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Unusual Neurological Complications of Immune Checkpoint Inhibitors used in Treatment of Cancer: Report of two cases.

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INTRODUCTION: Immune checkpoints are necessary molecules that either promote or inhinbit T-cell activation. Checkpoint inhibitors (ICI) that block these checkpoints allows T-cell to kill cancer cells. Neurological complications secondary to these novel cancer therapy are very rare and we report two such cases.

METHODS: Retrospective case series study.

RESULTS:

Case (1) 78 years old woman who presented with subacute onset of dysarthria and cerebellar ataxia with previously treated high grade urothelial cancer with Nivolumab. Her MRI, CSF, routine blood work and paraneoplastic panels were all negative. She responded partially with high dose steroids and 4 courses of IVIG but still requires ongoing attendent`s care.

Case (2) 70 years old man with subacute onset of dizziness, ataxia, orthostatic hypotension and autonomic dysfunction with previously treated bladder cancer with Pembrolizumab. His MRI shows enhancement in area postrema and (+) CSF anti-GAD65 antibody. He responded partially to high dose steroids, IVIG and plasma exchange. He continues to remain symptomatic with dizziness but his autonomic and area postrema symptoms had improved.

CONCLUSIONS: Serious but very rare, and delayed Neurological complications such as subacute cerebellar syndrome or autoimmune encephalitis due to ICI therapy for cancer should be suspected in those patients whose clincial presentation cannot be explained by other etiologies.

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Efficacy and Safety of Inebilizumab in Patients 50 years of age and older with Neuromyelitis Optica Spectrum Disorder: N-MOmentum Study Subgroup Analysis

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Background: Inebilizumab (INEB), an anti-CD19 B cell depleting antibody, is approved for the treatment of NMOSD in adults seropositive for aquaporin-4 antibody (AQP4-IgG+). The N-MOmentum study included participants with ages ranging from 18 to 74 years (yrs).

Objective: To evaluate the efficacy and safety of INEB in AQP4-IgG+ participants ≥50 yrs with NMOSD.

Methods: N-MOmentum (NCT02200770), a double-blind, phase 2/3 trial, assessed the efficacy and safety of INEB in adults with NMOSD, with a 28-week randomized controlled period (RCP) (INEB 300 mg or placebo [PBO] on days 1 and 15), and an open-label period (OLP) of ≥2 years. Post hoc analyses were conducted to analyze outcomes in AQP4-IgG+ participants ≥50 yrs.

Results: Of 213 AQP4-IgG+ participants, 65(30.5%) were ≥50 and 148(69.5%) were

Conclusion: This data supports the efficacy and safety of INEB in AQP4-IgG+ ≥50 yrs NMOSD although evaluation of larger populations is needed to confirm these results.

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Progressive Multifocal Leukoencephalopathy and Subacute Sclerosing Panencephalitis: Viruses, Antigens and Antibodies

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Progressive multifocal leukoencephalopathy (PML) is a rapidly progressive demyelinating infectious disease of the central nervous system with asymmetric brain damage. Caused by activation of human polyomavirus 2, which is carried by about 80 per cent of the US population. Human polyomavirus 2 or JC virus is one of six species of human polyomaviruses and was named after the initials of the patient John Cunningham, in whom it was first discovered in 1971. Its activation in the human body is preceded by significant suppression of the immune system: in the vast majority of cases, PML is a manifestation of acquired immunodeficiency syndrome (AIDS), in other cases, after immunosuppressive and immunomodulatory therapy, for example, as part of treatment with monoclonal antibodies or after organ transplantation, as well as hematological neoplasms, such as Hodgkin`s disease, chronic lymphocytic leukemia. Disease is especially common after bone marrow transplantation. Problem is the occurrence of PML in patients with multiple sclerosis treated with natalizumab.

Subacute sclerosing panencephalitis (SSPE) is a progressive neurodegenerative, most often fatal disease of the central nervous system caused by the measles virus. The disease is a slow viral infection; after the initial measles infection, there is an asymptomatic period that lasts an average of 7 years, but can vary from 1 month to 27 years.

