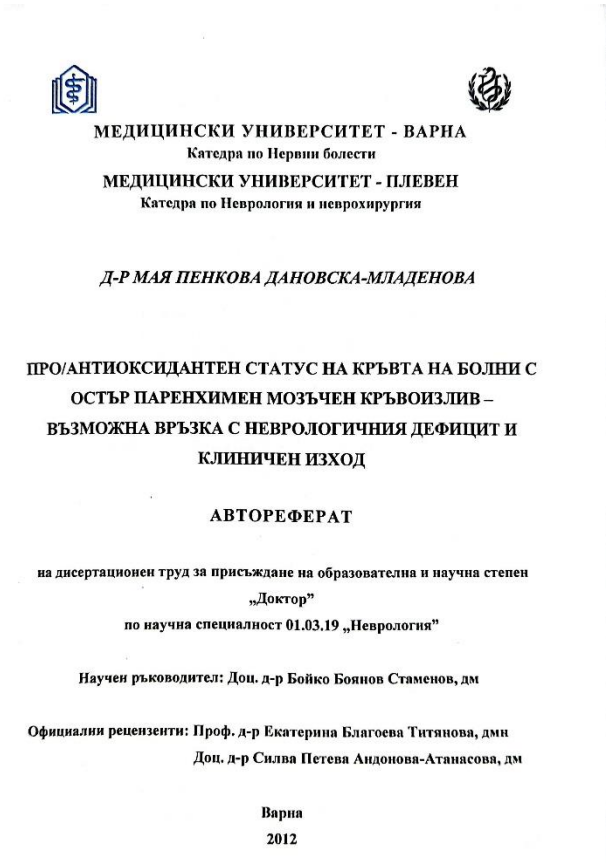
Резюмета

на отпечатаните в пълен текст научни трудове на доц. д-р Мая Пенкова Дановска-Младенова, д.м.

Във връзка с конкурс за заемане на академична длъжност „Професор“ в област на висшето образование 7. „Здравеопазване и спорт“, професионално направление 7.1. „Медицина“, по специалност „Нервни болести“ за нуждите на Катедра „Неврология и неврохирургия“, Факултет „Медицина“, за нуждите на Неврологична клиника, УМБАЛ „Г. Странски“ ЕАД, обявен в ДВ бр. 90/25.10.2024

А1. <u>Дановска, М</u>. Автореферат за дисертационен труд за придобиване на ОНС „Доктор“ на тема: „*Про/антиоксидантен статус на кръвта на болни с остър паренхимен мозъчен кръвоизлив - възможна връзка с неврологичния дефицит и клиничен изход*“



МЕДИЦИНСКИ УНИВЕРСИТЕТ - ВАРНА
Катедра по Нервни болести
МЕДИЦИНСКИ УНИВЕРСИТЕТ - ПЛЕВЕН
Катедра по Неврология и неврохирургия

Д-Р МАЯ ПЕНКОВА ДАНОВСКА-МЛАДЕНОВА

ПРО/АНТИОКСИДАНТЕН СТАТУС НА КРЪВТА НА БОЛНИ С ОСТЪР ПАРЕНХИМЕН МОЗЪЧЕН КРЪВОИЗЛИВ – ВЪЗМОЖНА ВРЪЗКА С НЕВРОЛОГИЧНИЯ ДЕФИЦИТ И КЛИНИЧЕН ИЗХОД

АВТОРЕФЕРАТ

на дисертационен труд за присъждане на образователна и научна степен „Доктор“
по научна специалност 01.03.19 „Неврология“

Научен ръководител: Доц. д-р Бойко Боянов Стаменов, дм

Официални рецензенти: Проф. д-р Екатерина Благоева Титянова, дмн
Доц. д-р Силва Петева Андонова-Атанасова, дм

Варна
2012

проследяване нивата възпалителни маркери, параметри от антиоксидантната система на защита и показатели за оксидативно увреждане в циркулацията.

7. Цялостният труд дава идеи за използване на нови провъзпалителни и оксидативни маркери за тежестта на неврологичния дефицит, клиничния изход и прогнозата на ПМК, които са достъпни за бързо определяне и могат да бъдат прилагани рутинно в клиничната практика за оптимизиране на терапевтичните подходи. Предлага се въвеждане определянето на hs-CRP в задължителния набор от лабораторни изследвания, утвърдени в лечебно-диагностичния алгоритъм на националния консенсус за мозъчно-съдови заболявания.

