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PROCEEDINGS

ORAL PRESENTATIONS – ABSTRACTS
(in alphabetical order of the first author)

The importance of intrasurgical TCD monitoring – new horizons in research

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Introduction. Transcatheter aortic valve implantation (TAVI) is a modern minimally invasive therapeutic alternative for the treatment of tight aortic stenoses.

Despite the obvious advantages associated with TAVI (percutaneous approach, avoidance of laborious surgery, much simplified postoperative care for patients treated by classical surgical methods), neurological complications are described in the literature, such as ischemic stroke, transient ischemic attack, or silent ischemic brain damage.

Long-term transcranial Doppler monitoring to detect abnormal embolic signals is a relatively new concept, first appeared in 2004, which allows real-time detection of possible spontaneous intracerebral emboli during surgery.

Methods. This work presents the results of the analysis of data collected from TCD records of five patients who received treatment with TAVI. Patients were monitored by peri- and post-procedural transcranial Doppler to determine the most embolic surgery times and the clinical and paraclinical factors that influence or are associated with an increased number of cerebral emboli.

Results. Spontaneous microembolisms have been observed during all surgery times. The highest incidence of spontaneous microembolism occurred during prosthesis expansion and cardiac resynchronization by pacing. Spontaneous and distant microembolisms were observed at the end of the surgery act, but with a different sound and appearance than the emboli intrasurgically detected.

Conclusions. The present study provides additional information on intraoperative brain damage and may allow the development of strategies to prevent and

reduce mortality and morbidity related to invasive interventional procedures.

Sleep and stroke: „Guilty by association“

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Research of the last 20 years has shown that sleep-wake disorders (SWD) and stroke are frequently associated and that their relationship may be causal and bidirectional.

On the one hand, SWD such as sleep disordered breathing (SDB), long sleep duration, and sleepiness/hypersomnia represent an independent risk factor for stroke. On the other hand, SDB, sleepiness/hypersomnia, insomnia, and restless legs syndrome (RLS) can appear “de novo” after stroke. Furthermore, SDB (and possibly also other SWD) appear to negatively affect stroke outcome and risk of recurrence. Finally, experimental and clinical studies give increasing support to the hypothesis that sleep (and its disturbances) modulates the acute ischemic cascade and neuroplasticity processes underlying stroke recovery.

More data, including interventional studies, are needed to assess the impact that a systematic management of SWD may have on stroke prevention and post-stroke outcome. While still incomplete, the evidence of a significant link between sleep, SWD and stroke is strong to call for more awareness and interdisciplinary collaborations between sleep, circadian and stroke clinicians and scientists.

The behavior of different subtypes of cultured T helper cells for precision treatment in multiple sclerosis patients

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Multiple sclerosis (MS) is a chronic and heterogeneous neuroinflammatory and neurodegenerative disease of the brain and spinal cord. In the pathophysiology of MS, T cells are involved early but also in the long-term host immune response. Substantial evidence implicating Th17 cells, as well as IFN- γ IL-17 double-positive Th17.1 cells, in MS pathogenesis has accrued.

The aim of our study was to isolate, culture and analyze subsets of human T lymphocytes harvested from naïve patients diagnosed with relapsing MS (RMS), assessment of a higher direct resolutive peripheral secretor profile of cells and, to determine the phenotypic cellular changes in these cells together with the characterization of the cytokines secreted in the presence of a certain DMT.

Material and methods. Phenotypic profile assessment of Th cells was determined from 32 RRMS naïve patients newly diagnosed and 12 HC with cell surface markers. Phenotyping Th cells: 1. use of cell surface markers (CD183/Th1, CD 161/Th17, CD196/Th17.1); 2. intracellular cytokine staining (CD3+ CD4+ T cells with an IFN- γ + IL-17-, IFN- γ - IL-17+, IFN- γ +IL-17+). The next step was to determine the modification of secretory profile of the cells in the presence of cladribine.

Results. The lymphocyte purity after PBMC isolation from whole blood had a median of 84,05%. Pearson correlations between the determined levels of above cytokines secreted by isolated cells: in Th17.1 cells direct correlations IL-17/IFN γ (0.001) found also after 7 respectively 14 day of Cladribine exposure (0.004, 0.002).

Conclusions. The Th17.1 subpopulations of Th lymphocytes is very rare in the periphery of MS patients but maintains its' secretory profile after 7/14 days of cladribine exposure. Using intracellular cytokines (IFN- γ and IL-17) allowed the selection of more cells than the rest of cell phenotyping methods.

The pathogenic effect of CCR6+ receptor in multiple sclerosis – preliminary results of an experimental model of lymphocyte isolation from multiple sclerosis patients

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Introduction. The curtain of uncertainty rises slowly above multiple sclerosis (MS) pathophysiology. The pro-inflammatory effect of T lymphocytes is actively mediated by the blood-brain-barrier and is subjected to the effect of various chemoattractant cytokines. CCR6 enhances the proinflammatory Th17 cells breach through the choroid plexus. In MS, activated Th17 lymphocytes therefore overexpress the CCR6 chemokine receptor. Cladribine (CLD) is a purine nucleoside analogue that disrupts the metabolic cycle of the lymphocytes.