It is estimated that on average 2 in 10,000 people who have measles develop it, with immunization being the main factor in the decline. In classic picture of the disease, death occurs between 1 and 3 years

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Acquired idiopathic generalized anhidrosis after COVID-19 infection

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Background: Acquired idiopathic generalized anhidrosis (AIGA) is an infrequent condition characterized by the sudden onset of an inability to sweat without accompanying neurologic features or sweat gland abnormalities, often leading to heatstroke. Several reports have postulated various pathogenesis about autoimmune responses in AIGA patients. The novel coronavirus (SARS-CoV-2) has been implicated in inducing autoimmune disease, prompting consideration of its potential role in the development of de novo autoimmune diseases. Case: We present a case of a 34-year-old male with 16-week history of decreased sweating. Two weeks after a confirmed SARS-CoV-2 infection, he experienced facial flushing. subsequently, with increasing ambient temperature, the patient developed tingling in the palm, and urticaria in response to exercise with an absence of overall body perspiration. Quantitative sudomotor axon reflex test by Q-Sweat revealed absent sweat output at all sites. Laboratory studies for autoimmune diseases were normal. A skin biopsy from the palm revealed mild lymphocytic infiltration around the secretary portion of eccrine gland. Intravenously administration of methylprednisolone (1000 mg/day for five consecutive days) resulted in significant improvement of anhidrosis within several days. Discussion: The hyperstimulation of the host immune system induced by SARS-CoV-2 infection and its vaccination has been linked to the development of autoimmune diseases. While the casual relationship between COVID-19 vaccination or infection and AIGA remains speculative, Nonetheless, the short incubation period and positive response to steroid in our case suggest a potential autoimmune association between AIGA and SARS-CoV-2 infection.

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Cerebral Cortical Encephalitis in a child with MOGAD and Hashimoto's Thyroiditis

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Cerebral Cortical Encephalitis (CCE) is a rare phenomenon of Myelin Oligocyte glycoprotein-associated disease (MOGAD). Having concurrent anti-thyroid antibodies has not been reported. The characteristic feature of CCE is its involvement of the cerebral cortex which is appreciated in the FLAIR images of MRI. CCE patients usually present with cortical signs. We hereby, describe a case of CCE in a Bangladeshi child who presented with a 3-week history of progressive behavioral abnormalities, bilateral visual impairment, and hemiparesis following an attack of seizure. Examination poor visual acuity (OD to finger counting and OS to light perception) with funduscopic evidence of bilateral papilledema, and right arm and leg weakness. MRI showed predominantly cortical but also subcortical hyperintense lesions with subtle contrast enhancement. Further investigations elicited positive anti-MOG IgG antibodies in the serum concomitantly with high titer of anti-TPO Antibody, high TSH, and low FT4. Coexistence of CCE phenotype of MOGAD with Hashimoto's Thyroiditis is a rare occurrence. Treatment with corticosteroids and Levothyroxine reversed the clinical manifestations within a few weeks. However, at 6 months follow up while on a low maintenance dose of Prednisolone and levothyroxine, serum anti-MOG IgG was still detected to be positive along with positive Anti TPO and TG antibodies despite complete recovery of symptoms. This finding persuaded us to continue oral steroid therapy for a longer duration. This case underscores the need to look for other associated antibodies in MOGAD as failure to do so may impact the outcome and monitoring the disappearance of the antibodies.

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Long-Term Comparative Efficacy of Inebilizumab in the AQP4+ Subpopulation from N-MOmentum Open-Label Period Versus Azathioprine and Immunosuppressants and Versus Placebo in Patients with NMOSD

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Background: Inebilizumab (INEB), an anti-CD19 B cell-depleting antibody, is approved for the treatment of neuromyelitis optica spectrum disorder (NMOSD) in adults seropositive for aquaporin-4 antibody (AQP4+). N-MOmentum (NCT02200770) consisted of a 28-week randomized-controlled-period (RCP) and an optional open-label-period (OLP, 2 years) in which all participants received treatment with INEB.

Objective: To evaluate the long-term comparative efficacy of INEB over N-MOmentum OLP vs azathioprine and other immunosuppressants (AZA/IST) and vs historical-placebo (PBO) in participants with NMOSD.

Methods: Two historical comparator groups (HCGs) of participants who received AZA/IST (N=132) or PBO only (N=106) were derived using data from published NMOSD studies and were used to evaluate the comparative efficacy of INEB (N=208) over the OLP. Hazard ratios (HR) for INEB vs HCGs were estimated using a Cox proportional hazards (PH) regression. Time to NMOSD attack was analyzed using parametric and flexible survival (spline) models that were fit to INEB and HCGs.

Results: The HR (95% CI) of time to NMOSD attack for the N-MOmentum PBO group compared to historical-PBO groups was 1.15 (0.67–1.91); P=0.58. The HR (95% CI) for time to NMOSD attack for INEB vs AZA/IST and PBO groups were 0.29 (0.17,0.42); P

Conclusions: INEB was associated with a statistically significant improvement in time to onset of an NMOSD attack and provided a long-term attack-free survival benefit over the OLP compared to the relative short-term benefit observed with AZA/IST.