SUMMARY

Spontaneous intracerebral hemorrhage (sICH) accounts for only 15-20% of all strokes, but is the cause of severe disability and is associated with the highest mortality rate. Despite the increasing stroke incidence sICH still remains an unsolved medical problem. Growing evidence suggests that inflammation and oxidative stress play a crucial role in the pathogenesis of sICH.

Objective: The aim of the present study was to evaluate pro/antioxidant changes in the blood of patients with acute sICH. The hypothesis was that the pro/antioxidant changes following sICH onset are reliable indicators of the brain damage and could serve as prognostic markers of the neurological deficit and clinical outcome.

Case material and methods: To test the hypothesis 171 patients were studied: 101 with sICH, 19 with vascular risk factors and 51 healthy controls.

Results: Leukocyte count, neutrophils and fibrinogen were found significantly increased in patients with sICH. Furthermore, they correlated with the neurological deficit severity and the clinical outcome. Serum CRP level correlated with the neurological state and hematoma volume. Some antioxidant parameters, TAS and ROOH were also found correlated with the neurological state and functional outcome. The impact of some modifiable risk factors, comorbidities and concomitant medication was also assessed. It was found that alcohol abuse and baseline hyperglycemia were associated with poor outcome while previous treatment with ACE-inhibitors and statins improved the functional outcome after sICH.

Binary logistic regression was used to assess the predictive value of the pro/antioxidant changes in the blood of patients with sICH. We found that serum CRP level and hematoma volume were significant predictors of short term mortality in sICH while serum ROOH concentration predicted poor outcome in sICH survivors. What is more, patients with sICH and serum CRP level > 22.4 mg/l had significantly lower chance to survive regardless of their age and sex.

Conclusion: On the base of the study results we can conclude that pro/antioxidant changes in the blood of patients with sICH are important indicators of the neurological deficit severity that could serve as additional laboratory markers of the clinical outcome after sICH.

The present study elucidates the important role of the pro/antioxidant changes in the acute stage of sICH thus enriching the basic and clinical knowledge. The study results show that some nonspecific markers – inflammatory and oxidative, that are easily measured, could serve as additional diagnostic and prognostic tool, thus providing an excellent opportunity for therapeutic interventions while the patient is still in clinic. We also recommend the routine evaluation of serum CRP level as early independent predictor of sICH outcome.

СПИСЪК НА НАУЧНИТЕ ПУБЛИКАЦИИ И СЪОБЩЕНИЯ ВЪВ ВРЪЗКА С ДИСЕРТАЦИЯТА

на д-р Мая Пенкова Дановска-Младенова,
гл.асистент към катедра"Неврология и неврохирургия" при МУ-Плевен

Публикации

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В. Хабилитационен труд - научни публикации в издания, които са реферирани и индексирани в световноизвестни бази данни с научна информация:

B1. **Danovska, M.**, Alexandrova, M., Totsev, N., Gencheva, I., Stoev, P. *Clinical and neuroimaging studies in patients with acute spontaneous intracerebral hemorrhage*. Journal of IMAB, 2014, Jan-Jun, 20(2): 489-494; ISSN: 1312-773X;

ISSN: 1312-773X (Online)

http://dx.doi.org/10.5272/jimab.2014202.489

Journal of IMAB - *Annual Proceeding (Scientific Papers)* 2014, vol. 20, issue 2

CLINICAL AND NEUROIMAGING STUDIES IN PATIENTS WITH ACUTE SPONTANEOUS INTRACEREBRAL HEMORRHAGE.

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ABSTRACT

Objective: To define the prognostic value of clinical and neuroimaging parameters on the 30-th day mortality and clinical outcome after spontaneous intracerebral hemorrhage (sICH).