Material and methods. Venous blood samples were harvested from newly diagnosed RR-MS patients and healthy controls (HC). The peripheral blood mononuclear cells were isolated, activated, cultivated and either exposed to CLD (CLD+) or remained unexposed (CLD-). They were ultimately assessed at baseline, 7 and 14 days (moment_0, 7, 14). The viability and proliferation index of the Th17 subpopulations were thoroughly assessed. Multiparametric flow cytometry analysis was performed using BD FACS ARIA III in order to identify the phenotypic profile of Th17 cells (Th17/Th17.1) and the CCR6 expression in all the stages of the experiment.

Results. The cell viability and proliferation were optimal throughout all the stages of the experiment ($p < 0.0001$).

Significant results were found in MS groups between Th17 moment_0 and CLD-7/14days and Th17.1 moment_0 and CLD-7/14days ($p < 0.0001$) favouring higher baseline CCR6 levels. We report a statistically significant result when comparing MS Th17.1 CLD-14days vs Th17.1 CLD+14 days ($p = 0.040$), favouring the latter, with higher CCR6 levels. When comparing HC vs MS Th17.1 CCR6 levels at both 7 and 14 CLD-, we found significant results for CCR6 at both 7 and 14 days ($p = 0.011$, $p = 0.005$), favouring higher levels for HC. We found no statistically significant results when comparing MS or HC Th17 (CLD +/- 7 or 14 days) populations.

Conclusions. The complexity of chemokine expression and lymphocyte interaction is still in the early stages of research. While CLD's mechanism of action is centred on B lymphocytes, studying the immune response from a Th17 perspective is needed. The Th17.1 HC CCR6-positive cells had a higher survivability rate in cultures. Our study indicates that perhaps under the effect of CLD, Th17.1 CCR6 cells tend to proliferate, but the evaluation of CLD cell cultures reveals a mixed response of CCR6 from a Th17/Th17.1 perspective.

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Innate and adaptive immunity for clinicians – principles

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The autoinflammatory syndromes represent a heterogeneous group of clinical syndromes produced by a dysfunction of innate immunity. They are caused by mutations of genes which control the regulatory mechanisms of nonspecific inflammation. Although patients with clinical manifestations suggestive for an autoinflammatory disease have been first described centuries ago, their genetic cause was identified only in 1997 when the link between the MEFV gene and Mediterranean fever was clearly proven. This gene was the first among many others discovered thereafter which led to development of the concept of autoinflammation in 1999. This concept is characterized by episodes of fever or systemic inflammation involving different organs or systems without an underlying source of infection or other determined cause. The innate immunity is the first to intervene as a non-specific defence mechanism in contrast with adaptive immunity which is specific.

While the presence of antibodies and activated B or T lymphocytes is characteristic for autoimmune diseases, these markers are not found in the vast majority of autoinflammatory syndromes. The cells involved in innate immunity are the monocytes, the macrophages and the dendritic and NK cells.

Nowadays there is a consensus regarding the existence of a broad spectrum of dysfunctions of the immune system including pure monogenic autoinflammatory diseases in which the innate immunity is altered, pure autoimmune diseases in which the adaptive im-

munity is deficient and mixed diseases in which both types of mechanisms coexist.

The concept of autoinflammatory diseases was constantly revised during the past years, today being defined as clinical alterations characterized by an abnormal level of inflammation determined by a dysfunction of innate immunity.

Autoimmune encephalitis: Diagnosis, treatment and prognosis – an epilepsy monitoring unit perspective

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Introduction. Autoimmune encephalitis (AE) represents an umbrella term for an expanding group of potential reversible neurological diseases with different underlying pathophysiological mechanisms. Its manifestations can vary greatly, making its recognition troublesome. Furthermore, AE is an increasingly recognized cause of seizures and epilepsy.

The aim of this presentation is to pinpoint the current aspects of diagnosis and management of patients with AE and the role of the epilepsy monitoring unit (EMU) in this context.

Methods. We present a case series of patients who were diagnosed with AE and managed in our Neurology Department.

Results. The patients' initial presentation was predominantly psychiatric. They were extensively assessed mostly for infectious encephalitis, acute psychosis and drug abuse. Consequently, they were referred to psychiatric or toxicology settings only after failure of specific treatment further testing was carried out. Brain imaging, blood and CSF work-up eventually emphasized an encephalitic process. As most of the patients exhibited epileptic fits, part of the integrative diagnostic work-up included videoEEG monitoring. Non-specific EEG alterations suggestive for an encephalitic process were found. Antibody panel and body imaging screening pinpointed autoantibodies indicative for either a sole autoimmune process or a paraneoplastic one. The patients were diagnosed with AE and were treated using immunomodulatory drugs and/or plasmapheresis with subsequent improvement.

Conclusions. This series highlights the importance of considering AE as potential cause of seizures and the

role of the EMU in its diagnosis and management. Abrupt-onset psychiatric manifestations and, as in our series, subtle cognitive impairment might account for underdiagnosing AE.

