Ref:Ro J Neurol. 2019;XVIII(Suppl)
DOI: 10.37897/RJN.2019.S.3

The 51st International Danube Symposium of Neurology
PROCEEDINGS

ORAL PRESENTATION – ABSTRACTS

Outcome aspects in patients with acute ischemic stroke and carotid artery occlusion

Andreea BANICA[1], Simona PETRESCU[1,2], Cristina Aura PANEA[1,2]

[1]"Elias" University Emergency Hospital, Bucharest, Romania
[2]"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Introduction. Symptomatic carotid artery occlusion represents a great disability risk in rather young patients due to compromised cerebral blood flow, while associated cardiovascular risk factors only serve to amplify the severity of the clinical outcome.

Objectives, method. To evaluate the outcome of symptomatic carotid artery occlusion and the influence of vascular risk factors on it. We retrospectively analyzed a cohort of 100 patients (71 males), in 2 years, with cervical segment occlusion of internal carotid artery (ICA) diagnosed using neurosonology methods, taking into account age, sex, associated cardiovascular risk factors and clinical outcome after the acute cerebrovascular event, ranked on the modified Rankin scale (mRS).

Results. 75 patients were diagnosed with symptomatic carotid disease, 38 with left and 32 with right ICA occlusion. Most patients were admitted for unilateral weakness and speech impairment.

Patients with symptomatic carotid occlusion and smokers had a less favorable outcome on the mRS scale ($p = 0.011$ and $p = 0.033$ respectively).

Arterial hypertension is correlated with symptomatic carotid occlusion ($p = 0.033$).

The mean mRS score for symptomatic carotid disease was 3.44, while asymptomatic patients scored a mean mRS of 2.52.

Conclusion. Carotid artery occlusion is a "volatile" condition, with multiple undervalued causes and consequences. In both preventing an acute cerebrovascular event and improving clinical outcome, along with adequate medical therapy, patients must be trained to also change their lifestyle, as this study goes to confirm.

Keywords: carotid artery occlusion, outcome, risk factors

Diagnostic challenges in autoimmune encephalitis

Liviu COZMA[1,2], Delia TULBĂ[1,3], Iulia OLARU[1,2], Zela COFOIAN-AMET[1], Andreea FLOREA[1], Cristina MITU[1], Bogdan Ovidiu POPESCU[1,2,4]

[1]Department of Neurology, Colentina Clinical Hospital, Bucharest
[2]Department of Clinical Neurosciences, "Carol Davila" University of Medicine and Pharmacy, Bucharest
[3]Colentina – Research and Development Center, Colentina Clinical Hospital, Bucharest
[4]Laboratory of Ultrastructural Pathology, "Victor Babeș" National Institute of Pathology, Bucharest

During the past decade, autoimmune encephalitis has risen from a fairly unknown entity to one of the most common causes of encephalitis, with a prevalence similar to that of infectious encephalitis. However, it is still poorly known and rarely diagnosed in Romania, with many patients being referred to infectious disease rather than neurology clinics, which leads to late diagnosis and treatment.

We showcase a series of patients with autoimmune encephalitis who presented to our department in the past years and raised several diagnostic dilemmas. In some of them the clinical picture was perfectly compatible with the detected antibodies, while others had antibodies with an unknown significance or unrelated to the disease. Many patients were suspected of having autoimmune encephalitis based on clinical and MRI features but no antibodies were found, therefore raising diagnostic challenges. In this regard, we retrospectively identified several issues that might have been responsible for the inappropriate detection of antibodies leading to diagnostic uncertainty. The most common mistakes were related to either antibody choice and sampling site or timing of detection (e.g. stepwise identification, sampling after corticosteroids, immunoglobulins or plasma exchange).

Taking these issues into account we discuss recommendations for antibody detection in autoimmune encephalitis and underline the importance of identification with panels of antibodies specifically tailored for

different phenotypes of autoimmune encephalitis. These should be applied promptly, followed by immediate treatment where a high index of suspicion exists.