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The relationship between autophagy and LCN2 secretion by reactive astrocytes

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Objective: Autophagy is a conservative lysosome degradation pathway, that can degrade and recover long-lived or misfolded protein and damaged organelles to maintain cell energy and function. LCN2 secreted by reactive astrocytes can induce the death of damaged neurons. Under inflammatory conditions, astrocytes secrete lipid delivery protein-2 (LCN2), which has recently been discussed as a valuable biomarker for predicting the clinical outcome of stroke patients. To summarize the relationship between autophagy and LCN2 and to explore whether autophagy can reduce the secretion of LCN2 by reactive astrocytes induced by OGD/R, which may be beneficial to neuroprotection. Methods: Through the databases of China Knowledge Network, PubMed, Wanfang, etc., we searched "autophagy", "LCN2" and "astrocytes" as keywords, collected related literature, and reviewed this problem. Results: Deferriamine improved the up-regulation of Lipocalin-2 induced by lipopolysaccharide through autophagy activation of primary astrocytes. Torin-1 can inhibit the activation of autophagy flux in non-reactive and LPS-induced reactive astrocytes by MTOR, resulting in faster degradation of LCN2, intracellular LCN2 can be degraded by autophagy lysosome pathway, and the activation of autophagy flux accelerates its degradation before secretion. However, some reports suggest that LCN2 can reduce autophagy flux, and the increase of LCN2 in RPE reduces autophagy and activates the process of inflammatory body-iron apoptosis in dry AMD mice. Conclusion: Regulating the autophagy of astrocytes to affect the secretion of LCN2 may be a new strategy in treating central nervous system diseases in the future.

Key words: astrocytes; autophagy; LCN2; ischemic stroke

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Hydroxy-safflower Yellow A Inhibited NLRP3 Expression In Microglia After Ischemic Stroke Through TLR4/NF-κB Signaling Pathway To Reduce Neuroinflammatory Injury

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Objective: NLRP3 expression in microglia after cerebral ischemia and hypoxia (CIH) increases brain injury, but its specific mechanism is not clear. Hydroxysafflower Yellow A (HSYA) has anti-ischemia and anti-inflammatory effects. However, whether it affects the expression of NLRP3 in microglia cells after CIH and its mechanism remains unclear. To investigate the effect of HSYA on NLRP3 expression in microglia after cerebral ischemia injury and its mechanism. Methods: The model of middle cerebral artery occlusion and reperfusion (MCAO/R) was established in male SD rats. BV2 was used to establish a glucose-oxygen-deprivation model in vitro. TTC staining, Western blot, immunofluorescence and ELISA were used to detect the relevant parameters. Results: Compared with the sham operation group, cerebral infarction volume in the MCAO/R group was significantly increased, and was reduced and nerve function improved after HSYA treatment. The expressions of TLR4, NF-κB and NLRP3 in the MCAO/R group were higher than those in sham group, and decreased after HSYA treatment. The levels of IL-1β and TNF-α in the MCAO/R group were higher than those in sham operation group, and HSYA inhibited the expressions. The expressions of TLR4, NF-κB and NLRP3 in the deoxygenated reoxygenated group were significantly higher than those in the control group, and were inhibited after the addition of HSYA. Conclusion: HSYA may inhibit NLRP3 expression in microglia after CIH by regulating TLR4/NF-κB signaling pathways, thereby alleviating brain injury.

Keywords: Hydroxy-safflower Yellow A; NLRP3; Ischemic stroke; TLR4/NF-κB signaling pathway

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Song and Yin are corresponding authors.

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Unveiling the Link: Hyponatremia as a Precursor to Guillain-Barré Syndrome Onset

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Guillain–Barré Syndrome (GBS) is an inflammatory polyradiculoneuropathy which is known to produce syndrome of inappropriate Secretion of Antidiuretic Hormone (SIADH).