Patent foramen ovale – a cause for acute ischemic stroke in the young adult

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Acute ischemic stroke in young adults has long been considered an uncommon condition, however, in the last decades we have witnessed an increase in its incidence. Taking into consideration also the high economic impact of this association, we must realize that we are facing a major health problem. There is a need of improving our diagnostic methods in order to better understand the magnitude of stroke in the young adults and to help us prevent it.

Paradoxical embolism through Patent foramen ovale (PFO) is considered one of the largely recognized etiologies for ischemic stroke. Approximately 1 of 4 persons still has this intracardiac shunt during adult life and that is the reason why there was a requirement for a more accessible method for its detection. Contrast-enhanced transcranial Doppler (c-TCD) has proven its value in effectively diagnosing the presence of right-to-left cardiac shunting.

Throughout 2019, patients, mostly young, were referred to our neurosonology laboratory after suffering a cerebral ischemic event without having an identified cause, or if there were asymptomatic hyperintense T2/FLAIR lesions identified on cerebral magnetic resonance imaging (MRI). C-TCD was performed with intravenous infusion of microbubbles and the number of emboli signals was recorded. The decision for medical treatment of PFO percutaneous closure was made by a multidisciplinary team and follow-up with c-TCD was set for 6 months after the intervention.

C-TCD is a non-invasive valuable tool in the diagnosis of PFO, offering a high accuracy at a low cost and at an increased comfort for the patient.

Left left me? Alien hand syndrome – Case report

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Introduction. Alien hand syndrome (AHS) is a common neurological disorder characterized by involuntary and autonomous movements. The cause of AHS varies from tumor, aneurysm to trauma, neurosurgical intervention and stroke.

Case presentation. We illustrate a case of a 68 years old patient with multiple vascular risk factor: diabetes mellitus type 2 insulin dependent, grade II hypertension, chronic atrial fibrillation and hyperlipoproteinemia type IIb. The patient presented to the hospital with symptoms of a left-hand paresthesia and confusional state.

Management and results. Magnetic resonance imaging of the brain showed a subacute ischaemic cerebral infarction in the splenium of the right corpus callosum, the precuneus of the right cingulate gyrus, with the psychological exam confirming the “alien hand syndrome”.

Conclusions. AHS remains a difficult diagnosis to make and manage given its low prevalence and requires more research and a multidisciplinary approach.

Autoimmune encephalitis in routine clinical practice

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Autoimmune encephalitis (AE) encompasses a wide spectrum of diseases, revolutionized after the discovery of NMDAR antibodies in 2007, with recent data suggesting a prevalence close to that of infectious encephalitis. We highlight the spectrum of various phenotypes of AE and the diagnostic challenges encountered in routine clinical practice.

Stiff-person syndrome and progressive encephalomyelitis with rigidity and myoclonus are in a spectrum that starts with increased muscle tone, most often due to GAD antibodies, while glycine receptor antibodies move this spectrum towards CNS features. Subacute cerebellar degeneration is one of the most common AE and is often paraneoplastic in nature.

Antibodies against VGKC are still routinely tested despite recommendations from experts to replace this with exclusive LGI1/CASPR2 testing. Their phenotypical spectrum includes both peripheral and central nervous system features in the case of CASPR2 antibodies, while LGI1-encephalitis is limited to CNS symptoms, presenting most commonly as a limbic encephalitis. The latter can be caused by a large number of antibodies and can be a part of various phenotypes, most notable of which is NMDAR-encephalitis.

Diagnosis of AE most often proves to be very difficult in routine clinical practice, where multiple questions arise: What clinical features should we pay attention to? Which antibodies to test, when to test them, by what method and what does the result mean? What other paraclinical work-up should be done? When to start treatment? We try to address some of these issues and answer with our own experience.

Sleep disturbances in patients with autoimmune encephalitis

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Autoimmune encephalitis (AE) is increasingly recognized as an important cause of subacute cognitive decline, seizures, and encephalopathy, with rising prevalence and a high potential for treatment responsiveness. As the understanding of the different clinical phenotypes increased, so too did the appreciation of the neurological impairments that can persist in some of the AE patients.

Sleep disturbances are detected in a majority of patients systematically screened for sleep complaints and may even be the presenting symptom in some patients with AE. It is yet unknown if their presence or persistence is linked to adverse neurological outcomes.

Sleep disturbances in AE can range from REM sleep behavior disorder in patients with antibodies against VGKC (now classified as antibodies against LGI1 or CASPR2), hypersomnia and fragmented sleep in the anti NMDA antibody syndrome, insomnia in patients with Morvan syndrome or sleep disordered breathing in patients with IgLON5 antibodies.

There is a clear need to define the prevalence and subtypes of sleep disturbances in AE patients, and to clarify the relationship between specific autoantibodies, sleep symptomatology, and outcomes.

We retrospectively reviewed the data of 15 patients diagnosed with AE in our clinic between 2016 and 2020. All of the patients underwent CSF examination, MRI scanning, standard EEG recording and an extended autoantibody screening upon admission. Sleep questionnaires, assessing daytime sleepiness, sleep disordered breathing, parasomnias or the presence and restlesslegssyndrome, were administered. Polysomnography was performed in patients with sleep complaints and/or a clinical indication.