A basilar roller coaster – case report

Adina Virginia CRACIUNOIU[1], Cristina Iulia CERNAT, Mihai Radu IONESCU[1], Patricia IOAN[1], Bogdan DOROBAT[1], Ovidiu Alexandru BAJENARU[1,2]

[1]Neurology Department, University Emergency Hospital, Bucharest
[2]" Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Stroke caused by acute basilar artery occlusion (BAO) is a relatively rare but especially dreaded occurrence, due to both high mortality and disability in surviving patients, compared to anterior and other posterior circulation syndromes. Studies investigating the superiority of endovascular treatment in BAO relative to intravenous thrombolysis have yielded variable results, especially regarding post-stroke disability, with the caveat that randomized controlled studies do not exist to support or refute this hypothesis. However, a trend seems to be emerging from the observational studies that have been conducted, namely that adding mechanical thrombectomy to the acute stroke treatment scheme in patients with BAO could improve the outcome significantly.

We present the case of a 64 year old woman, brought to the Emergency Department for acute onset vertigo, dysarthria and left hemiparesis. At presentation, the patient had a National Institute of Health Stroke Scale (NIHSS) score of 6 points. CT scan and CT angiography of supraaortic vessels were performed, revealing a pcASPECTS score of 10 and lack of basilar artery occlusion. Intravenous thrombolysis was started at 2 hours and 25 minutes after onset. 25 minutes after the initiation of alteplase, there was a 3 point aggravation in the clinical state of the patient, on account of anarthria and forceful gaze deviation, aggravation which resolved spontaneously in approximately five minutes. Intravenous alteplase was not discontinued. Ten minutes afterwards, the patient deteriorated again (with a 6 NIHSS points aggravation), this time on account of left hemiplegia, without aggravation of dysarthria. Intravenous alteplase was discontinued ant the patient had a repeat CT scan and CT angiography, negative for hemorrhage, but this time confirming the occlusion of the basilar artery. Whilst completing the intravenous alteplase, the patient was transported to the angiography laboratory, where, shortly after arterial puncture, entered deep coma. Mechanical thrombectomy was performed, with complete recanalization (Thrombolysis In Cerebral Infarction score 3), at approximately 5 hours after onset of symptoms. Subsequently, the patient regained consciousness and, one hour post endovascular treatment, was free from neurological deficits, except slight vertigo.

This case illustrates the difference that endovascular treatment can make in this particularly devastating subtype of stroke, as well as the importance of early successful recanalization in reducing disability. We can confidently say that, for this patient, it has made the difference between life and death.

Hypertension as important stroke risk factor: Early vascular and cognitive changes and the reversibility

László CSIBA[2], Enikő CSIKAI[1], Mónika ANDREJKOVICS[1], Bernadett BALAJTHY-HIDEGH[1], Gergely HOFGÁRT[2], László KARDOS[3], Ágnes DIÓSZEGI[4], Róbert ROSTÁS[2], Katalin R. CZURIGA-KOVÁCS[2], Éva CSONGRÁDI[2,5]

[1]Institute of Behavioural Sciences, Faculty of Public Health, University of Debrecen, Debrecen, Hungary
[2]Department of Neurology, Faculty of Medicine, University of Debrecen, Debrecen, Hungary
[3]Kenézy Gyula Hospital and Clinic, Debrecen, Hungary
[4]Department of Medicine, Faculty of Medicine, University of Debrecen, Debrecen, Hungary
[5]MTA-DE Cerebrovascular and Neurodegenerative Research Group, Debrecen, Hungary

The hypertension is one of the most important risk factors for stroke that can be modified. It can impair the vascular wall and results in multiorgan damage. Our aim was to investigate the morphological and functional damage of the vascular system in recently diagnosed asymptomatic hypertensive patient. The cognition was also investigated by validated neuropsychological tests. We summarize the results before and after antihypertensive therapy (3 and 12 months, respectively).

After one year therapy, lower IMT values were found. Pulse wave velocity showed a borderline significant decrease. During HUTT, several hemodynamic parameters improved. The patients performed better on neuropsychological testing and reached significantly lower scores on questionnaires evaluating anxiety.