In this report, we describe a rare presentation of GBS in a 64-year-old female, where hyponatremia preceded the typical muscle weakness, following a febrile illness a month prior, came to the emergency department with acute weakness and numbness. Remarkably, severe hyponatremia (116 mmol/L) was observed before the onset of GBS symptoms. Neurological examination revealed quadriparesis and sensory neuropathy with a distinct "glove and stocking" distribution. Extensive diagnostic investigations, including imaging and CSF analysis, ruled out alternative pathologies. The patient had a history of hospitalization for hyponatremia ten days before, and despite plasmapheresis and interventions for hyponatremia, no immediate improvement occurred. Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) was identified as the primary cause of hyponatremia, and a therapeutic regimen, involving Tolvaptan and fluid restriction, led to a gradual resolution of hyponatremia over two weeks. Notable neurological improvement was observed upon a follow-up, emphasizing the importance of a comprehensive diagnostic approach in cases where unexplained SIADH precedes GBS, especially in the context of antecedent febrile illness. This rare presentation underscores the need for nuanced evaluation for timely identification and management of GBS.

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A case of suspected tumor-like demyelinating disease with spinal cord involvement

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Background: Tumor-like inflammatory demyelinating disease (TIDD) is a rare primary demyelinating disorder of the central nervous system, also referred to as "demyelinating pseudotumor" , because of its magnetic resonance imaging (MRI) appearance. Bacause it manifests with focal lesions of demyelination larger than 2 cm with a mass effect, it can easily be mistaken, both clinically and radiologically, for brain malignancies, such as gliomas. Although TIDD primarily affects the brain, isolated spinal cord involvement occurs in a small number of instances.

Case presentation: We present a rare case of a 35-year-old man who experienced cervical spine pain, a distal sensory deficit that gradually affected the abdomen and thoracic areas, and urine incontinence. The initial blood samples, CSF analysis, serological and microbiological tests were negative. MRI of cervical and thoracic spine revealed two hyperintense lesions in the spinal cord on T2 - weighted images at C3-C4 and Th11 levels with a slight mass effect. Antibodies against aquaporin-4 and myelin-oligodendrocyte glycoprotein (MOG) were tested further and found to be within normal limits. Based on the neuroradiological criteria, demyelinating process and spinal cord malignancy were included in the differental diagnosis. A high-dose corticosteroid treatment was administered, with a slight clinical improvement. A follow-up MRI after one month revealed a reduction of spinal cord lesions.

Conclusion: A combination of clinical presentation, MRI features, and surgical biopsy is typically used to diagnose localized tumor-like demyelinating lesions. Given the fact that demyelinating processe are usually caused by autoimmune machanisms , corticosteroid therapy may be beneficial under particular circumastances.

Neuroimmunology

Epidemiological, clinical and radiological spectrum of connective tissue disease related neurological disorders — an ambispective observational study

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Background –Neurological manifestations are recognized increasingly in patients with connective tissue disorders (CTD) and account for a considerable proportion of morbidity and mortality associated with this disease.

Aim – To study the epidemiological, clinical-radiological features of connective tissue disease having neurological manifestations and impact of neurological manifestation on Quality Of life of CTD patients.

Materials and Methods – An ambispective study was carried out at a tertiary care center where 66 patients of CTD with neurological manifestations were recruited. Quality of life was assessed with Euro QOL 5D questionnaire .

Results – We recruited 66 patients of CTD having neurological manifestations. In 40 patients(60.6%), neurological manifestation were the presenting feature. Out of 66 patients, 17(25.8%) were of SLE , 14(21.2%) of primary Sjogren syndrome and 10 (15.2%) were of systemic sclerosis. The commonest neurological features were PNS manifestations, found in 35 patients(53%) ,followed by CNS manifestations in 34 patients(51.5%) and psychiatry manifestations in 11 patients(16.7%). CNS manifestation included headache in 30 patients(45.45%) , seizure disorder in 12 (18.2%) , myelopathy in 10 patients(15.2%) and CNS demyelination in 9 patients(13.6%). PNS manifestations were myopathy in 25 (37.9%) patients, followed by polyneuropathy in 10 (15.2%) patients. Most common psychiatry manifestations were Anxiety disorder 11 (16.7%) followed by mood disorder 10(15.2%). Quality of life measured by EURO-QOL 5D score were severely impaired in patients of APLA , Neuro-Behcet and MCTD.

Conclusion-As CTD is an uncommon disorder , this study is important to understand the various neurological manifestations associated with it in Indian population.

Neuroimmunology

Monitoring the intensity of oxidative stress, apoptosis and inflammation in rat brain during lipopolysaccharide-induced endotoxemia: modulatory effect of melatonin

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Introduction:Lipopolysaccharide(LPS) is an integral part of the cell walls of gram-negative bacteria, so it causes damage to many organs (brain, liver, heart). Lipopolysaccharide-induced endotoxemia leads to overproduction of proinflammatory cytokines and reactive oxygen species in brain tissue. Melatonin(MLT) is a neurohormone that is synthesized from tryptophan and exhibits antioxidant effect.