Materials and methods: we examined 88 patients with sICH admitted to Neurology Clinic, UMHAT Pleven within 48 hours after clinical symptoms onset. Glasgow Coma Scale (GCS) score was used to assess the primary stroke severity; neurological deficit on admission was assessed by National Institute of Health Stroke Scale (NIHSS); clinical outcome at discharge was evaluated by modified Rankin Scale (mRS) and by Glasgow Outcome Scale (GOS) on the 30-th day after sICH onset. Hematoma volume was measured by the formula of Kothari: AxBxC/2 in ml. The statistical analysis was performed by SPSS 19.0 and Statgraphics plus 4.1 for Windows.

Results: Initial assessment of primary stroke severity and neurological deficit by GCS è NIHSS, hematoma localization and volume were found strongly correlated with the clinical outcome on the 30-th day after the sICH onset. Age and vascular risk factors did not correlate with the clinical outcome. Male patients had better survival on the 30-th day compared with the female ones.

Discussion: Neurological deficit on admission, hematoma localization and volume were found reliable predictors of the 30-th day clinical outcome that could serve for early stratification of patients and optimal choice of therapeutic approach.

Key words: CT, neurological deficit, sICH, clinical outcome.

cular intensive care the parameters of sICH morbidity and mortality remain unchanged [2, 8]. Almost 40% of the patients die before the 30-th day after sICH, 66% of the survivors are severely disabled and only 20% recover their functional independence on the 6-th month after the sICH [22].

According to the guidelines of ÀÍÀ [American Heart Association] modern treatment of sICH is mainly supportive and is still one of the greatest challenges in the neurologicall practice [17]. The health and social policy of some countries, providing easy access to highly qualified medical professionals, effective primary prophylaxis and control of vascular risk factors, urgent admission to stroke units with modern intensive care equipment, results in stable reduction of sICH incidence during the last years [25, 26].

Unlike ischemic stroke sICH is less investigated in Bulgaria. There is a substantial lack of population-based studies on the problems of sICH in our country. No prospective studies, based on the hematoma volume measurement and correlative clinical and neuroimaging analyses of neurological deficit and clinical outcome are also conducted [3]. An urgent necessity for performing scientific investigations on sICH arises that could facilitate identification of patients with the highest mortality and disability risk and offer new therapeutic approaches.

The aim of the present study was to define the predictive value of some clinical and radiological parameters for the clinical outcome on the 30-th day after sICH.

MATERIAL AND METHODS

Patients

B2. **Danovska M.**, Peichinska D., Valkova M., Stamenov B. *Verbal choice in ischemic stroke patients with anomic aphasia*. Journal of IMAB, 2014, Jan-Jun, 20(2): 495-497; ISSN: 1312-773X;

http://dx.doi.org/10.5272/jimab.2014202.495

ISSN: 1312-773X (Online)

Journal of IMAB - *Annual Proceeding (Scientific Papers)* 2014, vol. 20, issue 2

VERBAL CHOICE IN ISCHEMIC STROKE PATIENTS WITH ANOMIC APHASIA

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ABSTRACT

Background and purposes: Anomic aphasia is common in patients with left hemispheric strokes. The purpose of this study was to explore the verbal production of ischemic stroke patients with anomic aphasia.

Contingent and methods: Fifty ischemic stroke patients admitted to the Neurology Clinic of University Hospital Pleven were studied by neuropsychological battery and CT scan of the brain. Verbal productivity changes found were analyzed in relation to the speech recovery education.

Results: All the patients showed lower scores at all nominative and reproductive speech subtests.

Discussion: Among the ischemic stroke patients with mild anomic aphasia comparatively great was the percentage of low frequency word actualization and verbal fluency impairment. The usage of nominatives in speech expression of ischemic stroke patients is less as compared with that one of predicatives. Actualization of particles, unions, prepositions and interjections was comparatively high thus compensating the difficulty in choice of a definite lexical number.

Conclusion: Future studies on testing of verbal choice in ischemic stroke patients should confirm its practical significance for the assessment of speech disorders concerning a special speech- recovery education.

Key words: Verbal choice, ischemic stroke, anomic aphasia

clinical signs [2, 3]. Two types of anomic aphasia have been described: phonological and semantic anomia [3].

Verbal productivity of patients with aphasia is extremely important for the correct diagnosis and adequate speech-recovery education [4, 5, 6, 7].

Testing of verbal choice is considered a reliable and objective method for assessment of speech disorders. For that reason verbal choice assessment is still an area of growing scientific investigations and analyses [8].