After 3 months therapy common carotid intima-media thickness (IMT) and brachial artery flow mediated dilatation (FMD) were detected by US. Arterial stiffness measured by augmentation index (AIx) and pulse wave velocity (PWV).

3-months ACE inhibition could not reach a significant level in the improvement of IMT, FMD, AIx and PWV values, but significant changes could be detected in cognitive tests after a short (3months ACE.inhibition) therapy.

The present study shows that early vascular changes and altered cognitive function observed in newly diagnosed hypertensive patients may improve with promptly initiated antihypertensive management.

Natural history of multiple sclerosis: Predictors of long term disability

Jelena DRULOVIC

Clinic of Neurology, CCS, Faculty of Medicine, University of Belgrade, Belgrade, Serbia

The natural history of multiple sclerosis (MS) is characterized by a marked variation when it comes to the gradual progression of disability. It has been demonstrated that about one-half to two-thirds of relapsing remitting (RR) MS patients would develop severe neurological disability 11 to 23 years from disease onset. Additionally, 2-3% of patients per year will convert to secondary progressive phase of the disease.

During the last 20 years, a significant number of disease modifying therapies (DMT)s for RRMS was introduced on the basis of their high efficacy in randomized controlled trials (RCT)s. Unfortunately, controlled trials provide limited data about the comparative efficacy of DMTs. Until now, no DMT has shown to be effective in all persons with MS. Rapid detection of suboptimal response to a DMT is thus very important, in order to switch to an alternative highly efficacious agent. It has been suggested that MS disability progression follows a two-stage process. It is assumed that a first stage is predominantly characterized by the inflammatory process. In that stage, number of relapses during the first two years and the deficit after the first relapse have been demonstrated to be the major predictive factors of disability progression. However, these factors are not predictive in the second stage, probably independent of inflammation. This notion have to be significantly considered because of its crucial therapeutic implications.

Restless legs syndrome – diagnosis and treatment

Cristian FALUP-PECURARIU, Ștefania DIACONU

Department of Neurology, County Emergency Clinic Hospital, Transilvania University Brașov, România

Restless legs syndrome (RLS) or Willis-Ekbom disease is a sensorimotor disorder, characterized by uncomfortable sensations in the legs and an irresistible urge to move the legs. These sensations occur during rest, generally in the evening or night, and are partially or totally relieved by movement, the occurence of these symptoms is not better explained by any other medical condition. RLS was first described by Karl-Axel Ekbom in 1945. In 1995 there were established the International Restless Legs Syndrome Study Group (IRLSSG) „minimal" criteria for diagnosis of RLS, in 2003 – the NIH/IRLSSG „essential" criteria for RLS diagnosis, and in 2014 was published the revision of the 2003 NIH/IRLSSG criteria.

Different epidemiological studies show that the RLS prevalence in the general population is estimated to be 5-10%.

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.

Regarding severity, RLS can be defined as being mild, moderate, severe or very severe, based on the International RLS Rating Scale. RLS is an important cause of insomnia and fatigue.

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 pharmacologic and non-pharmacologic strategies.

Pharmacological treatment includes dopaminergic agents (Pramipexole, Ropinirole, Rotigotine), iron supplimentation in iron deficits, anticonvulsivant calcium channel (alpha-2-delta) ligands, and opioids.

Non-pharmacologic treatment includes lifestyle changes, exercise, cold baths, limb massage, avoidance of RLS precipitants (ex. alcohol, caffeine, antidepressants).

Autoimmune syndrome induced by adjuvants (ASIA) – a controversial diagnosis

Nicoleta GHERGHEL[1], Adina STAN[1,2],
Nicu DRAGHICI[2], Dafin Fior MURESANU[1,2]

[1]Neurology Department, Emergency County Hospital, Cluj-Napoca
[2]Neuroscience Department, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj Napoca

We present the case of a 41-year-old woman who presented with severe gait and equilibrium difficulties, distal paresthesia, arthralgia and Raynaud phenomena starting four years after silicone breast augmentation surgery. ENMG showed severe axonal sensory polyneuropathy. Following an extensive immunological, infectious, neoplastic and metabolic workup, along with rectal biopsy, she was diagnosed with mixed connective tissue disease. After immunosuppressive therapy failure, a suspicion of ASIA syndrome was raised. ASIA syndrome is a recently described, controversial entity of aberrant autoimmune response triggered by exposure to adjuvants. Along with general manifestations, neurological features have been described. However, the controversiality of the subject asks for further studies.