The Aim:The objective of this research was to evaluate the effect of melatonin in the prevention of brain damage caused by Escherichia coli lipopolysaccharide, by analyzing: the level of oxidative stress (by monitoring malondialdehyde-MDA and carbonyl groups-PCC), apoptosis (DNase I and Caspase-3 activity) and parameters inflammation (NF-kB, IL-6 and TNF-α), as well as the effects of melatonin supplementation on the investigated parameters.

Material and Methods:Twenty-eight Wistar Albino rats were randomly divided into four groups (n=7) as follows: Control group, MLT group(50 mg/kg), LPS group(10 mg/kg) and LPS+MLT group.

Results:In the brains of rats treated with LPS, the concentrations of MDA and PCC, as well as the activities of DNase I and Caspase-3 were significantly increased(p0.001), while the administration of MLT led to a decrease in the level of these parameters(p0.01). Application of melatonin to animals with endotoxemia(LPS+MLT group) significantly normalized the high levels of NF-kB, IL-6 and TNF-α in the brain tissue, compared to the LPS group(p0.05).

Conclusion:This study showed a significant therapeutic effect of melatonin, by exhibiting antioxidant, antiapoptotic and anti-inflammatory effects, in brain tissue during endotoxemia. The authors would like to thank the Ministry of Science of the Republic of Serbia(project:451-03-47/2023-01/200113).

Keywords:Lipopolysaccharide, Melatonin, Oxidative stress, Apoptosis, Inflammation, Brain

Neuroimmunology

SEVERE OBSTRUCTIVE SLEEP APNEA IN MUSK-POSITIVE MYASTHENIA GRAVIS: A RARE PRESENTATION OF A RARE DISEASE?

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Background: Myasthenia gravis (MG) is a chronic autoimmune disorder of the neuromuscular junction characterized by fluctuating weakness of the ocular, bulbar, limb and respiratory muscles. MG with MuSK antibodies is more often associated with bulbar involvement and has a higher frequency of respiratory failure and myasthenic crises. Increasing evidence suggests a link between breathing sleep disorders such as obstructive sleep apnea (OSA) and MG.

Case presentation: We present the case of a 58-year-old female admitted to our hospital for isolated, severe, hypoxemic and hypercapnic respiratory failure that required noninvasive ventilation. The patient had been diagnosed with MuSK-positive MG, but denied fatigability, weakness, and other relevant symptoms over the past 20 years, despite not taking any immunosuppressive or anticholinesterase medication. The respiratory failure improved with corticotherapy and pyridostigmine. The sleep polygraphy performed after stabilization showed severe OSA (31 episodes of apnea-hypopnea per hour). A month later, the patient had another exacerbation compatible with myasthenic crisis, this time accompanied by bulbar deficits and limb weakness, that was successfully treated with plasma exchange therapy. Long-term treatment with pyridostigmine, oral methylprednisolone and azathioprine was started, with favorable outcome over the following year, apart from the further worsening of the OSA syndrome.

Conclusion: Our case reveals severe OSA in a normoponderal, middle aged, non-smoking, white female who has MuSK-positive MG with predominant respiratory muscle involvement. OSA is more prevalent among myasthenic patients compared to the general population, being encountered even in those without classical risk factors.

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Systemic Lupus Erythematosus transverse myelitis: a case report and literature review

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Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease which involves multiple organs. A severe complication of SLE is transverse myelitis (TM), affecting around 1-2 % of patients. The most frequent type of TM is longitudinal extensive myelitis (LETM) that includes three or more spinal cord segments on magnetic resonance imaging (MRI). The earlier an agressive treatment is introduced, the better the long-term prognosis of patients with TM is.

Methods

Clinical case report of a patient with a relapse of SLE TM and literature review.

Results

34 years old woman was admitted to the emergency department because of progressing tetraparesis, fever, headache and double vision. It was known from anamnesis that patient was diagnosed with SLE and had thoracic TM in 2015. Paraplegia and anesthesia of lower limbs and sphincter dysfunction remained after the first episode of TM. Examination revealed manifestation of coarse paraparesis of upper limbs. Lymphopenia, low complements, antiphospholipid syndrome, high titer of antibodies to double - stranded DNA and erythrocyte sedimentation rate was noted. Spine MRI showed C1-Th4 LETM. Other causes and possible comorbidity were ruled out. Treatment with pulse steroids and cyclophosphamide was initiated. In the absence of response to treatment intravenous human immunoglobulin and rituximab was continued. As a result, recovering hand strength was observed.