Hypersomnias of central origin

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Among sleep disorders, central hypersomnias require special attention due to their severity and negative impact on patients' quality of life. According to the International Classification of Sleep Disorders, Third Edition (ICSD-3), the entities considered to be part of central hypersomnias include narcolepsy type 1 and narcolepsy type 2, idiopathic hypersomnia, Kleine-Levin syndrome and other symptomatic hypersomnias (e.g. due to a medical disorder or due to medication/substance, hypersomnia associated with a psychiatric disorder). The key element for all these disorders is the presence of hypersomnolence. For a correct diagnosis, careful clinical history, sleep diaries, objective investigations of sleep (actigraphy, polysomnography, multiple sleep latency test) or even genetic tests or cerebrospinal fluid examination are necessary. Symptomatic treatment and behavioral modifications were shown to alleviate hypersomnolence in central hypersomnias, and there are also several stimulants known to have beneficial effects, especially in narcolepsy.

This lecture will focus on discussing the clinical presentation, pathogenesis, diagnostic criteria, differential diagnosis and management of main hypersomnias of central origin.

Restless legs syndrome

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Restless legs syndrome (RLS) or Willis-Ekbom disease is characterized by uncomfortable sensations in the lower limbs associated with an irresistible urge to move the legs. These sensations occur during rest, generally in the evening or night, are partially or totally relieved by movement, and are not better explained by any other medical condition. Since the first description of RLS by Karl-Axel Ekbom in 1945, there were established several criteria for RLS diagnosis by the International Restless Legs Syndrome Study Group (IRLSSG) – in 1995 and 2003, while the latest revision was published in 2014.

Different epidemiological studies have shown that the RLS prevalence in the general population is estimated to be 5-10%. Another condition often associated with RLS is represented by periodic limb movements of sleep (PLMS), which are repetitive involuntary movements of the legs occurring during sleep. Both RLS and PLMS are associated with important sleep impairments.

The pathophysiology of RLS is not completely understood. There are different factors involved, like brain iron deficiency (especially in the substantia nigra and putamen), genetic factors, or abnormalities in regulation of the dopaminergic system. Secondary RLS occurs in different diseases and conditions like uremia, celiac disease, diabetes mellitus, rheumatoid arthritis, pregnancy.

Augmentation is a phenomenon characterized by exacerbation and earlier onset of the symptoms during the day, and it may be induced by the medication intended to alleviate RLS.

Treatment options include non-pharmacologic and pharmacological strategies (dopamine agonists, iron supplementation, $\alpha 2 \delta$ ligands, opioids).

The presentation will focus on up-to-date information regarding diagnosis, pathophysiology, investigations, differential diagnosis and management of RLS in general population.

Rasmussen encephalitis – diagnostic and treatment features

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Rasmussen encephalitis is a rare neurological disorder, with an inflammatory and/or autoimmune pathophysiology, presenting with focal epileptic seizures and/or progressive unilateral neurologic deficits, and a gradually increasing, asymmetrical, cerebral atrophy.

With specific biomarkers lacking, diagnosis is currently made based on the Bien criteria and by excluding other disorders which could mimic the clinical or imaging picture.

Therapy is based on medical management of epileptic seizures, with a potentially added benefit from immune therapies and immunosuppressants; surgical treatment is probably the most effective in controlling refractory seizures, with the caveat of potentially disabling sequelae.

We will review some of the more important data related to the clinical presentation, pathophysiology, diagnosis, differential diagnosis, and therapy. Furthermore, we will present a case series of Rasmussen encephalitis patients from the Neurology Department of the University Emergency Hospital of Bucharest, with an emphasis on clinical features and treatment choices.

Neurologic symptomatology onset of mixed cryoglobulinemia in occult C virus infection

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Introduction. The diagnosis of mixed cryoglobulinemia is challenging because of the varied spectrum of manifestations. It is characterized clinically by a triad (purpura, arthralgias and Raynaud’s phenomenon) and involvement of other organs. There is a strong association between hepatitis C viral infection and mixed cryoglobulinemia.

Methods. A series of 3 cases – A 74-year-old patient with a history of rheumatoid arthritis presented for severe motor deficiency with an apparently acute onset.

The clinical examination revealed asymmetric tetraparesis and sensitivity disorder with a clinical picture suggestive of mononeuritis multiplex. Another 63-year-old patient known with cardiac disease history presented for horizontal diplopia with sudden onset. Clinically: right abducens nerve palsy, tactile bilateral lower limb hypoesthesia and purpura. The last patient, aged 60, with no pathological history, presents for oblique diplopia and palpebral ptosis in the right eye. Clinical examination: right oculomotor nerve palsy, without parasympathetic involvement.

Results. The clinical and electrophysiological context, demonstrate peripheral nervous system involvement. Hepatitis C viral infection was detected and cryoglobulin testing was intensely positive. Other causes of mononeuritis multiplex and mononeuritis of the cranial nerves were excluded through imaging and laboratory studies (compressive lesions, infectious causes, vascular, metabolic and other autoimmune systemic vasculitis).

Conclusions. Although the association between cryoglobulinemia and peripheral neuropathy is known in the literature, serum cryoglobulin levels are not routinely dosed, reason why this pathology being frequently underdiagnosed.