Dementia: New approaches and opportunites

Professor Vladimir HACHINSKI, MD, Dsc,
Dr. honoris causa X4

Department of Clinical Neurological Sciences, Western University, London, Canada

Over the past four decades, Alzheimer disease has become near synonymous with dementia and the amyloid/tau hypothesis as its dominant explanation. However, this monorail approach to etiology has failed to yield a single disease modifying drug.

Part of the explanation stems from the fact that most dementias in the elderly result from interactive Alzheimer and cerebrovascular pathologies. Stroke and dementia share the same risk factors and their control is associated with a decrease in stroke and some dementias. Additionally, intensive control of risk factors and enhancement of protective factors improves cognition. Moreover, anticoagulation of atrial fibrillation patients decreases their chance of developing dementia by 48%. Preliminary data suggest that treating blood pressure to a target of 120mm Hg systolic compared to a target of 140 mmHg decrease the chances of mild cognitive impairment by 19%.

The Berlin Manifesto establishes the scientific bases of "Preventing dementia by preventing stroke". Enlarging our vista of dementia to include cerebrovascular disease offers the opportunity of preventing not only stroke, but some dementias, beginning now[1].

Rerefences

1. Hachinski V. Dementia: New vistas and opportunities. *Neuro Sci.* online Jan 21 2019

Inflammatory neuropathies – a clinical approach

Tudor LUPESCU

Neurology Department,
„Agrippa Ionescu" Clinical Hospital, Bucharest

Peripheral neuropathies are frequent in the general population. Due to the high incidence and prevalence of diabetes mellitus worldwide, the most frequent form is diabetic neuropathy. The group of inflammatory immune-mediated neuropathies is important to recognize as early as possible, because they are treatable. IVIgs, plasma exchange, corticosteroids, and other drugs can be used, most of the time successfully, in these conditions. But it is not always easy. Sometimes different forms of inflammatory neuropathies are not easy to recognize, delaying the diagnosis; in other situations the clinical response to therapy is not so obvious, raising doubts on the diagnosis. In some cases it is not easy to differentiate between an AIDP and acute onset CIDP; what should we expect from the treatment? When can we say that one particular treatment fails, and what options should we consider? Is there a link between CIDP and diabetes mellitus?

Results of the CAPTAIN II trial – a new horizon in TBI treatment

Prof. Dafin MURESANU, MD, PhD

Professor of Neurology, Chairman Department of Neurosciences
"Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca, Romania

Background and aims. Traumatic brain injury (TBI) is a leading cause of injury-related disability and death worldwide. In 2016, an estimated 27 million new cases of TBI we added to the global burden. The CAPTAIN-RO trial enriches compelling evidence that currently exists for Cerebrolysin, an approved agent for neuroprotec-

tion and neurorecovery after TBI in many countries, using a novel approach: multidimensional analysis.

Methods. The study is an interventional, randomized, double-blind, controlled, single-center trial. The full protocol is available for consultation in the ISRCTN registry (no. 17097163). General and neurocognitive outcomes after TBI were measured using full scales, avoiding dichotomization of variables. The multidimensional analysis opens a new direction for clinical and statistical thinking in neurorehabilitation by adding precision to the measurement of complex health states for TBI.

Results. A total of 142 patients aged 19-79 with a diagnosis of TBI and a GCS score between 7 and 12 at the time of hospital admission were enrolled. Baseline, day 10, 30 and 90 assessments were collected using nine scales that measured cognitive function and emotional status.

Conclusion. CAPTAIN-RO is one of the first trials in TBI history with a truly multidimensional approach based on full outcome scales. We believe this strategy is superior to the single criterion paradigm, commonly used in neuroprotective treatment research. This trial delivers a unique perspective to decades of well-established positive effect trends of Cerebrolysin. These will be extensively discussed and evaluated for implications concerning future TBI research upon completion of data analysis.