Conclusions

This case report shows the nessesity of multidisciplinary cooperation in diagnosing and treating patients with TM, even though it remains controversial how widely investigation in this patient group should be perfomed.

Neuroimmunology

Factors associated with working status in persons with Neuromyelitis Optica Spectrum Disorders

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Aim: Neuromyelitis Optica Spectrum Disorders (NMOSD) can substantially affect employment and work-related outcomes. The present study aimed to explore factors associated with working status in persons with NMOSD (pwNMOSD). To the best of our knowledge, this is the first investigation dealing with this issue in NMOSD.

Methods: Fifty-four pwNMOSD, who fulfilled the 2015 NMOSD criteria, diagnosed and followed at the Clinic of Neurology, University Clinical Center of Serbia, Belgrade, were included in the cross-sectional study. The data related to the work status of pwNMOSD were collected by questionnaire. Severity of the disease was evaluated by the Expanded Disability Status Scale (EDSS). Presence of depressive symptoms, fatigue and pain were measured by the Beck Depression Inventory (BDI), Fatigue Impact Scale (FIS) and Pain Assessment Questionnaire, respectively.

Results: From the cohort of 54 pwNMOSD enrolled in the study, 42.6% were employed, and of those unemployed, 38.9% attributed their unemployment to the health-related issues. Multivariate logistic regression analysis showed that factors statistically significantly associated with unemployment status in our pwNMOSD were: higher level of disability measured by EDSS (OR=1.95, 95% CI=1.29-2.96, p=0.002), longer duration of the disease (OR=1.15, 95% CI=1.01-1.31, p=0.030), and lower level of education (OR=0.75, 95% CI=0.57-0.98, p=0.048).

Conclusions: In our study, predictors of unemployment in pwNMOSD were level of physical disability, duration of disease, and level of education. Treatment and interventions targeting these factors in pwNMOSD may be effective in helping individuals maintain employment.

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Frequency of comorbidities in patients with neuromyelitis optica spectrum disorder: the Serbian national registry data

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Aim: Neuromyelitis optica spectrum disorder (NMOSD) is associated with various comorbidities, including non-autoimmune and autoimmune conditions. The aim of this study was to investigate the frequency of autoimmune comorbidities in the Serbian NMOSD cohort.

Methods: The data on the demographic and clinical characteristics of NMOSD patients was obtained from the Serbian national NMOSD Registry. All patients fulfilled the 2015 NMOSD criteria. Severity of the disease was evaluated by the Expanded Disability Status Scale (EDSS). The frequency of comorbidities was compared between anti-aquaporin 4 antibody (AQP4-IgG) seropositive and seronegative patients.

Results: A total of 141 NMOSD patients were enrolled. The ratio of women to men was

4.2:1. The median age at onset was 40 years (range 4–73), and mean duration of the disease was 8.2+/-7.4 years. The median EDSS score at the last follow-up visit was 4.0 (range 0.0-10.0). Seventy-two (51.1%) patients reported at least one comorbidity. Fifty-one patients (36.2%) had autoimmune comorbidities: the most common disorders were autoimmune thyroiditis (N = 17; 11.1%), Sjogren's disease (N = 13; 9.2%), systemic lupus erythematosus (N = 7; 5.0%), and myasthenia gravis (N = 5; 3.5%). A significantly higher frequency of autoimmune comorbidities was observed in the AQP4-IgG positive patients (p=0.009). Autoimmune comorbidities were significantly associated with AQP4-IgG positivity (OR=3.2, 95% CI=1.3-7.5, p=0.009).

Conclusion: Our results show that half of the patients had comorbidities, suggesting screening for comorbidity as part of NMOSD care.

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Acute demyelinating encephalomyelitis (ADEM) in adults: postinfectious encephalomyelitis or something else?