The purpose of the present study was to examine and to analyze the verbal choice of patients with ischemic stroke and aphasic disorders of anomic type.

CONTINGENT AND METHODS

We studied 50 patients with anomic disorders (32 males and 18 females, 34 to 80 years old), who were admitted to the Neurology Clinic, University Hospital, Pleven. CT scan of the brain was performed to confirm the diagnosis ischemic stroke. Neuropsychological tests of A. R. Luria [8] were used for the evaluation of nominative and reproductive speech of patients with aphasic disorders (modified in Bulgarian language by P.Ovcharova et al) [9]:

· Neuropsychological battery for evaluation of nominative speech function

- naming of 6 objects, located in the visual field;
- naming of 6 objects, based on their description;
- verbal fluency: naming of 5 fruits for 5 seconds.

· Examination of reproductive speech - oral paraphrase of a definite text after it has been read once by

B3. **Danovska M.**, Ovcharov M., Ovcharova E., Mladenovski I., Shepherd N. *Surgical Versus Conservative Treatment of Spontaneous Intracerebral Hemorrhage*. Journal of IMAB, 2019, Apr-Jun, 25(2): 2471-2475; ISSN: 1312-773X; *SJR 0,108*.

Journal of IMAB
ISSN: 1312-773X
https://www.journal-imab-bg.org

https://doi.org/10.5272/jimab.2019252.2471

Journal of IMAB - *Annual Proceeding (Scientific Papers)*. 2019 Apr-Jun;25(2)

Original article

SURGICAL VERSUS CONSERVATIVE TREATMENT OF SPONTANEOUS INTRACEREBRAL HEMORRHAGE

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ABSTRACT

Background: Spontaneous intracerebral hemorrhage (sICH) causes severe disability and high mortality. Today it is still an unresolved medical problem. The choice of optimal management - surgical or conservative, remains a difficult and controversial one. Early evacuation may restrict hematoma expansion and limit the secondary brain damage, improving the outcome for the patient.

Objective: To compare the effectiveness of surgical to conservative treatment of sICH.

Material and Methods: We examined 94 patients with sICH admitted to the Neurology Clinic within 24 hours ofonset. Forty seven patients underwent surgical evacuation and the remaining 47 received conservative medical therapy. Neurological deficit and clinical outcome were assessed by Glasgow Coma Scale (GCS), National Institutes of Health Stroke Scale (NIHSS) and Glasgow Outcome Scale (GOS). Each patient was assessed on two occasions, the first on admission and the second after one month. The statistical analysis was performed with the Statistical Package for Social Sciences, version 13.0 (SPSS).

Results: Neurological deficit, hematoma volume and location displayed correlation with GOS in the conservative group ($p>0.05$), while no statistical significance between GOS and hematoma volume in the surgical group ($p<0.05$) was observed. Surgically treated patients with a baseline GCS>12 had a better final GOS relative to conservatively treated ones. There was no statistically significant difference in GOS on the 30th day of treatment for both groups. The mortality of 4.3% was significantly lower in the surgical group ($p<0.05$).

Conclusion: Early surgery for sICH might be a safe and effective treatment, especially for large hematomas (>60cc) in male patients with progressive impairment of consciousness.

Keywords: Spontaneous intracerebral hemorrhage, surgical treatment, conservative management.

INTRODUCTION

Spontaneous intracerebral hemorrhage (sICH) is the second most common type of stroke due to a leakage of blood into the brain parenchyma caused by a vessel rupture [1]. Although sICH accounts for only 15-20% of all strokes, it is associated with the highest mortality and disability rate [2]. Regardless of modern achievements in neuroimaging techniques and advanced therapeutic options of neurovascular reanimation, the parameters of sICH morbidity and mortality remain unchanged [3]. Almost 40% of the patients die before the 30th day of sICH, 66% of the survivors suffer severe and permanent disability and only 20% recover their functionality by the 6th month [2]. According to the AHA (American Heart Association) guidelines, the modern sICH treatment is mainly symptomatic and has been one of the greatest challenges in the neurological practice [4]. Making the right decision as to whether and when the hematoma should be evacuated has been incredibly difficult and controversial. Early surgical treatment could minimise mechanical compression of the brain parenchyma and eventually prevent the toxic effects of blood degradation products thus limiting the secondary brain damage. On the other side, the risk for the patient from continuous bleeding could be greater, and the craniotomy itself could further damage healthy brain parenchyma. According to some authors, early evacuation of the hemorrhage shortens the hospital stay, lowers financial costs and hastens the patients' return to their daily routine [5]. Still the results from International Surgical Trial inIntracerebral Hemorrhage (STICH) failed to prove significant advantages of early surgical evacuation compared to the conservative treatment [6, 7]. Up to now, multiple surgical approaches as conventional craniotomy, stereotactic guidance with aspiration and thrombolysis, image guided stereotactic endoscopic aspiration and decompressive craniotomy, have presented with varying degree of success. Although hematoma evacuation may be lifesaving, the efficacy of surgical treatment of sICH is still under debate due to the fact it does not improve functional outcome.