Keywords: randomized controlled trial, traumatic brain injury, multidimensional analysis

Recognizing and treating hereditary transthyretin amyloidosis

Laura OBICI, MD

Amyloidosis Research and Treatment Centre, Fondazione IRCCS Policlinico San Matteo, Pavia, Italy

Hereditary transthyretin amyloidosis (hATTR) is characterized by high genetic and phenotypic variability, with differences in disease presentation and progression across different populations and geographical regions. The most common *TTR* pathogenic variant, Val30Met, clearly exemplifies such significant heterogenity in clinical presentation and disease course, being associated with two different phenotypes, indicated as early-onset and late-onset respectively. Differences include not only the age at disease onset but also the pattern of organ involvement, with small-fibre neuropathy, severe autonomic dysfunction and nephrotic renal damage dominating in the first case, whereas in patients with the late-onset phenotype the disease is heralded by bilateral carpal tunnel syndrome and usually manifests with early involvement of larger sensory and motor nerve fibres and mild autonomic neuropathy. Moreover, a progressive cardiomyopathy with a hypertrophic phenotype typically occurs in late-onset patients but it is not observed in the early-onset population. Finally, differences occur also in response to treatment, with higher beneficial effect from liver transplantation and treatment with tafamidis in early-onset patients, resulting in better outcome. Neuropathy progression occurs relentlessly in the absence of treatment, with walking impairment and wheel-chair requirement within a few years. The rate of disease progression and outcome may vary according to the underlying *TTR* mutation.

Tetramer disassembly followed by monomer aggregation is a critical, rate-limiting step for transthyretin amyloid fibrillogenesis. Stabilization of the protein quaternary structure is therefore a key molecular target that can be exploited for therapeutic purposes using compounds that interact with the thyroxine binding sites of transthyretin. Tafamidis, as analogue of thyroxine, is the first properly designed molecule to target such a key pathogenic event. Diflunisal, another structural analogue of thyroxine, proved its safety and efficacy in slowing neurological deterioration irrespective of genotype and disease stage in a phase III controlled trial. However, off-label indication, limited access in Europe and possible renal and gastrointestinal side-effects restricted its use in real-life practice. Novel treatment options that prevent hepatic TTR synthesis by degrading its mRNA are now available. The antisense oligonucleotide inotersen and the RNAi agent patisiran have both proved effective in halting neurological progression and improve quality of life in two phase III trial, representing novel treatment opportunities for a larger number of patients.

Functional movement disorders – a shift from classical psychopathological view to recent neurobiological evidence

Oana OBRISCA[1], Mark J. EDWARDS[2,3], Amalia ENE[1], Ovidiu A. BAJENARU[1,4]

[1]Neurology Department, Emergency University Hospital of Bucharest, Romania
[2]Neuroscience Research Centre, Institute of Molecular and Clinical Sciences, St George's University of London, UK
[3]Atkinson Morley Regional Neuroscience Centre, St George's University Hospital, London, UK
[4] "Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Functional movement disorders (FMD), along with other functional neurological disorders, are commonly

encountered in clinical neurological practice, accounting for approximately 16% of patient referrals to neurology clinics.

The focus in terms of pathophysiology was on psychological factors, such as traumatic and stress-related events, but this view tends to change in light of modern research. The DSM-V criteria for conversion disorders (now including the term "functional") emphasize the importance of a positive neurological diagnostic and acknowledge that significant psychological factors may not be present.

The main difficulty in assessing FMD is knowing whether the abnormal movements are voluntarily produced (distractibility and resolution to placebo are shared features with voluntary movements), thus feigned, or if they are perceived by the patient as involuntary, suggesting a disrupted neural circuit. Experimental evidences suggest that impairment in neural systems conferring a sense of agency for movement is responsible of the maladaptive response, so that movements that appear voluntary are not perceived as such.

Modern functional imaging studies objectified temporoparietal junction hypofunction, a region important in comparing actual with expected sensory feedback during movement, and reflected abnormal connectivity between motor and limbic areas as well.