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Introduction: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a rare, antibody-mediated inflammatory demyelinating disorder of the central nervous system presented by various phenotypes that may vary with age, such that ADEM-like lesions are more likely to affect children, whereas optic neuritis and myelitis tend to be more common among adults.
Case presentation: We report the case of a 28 years old female presented to the Emergency Department with a 3-day history of fever, leg weakness and numbness, imbalance, gait disturbances and difficulty urinating. The neurological examination revealed conductive hypoesthesia from Th4-Th5 level, mild paraparesis with muscle hypotonia and hyperreflexia, Babinski reflex, severe ataxia, positive meningeal signs, and urinary retention. Contrast-enhanced MRI of the brain and spinal cord revealed transverse myelitis with extensive spinal cord involvement from C3 to the conus medullaris, and cerebral lesions with demyelinating appearance in the optic thalamus, parietal, periaqueductal, medulla oblongata, pons, area postrema. Cerebrospinal fluid (CSF) analysis demonstrated lymphocytic pleocytosis (160 cells, 98% lymphocytes, protein 0.99 g/L). PCR tests for EBV, CMV, HSV1, HSV2, and enterovirus in CSF were negative. Oligoclonal bands were negative. Immunological screening revealed positive serum anti-MOG and negative anti-aquaporin 4 antibodies. The patient received intravenous Methylprednisolone 1 g/day for 5 days and progressive improvement was noticed. After discharge she continued with Prednisolone 1 mg/kg/day, with complete resolution of symptoms after one month.
Conclusion: MOGAD is a rare demyelinating pathology and is rarely presented with ADEM in adults. In this case it was important to do a differential diagnosis with NMOSD (neuromyelitis optica spectrum disorders) and MS (multiple sclerosis) in order to establish the treatment as well as the prognosis that seems to be more favorable in case of MOGAD.

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Isolated neurosarcoidosis presenting as an extensive form of encephalomyelitis

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Introduction

Sarcoidosis is a systemic inflammatory disease affecting multiple organs. Neurosarcoidosis, especially as an initial and isolated presentation, is rare, diagnostically challenging and potentially life-threatening when the lesions are extended cerebromedullary, as reported in this case.

Methods

A 46-year-old woman presented in our clinic with paraparesis, speech impairment, action tremor and seizures, developed progressively over 3 months. The initial magnetic resonance imaging (MRI) examination, humoral tests and lumbar puncture pointed to an ill-defined inflammatory disease of the central nervous system. Further workup included full-body positron emission tomography and computed tomography and brain biopsy.

Results

Cerebral and medullary MRI revealed extensive white matter lesions in the left cerebral hemisphere with mass effect and a longitudinal lesion covering 11 vertebral segments with heterogeneous contrast enhancement. Cerebrospinal fluid (CSF) examination revealed 104 cells/microliter (99% mononuclear), elevated proteins, moderately low glucose and the absence of oligoclonal bands or microbial agents, including Mycobacterium tuberculosis. Systemic autoimmunity screening, antiMOG and antiAQP antibodies, onconeural antibodies, CSF GFAP antibodies, tumoral markers, serum angiotensin-converting enzyme and interleukin2 receptor tested negative. No lesions were found in other organs. The brain biopsy showed no evidence of lymphoma, vasculitis or primary angiitis of the central nervous system, but was highly suggestive of neurosarcoidosis. Evolution was promptly favourable under corticosteroids.

Conclusion

Isolated neurosarcoidosis is uncommon in clinical practice and can be difficult to diagnose. In this case, despite the initial severity, the disease was monophasic and most symptoms remitted under corticotherapy. Overtime management required immunosuppressive therapy.

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Treatment dilemmas of neuro-tuberculosis: Paradoxical response

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Introduction

Neuro-tuberculosis, particularly meningeal tuberculosis, poses a persistent global health challenge with cases demonstrating clinical dilemmas. This study addresses the complex issue of treatment escalation in clinically asymptomatic patients with persistent cerebral-spinal fluid (CSF) reactivity and worsening imaging findings.

Case report

A 24-year-old university girl initially treated for Kikuchi disease with immunomodulatory therapy was later diagnosed with smear-positive pulmonary tuberculosis after two months. Despite initiating CAT1 anti-TB treatment, she experienced recurrent fever, meningitic symptoms, and new focal neurological signs and was ultimately diagnosed with meningeal TB. Complications included multiple tuberculomas and cerebral venous sinus thrombosis, necessitating the escalation of glucocorticoid treatment and a switch to individualized anti-tuberculosis drugs.

After ten months of treatment, despite clinical wellness, the patient exhibited persistently reactive CSF and a large tuberculoma mimicking an abscess. In a multidisciplinary decision-making process, brain biopsy before second-line immunotherapy with thalidomide or infliximab was considered, but the patient declined. Tailoring off immunotherapy based on clinical resolution led to discontinuation of anti-TB treatment after 18 months, resulting in gradual lesion resolution. The patient presently functions well without disability or cognitive impairment.

Conclusion

This case highlights the challenge of managing paradoxical response in central nervous system tuberculosis. It underscores the need for further studies to determine the optimal timing and extent of treatment in such cases.

