for publication by all authors.