A better understanding of the proposed mechanisms that underpin FMD definitely will enlarge our knowledge and ideally, influence our clinical judgement. Addressing more carefully to FMD patients and offering them an objective explanation for their symptoms may lead to better management of this category of patients, often situated in an uncertain, grey area between neurologists and psychiatrists.

Cognitive dysfunction in multiple sclerosis

Cristina PANEA, Simona PETRESCU

"Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

Elias University Emergency Hospital, Bucharest, Romania

Introduction. Cognitive impairment, often underrecognized or misdiagnosed as depression or stress, occurs in almost 70% of patients with MS and contributes significantly to a poor quality of life. It seems to be linked to cortical pathology as well as to white matter pathology and thalamus atrophy.

Goals and method. To identify cognitive disability and its relationship with extension of lesion burden, fatigue and quality of life in MS patients. 172 patients (68.02% female, mean age 38) with RRMS (75%), SPMS (16.27%), PPMS (4.06%) and CIS (4.67%) have been evaluated with specific tests for: cognition – MMSE, MoCA, BICAMS; physical disability - EDSS, MSFC; fatigue - Multiple Sclerosis Fatigue Impact Scale (MFIS); quality of life – self-reporting scale EuroQol 5-Dimension, with EQ-5D-index and EQ-Visual Analogue Scale (EQ-VAS).

Results. 61.04% of all patients were cognitively affected (MMSE and MoCA less than 26 points) but in different degrees, according to MS form. EDSS is significant statistically negative correlated with MMSE score (r= -0.44, p=0.0001), MoCA score (r= -0.45, p=0.0001), PASAT score (r=- 0.47, p=0.0001), and SDMT score. There is a strong correlation between cognition (all scales) and fatigue (p=0.001) and QoL (p =0.0002).

Conclusions. The patients with MS, especially those with PPMS and SPMS, are cognitively impaired in a significant proportion, regardless of age or disease duration. They also have higher disabilities, higher level of fatigue and poorer quality of life.

Keywords: cognition, disability, fatigue, quality of life

Brain cleaning systems and neurodegeneration

Bogdan O. POPESCU

„Carol Davila" University of Medicine and Pharmacy, Bucharest, Romania

„Victor Babes" National Institute of Pathology, Bucharest, Romania

Colentina Clinical Hospital, Bucharest, Romania

Our brain (and body in general) produces molecular garbage and has cleaning systems to clear it away and to allow physiological functions. These cleaning systems are organized on different levels, namely cellular level, where the proteasome and the lysosome systems are active, brain parenchyma level, where microglia and other cells are able to remove abnormal molecules, blood-brain barrier level, where ABC cassette transporter pumps are removing foreign molecules and eliminate them in the blood stream and the global brain level, where the recently described glymphatic system drives debris to the venular blood trough convective flow. Neurodegeneration is characterized by progressive accumulation of aggregated proteins, and an important pathogenic mechanism might be in sporadic cases the weakening of the brain cleaning systems with ageing.

Bilateral cerebellar hemorrhage – a case report

Adina STAN[1,2], Nicoleta GHERGHEL[1], Simona MANOLE[3], Horatiu STAN[2,4], Dafin Fior MURESANU[1,2]

[1]Neurology Department, Emergency County Hospital, Cluj-Napoca
[2]Neuroscience Department, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca
[3]Radiology Department, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca
[4]Neurosurgery Department, "Iuliu Hatieganu" University of Medicine and Pharmacy, Cluj-Napoca

A 32 years old male patient was admitted for severe nausea, pulsating tinnitus, dizziness, equilibrium problems, symptoms onset being one week before admission. Initial MR angiography was normal, but 24 hours later the neurological status aggravated, with meningeal signs, severe nystagmus and bilateral ataxia. The brain CT-angiography revealed bilateral cerebellar hemorrhage. After rapid neurosurgical intervention extensive radiological investigations were done. A small dural fistula between a branch of right external carotid artery and confluence of right sigmoid and transverse sinuses was discovered and embolization was performed. Bilateral cerebellar hemorrhage in young patients without previous medical history is a provoking diagnosis and dural fistula should be kept in mind.