The aim of the present study was to compare clini-

B4. Ovcharova, E., **Danovska, M.**, Marinova, D., Pendicheva-Duhlenska, D., Tonchev, P., Atanasova, M., Ruseva, A., Shepherd, N., Tzveova, R. *Adapted Mediterranean Diet Impact on the Symptoms of Chronic Fatigue, Serum Levels of Omega-3 Polyunsaturated Fatty Acids (PUFAs) and Interleukin 17 (IL-17) in Patients with Relapsing-Remitting Multiple Sclerosis undergoing Disease-Modifying Therapy: A Pilot Study*. Journal of IMAB, 2022, Jan-Mar, 28(1): 4297-4304 ISSN: 1312-773X; *IF 0,228; SJR 0,225.*

Journal of IMAB
ISSN: 1312-773X
https://www.journal-imab-bg.org

https://doi.org/10.5272/jimab.2022281.4297

Journal of IMAB - *Annual Proceeding (Scientific Papers).* 2022 Jan-Mar;28(1)

Original article

ADAPTED MEDITERRANEAN DIET IMPACT ON THE SYMPTOMS OF CHRONIC FATIGUE, SERUM LEVELS OF OMEGA-3 POLYUNSATURATED FATTY ACIDS (PUFAS) AND INTERLEUKIN 17 (IL-17) IN PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS UNDERGOING DISEASE-MODIFYING THERAPY: A PILOT STUDY

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SUMMARY

Purpose: This pilot study was designed to investigate the impact of a moderate-calorie Mediterranean diet compared to a regular diet with omega-3 PUFAs (eicosapentaenoic and docosahexaenoic acids) supplementation on fatigue symptoms in patients with relapsing-remitting multiple sclerosis (RRMS) and to assess the optional benefit of the diet on their quality of life.

Material/Methods: This 12-month pilot study was conducted in 2021 at the Department of Neurology, Medical University – Pleven, Bulgaria. A total of 60 patients with RRMS aged 18-64 were selected from the database of the Neurology Clinic at the University Hospital "Dr Georgi Stranski" – Pleven. From the selected patients, only 30 were included in the pilot phase and respectively assigned to the nutritional arms. Blood samples were collected twice – at the first and second visit in 3 months, for metabolic and dietary parameters analysis. Symptoms of fatigue were assessed with Fatigue Scale for Motor and Cognitive Functions (FSMC) and Modified Fatigue Impact Scale (MFIS).

Results: From the 30 participants included in the study, 17 patients attended the clinic centre for complete follow-up; the remaining 13 were only partially observed. The dynamics of the followed-up parameters showed a statistically significant change in the body mass index (BMI), the fatigue symptoms in the FSMC and MFIS scales, total cholesterol and triglycerides levels, and the serum concentrations of IL17A, EPA and DHA. The metabolic caloric values were also found to be significantly changed.

Conclusions: Despite the small study size limitation, this pilot study might be of benefit for further extensive research on the potential favorable impact of diet and lifestyle modifications on the symptoms of fatigue in multiple sclerosis patients.