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The great pain of small fiber neuropathy: a case of immune-mediated small fiber neuropathy

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Introduction: Small fiber neuropathy (SFN) is the result of somatosensory and autonomic A-delta and C fibers injury. Although most of the cases are idiopathic, SFN may also occur due to metabolic, immune-mediated, infectious, hereditary, or toxic etiologies. In idiopathic SFN, the fibers are usually involved in a length-dependent manner, whereas a non-length-dependent distribution would rather suggest a paraneoplastic or immune-mediated pathology.
Methods: A 31-year-old woman, diagnosed with mixed connective tissue disease one year prior and undergoing combination therapy with corticosteroids and mycophenolate mofetil, was admitted to our clinic for diffuse burning pain, tingling and numbness, primarily in the palms and soles. She also complained of recent gastrointestinal disturbances, orthostatic dizziness and palpitations, fatigue, and general malaise. Neurological examination revealed mild proximal tetraparesis and normal sensory examination and tendon reflexes.
Results: An extensive work-up for metabolic (diabetes, vitamin B12 deficiency, hypothyroidism), infectious (HIV, hepatitis C, Lyme disease), hereditary and immune-mediated diseases was performed, revealing positive anti-dsDNA and anti-U1RNP antibodies. Apart from minimal myopathic changes, the electroneuromyography results were unremarkable. Subsequently, SUDOSCAN revealed prominent sudomotor dysfunction highly suggestive of small fiber neuropathy, most probably secondary to mixed connective tissue disease. The patient received intravenous immunoglobulin (2g/kg), with marked symptomatic improvement within days.
Conclusions: Small fiber neuropathy should be suspected in patients presenting with positive sensory phenomena and autonomic dysfunction who have normal nerve conduction studies. Furthermore, patients should be thoroughly screened for reversible causes of small fiber neuropathy and benefit from appropriate etiological and symptomatic treatment.

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Immune reconstitution for the treatment of myasthenia gravis- the case for cladribine

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Autoimmune myasthenia gravis (MG) is a neuromuscular junction (NMJ) disorder marked clinically by fatigable muscle weakness and serologically by the presence of autoantibodies. Autoantibodies against acetylcholine receptors (AChRs), muscle-specific kinase (MuSK), and lipoprotein-related protein 4 (LPR4) have been proven to be pathogenic.

Pathological B- and T-cell subtypes are implicated, including memory B and plasma cells, with concomitant reduced regulatory B(reg) and Treg cells activity. This implicates that acting selectively on pathogenic T and B cells might be important strategy to suppress MG activity in order to prevent the downstream damage in the neuromuscular junction.

Immune reconstitution IIR) has become attractive approach to control different types of autoimmune diseases with multiple sclerosis as the best studied condition. Cladribine is one of the prototype drugs to induce IR with long lasting therapeutic effects (Giovannoni and Mathews, 2022).

It was tempting to use CLAD in MG patients to test this hypothesis. Indeed, in the first pilot clinical study we demonstrated the efficacy together with appreciable safety profile of cladribine (Rejdak et al., 2018). Initial findings encouraged us to organize randomized, double blind placebo controlled trial currently being conducted in 9 clinical centers in Poland. In this presentation the study rationale and design of ongoing trial (EudraCT Number: 2020-005762-34) will be discussed.

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E-Poster

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Focused ultrasound thalamotomy for tremor due to chronic inflammatory demyelinating polyneuropathy

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Background: Unilateral MRI-guided focused ultrasound (FUS) ablation has established efficacy in tremor relief.

Objective: To describe a patient that underwent FUS thalamotomy for tremor due to chronic inflammatory demyelinating polyneuropathy (CIDP).

Methods: Tremor was assessed in the treated hemibody using the Clinical Rating Scale for Tremor (hemi-CRST).

Results: A 63-year-old male suffered from severe disabling tremor for 8 years due to CIDP. He had marked sensorimotor impairment. He was offered FUS treatment. Immediately following treatment there was improvement in tremor, from a baseline hemi-CRST score of 14 to a score of 7. At 1 month tremor had partially returned with a hemi-CRST score of 11. At 6 months tremor was almost as severe as before treatment with the hemi-CRST score rising to 13 and remaining unchanged at 1 year. The patient reported subjective gait unsteadiness and lip parasthesias that resolved within 1 month.

Conclusions: To the best of our knowledge this is the first report of a single patient who underwent FUS thalamotomy for tremor due to CIDP. Our experience does not support the use of this technology in this condition.