Stent-graft – a good choice of therapeutic approach in some clinical cases

Daniela STEFAN[1], Athena RIBIGAN[1,2], Vlad TIU[1], Bogdan DOROBAT[1], Ovidiu BĂJENARU[1,2], Florina ANTOCHI[1]

[1]Neurology Department, Emergency University Hospital, Bucharest
[2]"Carol Davila" University of Medicine and Pharmacy, Bucharest

Introduction. Stent-grafts are now increasingly used for endovascular treatment of different pathologies of intracerebral vessels although they were initially designed for aortic and peripheral aneurysms and arteriovenous fistulas. The aim of our presentation is to illustrate the utility of stent-grafts in different clinical situations.

Methods. We present a series of five patients: a 46-year-old female with a giant aneurysm in the intracavernous segment of the left internal carotid artery, a 37-year-old female with an aneurysmal dilation of 1.5 cm at the origin of the left internal carotid artery, a 36-year-old male with a post-traumatic right internal carotid artery dissection with a pseudoaneurysm in the C1 segment, a 47-year-old female with post-traumatic right direct carotid-cavernous fistula and a 73-year-old female with an iatrogenic lesion of the left vertebral artery after surgery for a herniated disk with secondary myelopathy.

Results. All patients underwent digital substraction angiography of the cervical and cerebral vessels and endovascular treatment with stent-graft, with optimal results and no other findings at their follow-up visits.

Conclusion. Stent-grafts represent a safe, effective and minimally invasive therapeutic approach for a variety of cervical and cerebral vascular pathologies.

Implementing stroke action plan 2018-2030 in Romania

Cristina TIU, Elena TERECOASĂ, Vlad Eugen TIU, Răzvan Alexandru RADU, Ovidiu BĂJENARU

Department of Clinical Neurosciences, UMF "Carol Davila", Department of Neurology, University Hospital, Bucharest

All eastern European countries are confronted with a high incidence, prevalence, mortality and morbidity of stroke, but Romania is amongst the most affected. Various factors contribute to this reality, and it is a real challenge to improve the situation, as it implies a lot of economic and social corrective measures, education for population and medical professionals, equipment for hospitals, human resources and enough centers for neuro-rehabilitation.

Intravenous thrombolysis has dramatically changed the faith of stroke patients, and in developed countries the treatment is accessible for the vast majority of patients. In Romania, the first attempts to organize stroke care were made in 2004, but it took a long way to change mentalities, and it was only in 2019 that the method started to be applied in almost all the regions of the country.

The percentage of people treated by endovascular methods is still very low, and the main reason is the lack of doctors trained for neuro-radiological interventions.

The seven pillars of the stroke action plan 2018-2030 have clear objectives, and it may seem too ambitious for a country like Romania, but the achievements of the last 3 years, with a rapid increase in the number of thrombolysis and the establishment of the Romanian Registry of Interventional Treatment in Stroke show us that perseverance can move the mountains of indifference.

The phenotypic spectrum of motor neuron disease

Delia TULBĂ[1,2], Liviu COZMA[1,3], Iulia OLARU[1,3], Antonia LEFTER[1], Cristina MITU[1], Bogdan Ovidiu POPESCU[1,3,4]

[1]Department of Neurology, Colentina Clinical Hospital, Bucharest
[2]Colentina – Research and Development Center, Colentina Clinical Hospital, Bucharest
[3]Department of Clinical Neurosciences, "Carol Davila" University of Medicine and Pharmacy, Bucharest
[4]Laboratory of Ultrastructural Pathology, "Victor Babeș" National Institute of Pathology, Bucharest

Motor neuron disease (MND) is a neurodegenerative disorder primarily involving motor neurons in the cerebral cortex, brainstem and spinal cord. Its diagnosis requires evidence of both upper (UMN) and lower motor neuron (LMN) progressive degeneration unexplained by other diseases. Since the discovery of MND by Charcot at the end of the 19th century, emerging recognition of various pathogenic gene mutations, widespread pathology and overlap with frontotemporal dementia has pointed towards a spectrum disorder rather than a single disease.