Keywords: relapsing-remitting multiple sclerosis, Mediterranean diet, chronic fatigue, polyunsaturated fatty acids,

INTRODUCTION:

Multiple sclerosis (MS) is a chronic, autoimmune, demyelinating and neurodegenerative disease of the central nervous system (CNS) with female predominance and usual debut in the third or fourth decade of life. The molecular and tissue manifestation of systemic inflammation and varying degree of autoimmune process activation

B5. Dimitrov G., **Danovska M.**, Simeonova Y., Gencheva I., Stoev P., Ovcharova E., Marinova D. *Comparative Evaluation of Risk Factors in Young and Middle-Age Patients with Acute Ischemic Stroke*. Journal of IMAB, 2020, Jan-Mar, 26(1): 2926-2930; ISSN: 1312-773X; *SJR 0,225*.

Journal of IMAB
ISSN: 1312-773X
https://www.journal-imab-bg.org

https://doi.org/10.5272/jimab.2020261.2926

Journal of IMAB - *Annual Proceeding (Scientific Papers)*. 2020 Jan-Mar;26(1)

Original article

COMPARATIVE EVALUATION OF RISK FACTORS IN YOUNG AND MIDDLE-AGE PATIENTS WITH ACUTE ISCHEMIC STROKE

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ABSTRACT

Background: Ischemic stroke (IS) in young adults has different etiologies and risk factors (RF). A better understanding of the contribution of potentially modifiable RF to the global burden of IS in young adults is crucial for successful prevention strategies.

Objective: To evaluate the incidence and prevalence of different RF in young and middle-age acute IS patients.

Material and Methods: In the study were included 63 patients with acute IS, admitted to the Neurology Clinic Pleven. They were classified in two groups: Group A (n=10) of young (18-44 y) and Group B (n=53) of middle-age (45–59 y) IS patients. Comparative evaluation of the following RF: age, sex, family history of stroke, arterial hypertension (AH), smoking, dyslipidemia, alcohol consumption, low physical activity, obesity and diabetes mellitus (DM) was done. The statistical analysis was performed with the Statistical Package for Social Sciences, version 24.0 (SPSS).

Results: Out of the 63 patients, 42 (66,7%) were males and 53 (84,1%) were 45-59 years old. No gender difference was found in group A, while in Group B, the prevalence of male patients (69,8%) was found, though statistically not significant (p=0.223). A first-degree family history of stroke had 30 (93.8%) of the middle-aged IS patients, as compared to only 2 of the young ones (6,3%), which was statistically significant (p=0.034). Group B showed prevalence of smoking (82,2%), alcohol consumption (83%), body overweight (90,5%), low physical activity (80%), AH (87,3%) and DM (87,3%).

Conclusion: The higher incidence of some RF in middle-age acute IS patients indicates that early identification and control of the RF is the best strategy for reducing stroke mortality and morbidity.

Key words: Ischemic stroke, risk factors, young and middle-age patients,

INTRODUCTION

Stroke is a leading cause of death, physical and mental disability worldwide. Although stroke has been considered a privilege of the older population, recent data reveals the increasing number of "young" strokes [1, 2]. The incidence of IS in the age range 18-50 years is 10.8 to 100 000 population [3]. Approximately 10% of the young and middle-age IS patients remain severely disabled, half of them do not return to work with worsen quality of life thus causing serious economic consequences to their families and the society [4]. Annual expenses for treatment and rehabilitation of IS outpatients are assessed to 5.7 billion US dollars [4]. As the treatment of IS remains limited, the best approach to reduce stroke mortality and morbidity is the primary prevention through RF modification.

IS in young adults is considered a multifactorial disease involving genetic predisposition and a number of modifiable factors. The hypothesis that "young" stroke is associated only with rare RF is still under debate [1]. Regardless of the cumulating information that well-defined traditional RF are widely present in young male patients, undoubtedly IS in young adults has different etiologies and risk factors (RF) from the older population.

Although most of the RF for IS are potentially modifiable (smoking, low physical activity, irrational nutrition, alcohol consumption, dysplipidemia, hyperhomocysteinemia, asymptomatic carotid stenosis, AH, DM and others), their control and management are still a medical and social challenge.

For the purpose of primary stroke prevention in young adults, a multidisciplinary approach, integrating innovative screening and educational programs for early identification and control of the specific modifiable RF, is recommended [3, 4, 5].

The aim of the present study was to evaluate the incidence and prevalence of different RF in young (18-

B6. Yanakieva M., **<u>Danovska M.</u>**, Ovcharova E., Marinova D., Shepherd N. *Tumefactive multiple sclerosis: a diagnostic enigma*. *A case report*. Journal of IMAB, 2023, Apr-Jun, 29(2): 4943-4946; ISSN: 1312-773X; *IF 0,1*.