Pitfalls in the diagnosis and management of convexity subarachnoid hemorrhage

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Convexity or cortical subarachnoid hemorrhage (cSAH) is increasingly recognised as a separate clinical entity in the spectrum of cerebro-vascular diseases. It is characterised by the presence of blood limited to the subarachnoid space overlying the hemispheric convexity, without extension into the basal cisterns, ventricular system or brain tissue. Although it is well known that approximately 15-20% of subarachnoid hemorrhages (SAH) are nonaneurysmal, cSAH is emerging as a distinct category, with an estimated share of 5-6% of the total SAH. Over the past 10 years there have been several studies that tried to clarify first and foremost the etiology,

as well as the clinical course, optimal treatment and prognostic of cSAH. Unfortunately, given the low incidence, the data are sparse. cSAH constitutes a challenge not only because of the clinical presentation that is diverse and often atypical for a "classic" SAH, but also because of the multitude of possible etiologies which entail different management approaches as well as different prognosis. This presentation is based on a clinical case and aims to bring the current data on the pitfalls in diagnosing and managing this extremely interesting pathology up to date.

Sleep disturbance and epilepsy

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Sleep disturbance is a common occurrence in epilepsy. It could be related to seizures but also to antiepileptic treatment. Sleep fragmentation is a common finding with variable causes in people with epilepsy. A polysomnography could show other sleep related comorbidities, the most common being sleep apnea. Neurocognitive deficits especially for memory are known to be prevalent in people with epilepsy. The role of poor sleep and impact on memory processing and consolidation is well recognized highlighting the importance of exploring sleep in cognitively impaired patients independent of seizure control.

Epileptic events are believed to be activated by sleep and particularly nonrapid eye movement (NREM) sleep. Reciprocally, epilepsy alters the sleep-waking cycle and sleep architecture. The sleep-epilepsy relationship differs according to the type of epilepsy or epileptic syndrome. Although sleep epilepsies are not considered to be entities in their own right, some epilepsies are activated by sleep, and in others sleep deprivation leads to sensitization to seizures.

The association of blood pressure values with ischemic stroke prognosis

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Introduction. Ischemic stroke is the most frequent neurological disease in adults and the second cause for

mortality and morbidity after cardiovascular disease. High blood pressure is the most important modifiable vascular risk factor for stroke. The aim of this study is to analyse the influence of blood pressure values on the prognosis of patients with ischemic stroke.

Materials and methods. We conducted a retrospective study that includes 344 patients admitted in the Neurology department of Elias University Emergency Hospital from February to August 2020, with the diagnosis of ischemic stroke. We collected data from the medical charts. We analysed blood pressure values at admission, at 24 hours and 48 hours after admission and at discharge. The patients' evolution was established by NIHSS score progression, complications and length of hospital stay. We carried a statistical analysis of the data collected.

Results. We observed that the patients who had a negative outcome had higher mean blood pressure values and a wider variation of blood pressure values. We found a significant association between systolic blood pressure at 48 hours after admission and the neurological evolution, as the mean systolic blood pressure values in the group with a negative outcome were with 15.08% higher than the mean systolic blood pressure values in the group with a positive outcome ($p = 0.002$).

Conclusions. Blood pressure values influence the prognosis of ischemic stroke; our results show that systolic blood pressure at 48 hours after admission is statistically significant for the prognosis of ischemic stroke.

Keywords: stroke, blood pressure, outcome

The influence of neurocognitive dysfunction on pain in patients with Parkinson's disease

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Introduction. Parkinson's disease is the second most frequent neurodegenerative disorder in the general population, after Alzheimer's disease. Neurocognitive impairment is present from the onset, although it may initially remain undetectable using commonly used neurocognitive tests. When evaluating non-motor symptoms, pain, together with fatigability, are very frequent. The purpose of this study is to determine the influence of the cognitive dysfunction on pain related symptoms.

Materials and methods. We conducted a retrospective study on 134 patients with Parkinson's disease

admitted in the Neurology Department of Elias University Emergency Hospital from July 2014 to July 2019. We diagnosed the presence of neurocognitive disorder by MMSE score. Pain was evaluated using Parkinson's well-being map. For motor symptoms evaluation, we used UPDRS III. We performed a statistical analysis of the data collected.

Results. Out of the 51 patients with neurocognitive dysfunction, 45.1% had mild neurocognitive disorder, 35.3% had a moderate form of major neurocognitive disorder and 19.6% had a severe form of major neurocognitive disorder. Interestingly, 88% of the patients with neurocognitive disorder experienced painful events. We found a statistically significant correlation between the presence and intensity of painful episodes and the MMSE score ($p = 0.016$) and also an association with motor dysfunction.

Conclusions. The presence and the intensity of pain related symptoms is correlated with the presence and the severity of cognitive dysfunction in patients with Parkinson's disease.

Keywords: Parkinson's disease, cognitive disorder, pain

Sleep study in the diagnosis of REM sleep behavior disorder

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Background. REM sleep behavior disorder (RBD) is a REM parasomnia in which patients act out their dreams.