We present a series of patients diagnosed with *amyotrophic lateral sclerosis* (ALS) according to the Revised El Escorial/Awaji Criteria, emphasizing the differences in onset and clinical features and their prognostic value. We exemplify two cases of pure UMN and LMN involvement, discussing the differential diagnosis between *primary lateral sclerosis* (PLS) and UMN-dominant ALS and *progressive muscular atrophy* (PMA) and LMN-dominant ALS. We report a patient with *facial-onset sensory and motor neuronopathy* (FOSMN), a recently described entity featuring progressive facial-onset sensory deficits and LMN signs, with occasional TDP-43 pathology. We also present a case of ALS and subsequent breast cancer diagnosis with amphiphysin antibodies, bringing into question the controversial paraneoplastic MND.

Provided that phenotypes such as PLS, PMA and FOSMN cannot be listed as ALS according to current diagnostic criteria although having (at least occasionally) TDP-43-mediated neurodegeneration, revisions are warranted. Moreover, since MND phenotypes have different rates of progression and functional decline, an improved prognosis stratification taking into consideration the onset mode, UMN versus LMN burden, progression rate and cognitive-behavioral changes is requested.

Kynurenines and neurological disorders: Biomarkers and therapeutic possibilities

László VÉCSEI

Department of Neurology, University of Szeged
MTA-SZTE Neuroscience Research Group, Szeged, Hungary

The kynurenine pathway (KP) is the main metabolic route of tryptophan degradation, in the course of which several neuroactive compounds generated. The imbalance of the neurotoxic and neuroprotectant metabolites can lead to excitotoxicity and overproduction of reactive oxygen species, which both contribute to the progression of different neurological disorders. Recently, clinical investigations have shown that during the acute phase of ischemic stroke, KP is activated and peripheral levels of metabolites correlated with worse outcome. Migraine is a primary headache of imprecisely known mechanism, but activation of the trigeminovascular system appears to be essential during the attack. Intensive research has recently focused on pituitary adenylate-cyclase-activating polypeptide (PACAP) and the KP as potential pathogenic factors. In our studies we found that kynurenic acid inhibits the electrical stimulation induced elevated PACAP expression in trigaminal nucleus caudalis. These data suggest that KP plays important role in the development of several neurological disorders. Therefore, it is possible that influencing KP has therapeutic potential.

References

1. Boros FA, Klivényi P, Toldi J, Vécsei L. Indoleamine 2,3-dioxygenase as a novel therapeutic target for Huntington's disease. Expert. Opin. Ther. Targets 23:39-51, 2019.
2. Boros FA, Bohár Z, Vécsei L. Genetic alterations affecting the genes encoding the enzymes of the kynurenine pathway and their association with human diseases. Mutat Res. 776:32-45, 2018.
3. Fakan B., Szalardy L, Vecsei L. Exploiting the therapeutic potential of endogenous immunomodulatory systems in multiple sclerosis- specific focus on the Peroxisome Proliferator-Activated Receptors (PPARs) and the kynurenines. Int. J. Mol. Sci. 20, 2019.
4. Hertelendy P, Toldi J, Fülöp F, Vécsei L. Ischemic stroke and kynurenines: Medicinal chemistry aspects. Curr. Med. Chem. in press, 2019.
5. Körtesi T, Tuka B, Tajti J, Bagoly T, Fülöp F, Helyes Z, Vécsei L. Kynurenic acid inhibits the electrical stimulation induced elevated Pituitary Adenylate Cyclase-Activation Polypeptide expression in the TNC. Front. Neurol. 16;8:745, 2018.
6. Vecsei L, Szalardy L, Fülöp F, Toldi J. Kynurenines in the CNS: Recent advances and new questions. Nat. Rev. Drug. Disc. 12:64-82, 2013.
7. Zádori D, Veres G, Szalardy L, Klivényi P, Vécsei L. Alzheimer's disease: Recent concepts on the relation of mitochondrial disturbances, excitotoxicity, neuroinflammation and kynurenines. J. Alzh. Dis. 62:523-547, 2018.