Patients and method. We included patients that underwent sleep studies in the Epilepsy and Sleep Unit at the University Emergency Hospital Bucharest. Polysomnographic recordings were performed using a particular, extended EEG montage, 10-20 system; additionally, we monitored limb movements using four EMG motion sensors placed on each limb, electrooculogram to record eye movements and determine REM stage, chin EMG sensor to detect muscle tonus, thoracic belt, respiratory airflow and pulse oximetry to monitor the respiratory effort and EKG.

Results. Between 2014 and 2020 we explored over 200 patients using polysomnography and we were able to identify 30 patients with RBD. Most often patients presented brisk upper limb movements, kicking using the lower limbs, talk or smiled during the episodes. If

awakened, they could correlate their movements with their dreams. These patients were diagnosed with multiple system atrophy, parkinson disease or RBD was idiopathic meaning that patients did not yet present with additional symptoms of a neurodegenerative disorder.

Conclusion. Our experience is concordant with up to date sleep studies in terms of diagnosis and evolution of RBD.

Sleep disorder and headache – how do we approach?

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Introduction. Sleep disorders and headache are frequent complaints in clinical practice and is not unusual to coexist, whatever is dominant. They share anatomical pathways, physiology and treatment in some cases, so is reasonable to approach them together

Objectives. To analyze the possible etiologies and the necessary steps to get them, underlying mechanisms and therapeutical options

Materials and methods. among patients addressed to sleep lab for sleep disorders we indentified those with headache also; we used headache and sleep diaries and severity scales, sleep, anxiety, depression and QoL questionnaires and standard neurological evaluation (clinical, EEG, vascular ultrasonography and brain MR imaging); in selected cases we performed standard polysomnography

Results. We identified 54 patients patients with sleep disorders (insomnia, daytime sleepiness, circadian rhythm slepp disorders) and headache. In 22 (40,7%) cases we found sleep disorders and other 13 (24%) undiagnosed primary headaches as main cause for presentation. The other cases 19(35,18%) had various (psychiatric, vascular, infectious) origins

Conclusions: Although frequent and apparently easy to approach, the association of sleep disorder an headache may hide conditions with aggravating potential, so they must be addressed together by specialists with comprehensive knowledge of neurology and sleep medicine

Keywords: sleep disorder, headache, diagnosis

Sleep in degenerative parkinsonism

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Introduction. Sleep disorders are non-motor symptoms of Parkinson’s syndromes, which is a recently introduced but much studied topic in literature. Some sleep disorders have been shown to act as a biomarker, facilitating early and differential diagnosis, especially in Parkinson’s disease (BP).

The etiology of sleep disorders is multifactorial and not entirely elucidated being attributed to the degeneration of the sleep center and the motor symptoms themselves, but also to the dopaminergic medication.

The estimated prevalence is between 70-98%, holding a significant impact on the quality of everyday life. The most common sleep disorders are REM behavioral sleep disorder, excessive daytime sleepiness, insomnia and parasomnia. Sleep assessment is required based on the anamnestic data provided by both the patient and their relatives. Questionnaires such as “Parkinson’s Disease Sleep Scale “ and “ The Scales for Outcomes in PD (SCOPA) “ can be particularly useful in quantification and follow-up of specific complaints. For diagnostic purposes, however, the gold standard remains polysomnography with continuous recording during the nights.

Conclusion. The paper summarizes the main changes regarding sleep in degenerative parkinsonism, emphasizing the specific features of each entity.

Oligoclonal bands in multiple sclerosis – correlative interpretation

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Oligoclonal bands (OB) are present in more than 90% of patients with multiple sclerosis and their inclusion into the updated McDonald criteria has improved clinical diagnosis.

OBs are considered now one of the diagnostic biomarkers of the disease, although these immunological

abnormalities in cerebrospinal fluid (CSF) are also found in other neurological disorders.

Recent studies on biomarkers in multiple sclerosis found the presence of OB (both IgG and IgM) is correlated with a worse prognosis.

No association between OB and magnetic resonance imaging (MRI) features has been found (such as anatomical location of lesions or brain atrophy).

Different CSF biomarkers could help improve diagnostic accuracy, allow a personalized therapy of MS patients and provide valuable feedback regarding the course of the disease.

Keywords: multiple sclerosis, oligoclonal bands, biomarkers

Dysphagia therapy in a stroke rehabilitation unit: What factors influence dysphagia severity on discharge?

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Introduction. A proportion of stroke patients continue to experience dysphagia both during the subacute phase and after their admission to rehabilitation units (RUs). Here, we investigated how stroke-and dysphagia-specific factors can influence the outcome of rehabilitative dysphagia therapy.

Methodology. Data from consecutively admitted stroke patients to the dysphagia clinic of an RU in Western Greece were examined retrospectively over a 12-month period. Dysphagia scores – Dysphagia Severity Rating Scale (DSRS) and Functional Oral Intake Scale (FOIS) – and stroke-specific measurements (NIHSS, type of lesion, previous history of stroke and others) were collected on admission and discharge. Data for the duration and intensity of dysphagia therapy were also captured. Factors for positive changes in dysphagia status, cognitive and motor abilities were examined

(chi-square tests and multiple regression analysis, SPSS, v.23).

Results. 95 patients were included (54 men, 74.1±11, mean (±SD) age) with mean length-of-stay 114±59 days. Patients with right hemispheric (RH) lesions experienced more severe dysphagia compared to left-sided (LH) lesions (p=0,009). Initial moderate-to-severe dysphagia (76.8%) was reduced to 24.5% on discharge (p<0.001). Dysphagia severity was significantly improved in both RH and LH patients but not in patients with bilateral lesions. Improved dysphagia status on discharge was more likely in patients with unilateral lesions (p = 0.037, R² = 0.342).

Conclusion. Stroke-specific factors exert an important influence on the outcome of dysphagia therapy delivered in RU subacute stroke patients. Further research is required investigating how these factors interact with SLT-led dysphagia therapy, and whether patient stratification would improve such care.

Lupus erythematosus – neurologic complications

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Introduction. Systemic lupus erythematosus (SLE) is characterized by numerous immunological abnormalities that lead to multiorgan involvement. The central and/or peripheral nervous system are frequently affected in patients with SLE. It is estimated that 10-80% of patients with SLE develop neurologic and psychiatric symptoms.

Materials and methods. In this paper the neurological complications of SLE will be presented and supported by two case presentations. First female patient of 64 years old was transferred to our Neurology Department for multiple oculomotor nerves palsies and motor weakness of the lower limbs with the absence of deep tendon reflexes. Serial cerebral magnetic resonance imaging revealed cavernous sinus thrombosis that extended despite anticoagulation. Nerve conduction studies showed sensorymotor axonal polyneuropathy. The second patient of the same age was transferred from the Cardiology Department, where she was admitted for Libman-Sacks endocarditis, for abrupt onset of right hemiparesis and aphasia, 3 hours before. Cerebral computed tomography with iv contrast revealed left middle

cerebral artery M1 segment occlusion. She also presented thrombocytopenia (61000/microliter).

Results. The first patient was diagnosed with SLE and received treatment with cyclophosphamide with improvement of the symptoms but one week later she presented severe anemia secondary to a large retroperitoneal hematoma. The patient underwent surgery and died few days later. The second patient underwent thrombectomy with complete remission of the symptomatology.

Conclusion. We chose to present this paper in order to highlight the neurologic complications of SLE and the importance of an early diagnosis and treatment of this pathology.

Plasmapheresis and double filtration plasmapheresis in severe neuroimmune disorders

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Therapeutic plasma exchange (TPE) is an extra-corporeal blood purification technique designed to remove large molecular weight particles from plasma such as circulating autoantibodies, immune complexes, cytokines, monoclonal proteins, toxins and other inflammatory mediators. TPE is accepted by the American Society for Apheresis as first line treatment for some severe neuroimmune disorders-Guilaine Barré syndrome (GBS), myasthenia gravis in severe crisis, chronic inflammatory demyelinating polyneuropathy and fulminant forms of Wilson disease. Plasmapheresis is accepted as second line therapy in Lambert-Eaton myasthenic syndrome, multiple sclerosis relapsing-remitting form, acute disseminated encephalomyelitis (ADEM) and in neuromyelitis optica (NMO) unresponsive to high-dose corticosteroids.

Double filtration plasmapheresis (DFPP) is a newer technique in which plasma is not entirely removed, only the antibodies, using special filters. High-dose intravenous immunoglobulins are an alternative treatment for these patients but are much more expensive. We report the experience with TPE and DFPP performed between 2012 and 2020 in a lot of patients with severe neuroimmune disorders that were admitted in our hospital.

Neurologic manifestations of the ADA2 associated vasculopathy

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First described in 2014, deficiency of adenosine deaminase 2 (DADA2) is a monogenic autoinflammatory disorder of children and less often adults, characterised by an early onset vasculopathy with skin rash associated with systemic manifestations, nervous system involvement and mild immunodeficiency. This condition is secondary to autosomal recessive mutations of CECR1 gene, mapped to chromosome 22q11.1, that encodes the enzymatic protein adenosine deaminase 2 (ADA2).

The pathogenetic mechanism of DADA2 is still unclear but abnormalities in adenosine breakdown are considered to play a key role. The diagnosis is established through detection of reduced activity level of the ADA2 and/or identification of bi-allelic mutations in the ADA2 gene.

From the clinical point of view, this disease is characterized by a wide spectrum of severity. Chronic or recurrent systemic inflammation with fever, elevation of acute phase reactants and skin manifestations is the typical clinical picture. While in some patients the disease is mild and skin-limited, others present a severe, even lethal, disease with multi-organ involvement. Neurologic involvement is estimated to occur in 50–75% of patients, the most frequent manifestations being ischemic or hemorrhagic strokes. Meningitis, encephalitis and PNS involvement with mononeuritis multiplex, cranial neuropathies, and polyneuropathy (sensory or motor) have also been reported.

Due to its rarity, the response to treatment of DADA2 is still anecdotal. The first-line treatment consists of TNF-inhibitors which are effective in controlling inflammation and in preserving vascular integrity. Steroids can control the disease's manifestations at high dosage.

Immunologic consequences of acute ischemic stroke

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Acute stroke holds the second place after acute cardiac ischemia regarding worldwide death causes. Significant progress has been achieved in recent years by using both chemical and mechanical revascularisation techniques for acute ischemic stroke treatment. However, there is a constant need for complementary therapies in order to improve quality of life and survival rates after stroke.

Inflammation is the key event that triggers immunologic cascades within the central nervous system. The immune system acts through both pathways: innate and acquired. The innate immune system determines immediate activation of non-specific leukocytic cells, granulocytic cells and innate lymphoid cells. These innate immune cells secrete cytokines and chemokines that recruit other innate cells, signal other pathways and activate secondary immunologic cascades. The adaptive immune system is initiated within hours to days from the acute event. It uses cell mediated immunity (T cells) and humoral mediated immunity (B cells). The antigen-specific response is characteristic for the adaptive immunity, as well as the ability to have immunological memory.

Current literature states that there is no certain cell population defined as main pathogenic effector in stroke. Neutrophils, followed by macrophages and natural killer cells are the first to migrate in the brain parenchyma in the first hours up to days after the ischemic event. B and T lymphocytes are later involved in the inflammatory event. Consequently, immediate immune system approach should be attempted in the very early stages of an acute ischemic event in order to improve outcome.

The inflammatory cascade is responsible for molecular alterations in the blood brain barrier triggered by arterial vessel occlusion. Although the purpose of this mechanism is to restore homeostasis, inflammation can also alter the penumbral tissue. A better understanding of the intricate connections between ischemic stroke and the immune system could help neurologists alter the effects of inflammation towards protection and away from tissue damage.

Common mistakes in neurocritical care

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A brief review of the most common local practices in caring for the neurocritical patient, exploring the evidence each of these therapeutic gestures is based on.

The dos and don'ts of hyperosmolar therapy, proton pump inhibitors overprescription, orotracheal intubation that overstays its welcome, microdosing statins, how training residents in acute stroke care lowered the annual furosemid consumption by almost a third and other hot topics will be brought under the spotlight.

While sorting guideline indications from folklore, the authors explore the medical and pharmaco-economic impact generated by common mistakes in day to day practice.

Keywords: neurointensive care, guidelines, errors

Diagnostic approach to central nervous system lymphomas: A case series

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Central nervous system lymphomas (CNSL) comprise a diverse group of rare hematologic malignancies resulting from monoclonal lymphocyte proliferation. They are divided into two subtypes, primary CNSL (that primarily arise in the CNS) and secondary CNSL (metastatic). Considering their heterogeneous clinical presentation that ranges from paucisymptomatic to acute multifocal symptoms, particular imaging findings should raise a high index of suspicion. Provided that contiguity with a cerebrospinal fluid (CSF) space occurs, lumbar puncture might assist diagnosis. Nevertheless, histopathologic confirmation is warranted.

We present ten patients aged 23 to 71 years old with primary or secondary CNSL. Main clinical manifestations were cerebellar signs, intracranial hypertension syndrome, limb motor deficits, cranial nerves palsies and epileptic seizures. Most patients had bilateral parenchymal involvement on MRI, one had leptomeningeal infiltration and one had normal imaging. In two cases CSF

analysis identified atypical lymphoid cells and three had mild lymphocytic pleocytosis.

Consistent with the literature, the immunocompetent patients had late onset of primary CNSL, whereas the only one with HIV infection was diagnosed at age 30. All primary CNSL in our group were diffuse large-B cell lymphomas (DLBCL), one being confirmed at necropsy and one requiring two biopsies. Three patients had CNS involvement by primary extranodal DLBCL (mediastinal and ovarian) and nodular sclerosis Hodgkin lymphoma, respectively. In one patient brain biopsy failed to probe the diagnosis of Bing-Neel syndrome.

In conclusion, CNSL are “great imitators”, with heterogeneous clinical presentations and imaging features. Diagnostic approach is difficult and sometimes requires sequential brain biopsies.

Immunological features of giant cell arteritis

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Giant cell arteritis (GCA) is the most common idiopathic systemic vasculitis in persons aged 50 years or older, with increased risk of vertebral artery stroke and

optic nerve ischemia. In particular, carriage of HLA-DRB1*0401 and DRB1*0404 haplotypes are more prone to interact with a probable environmental infectious agents or autoantigens and activate arterial wall dendritic cells. Activated vascular dendritic cells are able to attract and activate T lymphocytes and macrophages through production of specific chemokine and cytokine and further initiate and maintain arterial inflammation and granuloma formation. In the adventitia, activated M1 macrophages primarily secrete proinflammatory cytokines like IL-1 and IL-6, while M1 macrophages in the medial layer degrade the arterial matrix through secretion of matrix metalloproteinases and damage vascular smooth muscle cells and endothelial cells. CD4+ T effector cell subtypes have been identified as key regulators in vasculitic lesions of GCA; type 17 helper T cells and type 1 helper T cells. Although a major immunologic role of B cells is the production of antibodies, B cells can also regulate T cell responses in auto-immunity through the secretion of both pro-inflammatory (TNF- α and IL-6) and anti-inflammatory (IL-10) cytokines. Beyond standard cortisone therapy the above immune mechanisms are targeted by new therapeutic agents, including abatacept and ustekinumab but also tocilizumab which has shown clear benefit in both newly diagnosed and relapsing patients with GCA.