Journal of IMAB
ISSN: 1312-773X
https://www.journal-imab-bg.org

https://doi.org/10.5272/jimab.2023292.4943

Journal of IMAB. 2023 Apr-Jun;29(2)

Case report

TUMEFACTIVE MULTIPLE SCLEROSIS: A DIAGNOSTIC ENIGMA. A CASE REPORT

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ABSTRACT

Purpose: To present a clinical case of tumefactive multiple sclerosis (TMS), which is an inflammatory demyelinating disease of the central nervous system considered to be a rare form of multiple sclerosis (MS). It belongs to the group of borderline forms of MS – a collective term used to define a spectrum of demyelination-associated neurological conditions that share similar clinical, neuroimaging and histopathological features but vary widely in severity, clinical course and outcome.

Materials/Methods: We describe the case of a 31-year-old female who was admitted to the Neurology clinic of UMHAT "Dr Georgi Stranski" in Pleven, Bulgaria, with a rapid onset of neurological deficit including right-sided hemiparesis, dysarthria, imbalance, cognitive impairment and urinary incontinence. MRI of the brain showed several tumor-like concentric lesions of demyelination surrounded by moderate brain edema, consistent with the radiological criteria for the demyelinating disease.

Results: High-dosage corticosteroids were applied intravenously for this patient as acute therapy. A progressive improvement in the patient was achieved after the extended pulse corticosteroid therapy in combination with physiotherapy. Glatiramer acetate as a disease-modifying treatment was initiated within three months and had substantial efficacy.

Conclusions: The diagnosis of TMS is always difficult and requires not only complex clinical and neuroimaging investigations but also an extensive follow-up of the patient. It is believed that TMS usually has a progressive course and an unfavorable outcome, but a relapsing-remitting course of TMS, albeit rare, is also possible. Our case report confirms that such benign variants of TMS exist. We believe that highlighting such complex clinical cases will contribute to a better understanding of the mystery of MS.

Keywords: demyelinating disease, multiple sclerosis, tumefactive MS, magnetic resonance imaging,

a neoplasm such as size >2 cm, mass effect, edema and ringlike or open-ring enhancement which is usually demonstrated by magnetic resonance imaging (MRI) [1]. It belongs to a group of borderline forms of MS – a collective term used to unify several demyelination-associated neurological conditions that share similar clinical, neuroimaging and histopathological features but vary widely in severity, clinical course and outcome [2]. Some notable disorders in this entity include Balo's concentric sclerosis, Marburg disease, neuromyelitis optica and Schilder's disease [3]. The existing overlap among their clinical and neuroimaging presentation raises the question of whether they manifest as separate diseases or coexist together under the MS spectrum.

The incidence of TMS is from one to three of every 1,000 cases of MS [1]. It is extremely rare, and when encountered, it requires a carefully thought-out and structured diagnostic process. Before the era of MRI, TMS was considered an aggressive, rapidly progressive condition with predominantly fatal outcome [3]. Currently, no therapeutic guidelines for TMS exist, but a remarkable response to high-dosage corticosteroids has been reported in the literature [4]. Nevertheless, the specific MRI findings enable earlier diagnosis and treatment and, thus, a better prognosis of the disease [5].

MATERIALS AND METHODS:

A previously healthy 31-year-old female was admitted to the Neurology clinic of UMHAT "Dr Georgi Stranski" in Pleven, Bulgaria, with weakness of the right extremities, facial asymmetry, cognitive impairment and urinary incontinence. These symptoms appeared a month prior to her admission to the clinic and progressed considerably to the point where she could no longer walk on her own and had to use a wheelchair. The patient did not report any previous diseases or use of medications. She denied any febrile illness prior to the onset of these

B7. Mladenovski I, Mladenovski M, Stoev P, Vasilkova S, **Danovska M**. *Cortical blindness due to bilateral strokes – a case report of Anton syndrome*. Journal of IMAB, 2023, Apr-Jun, 29(2): 5006-5008; ISSN: 1312-773X; *IF 0,1*.

Journal of IMAB
ISSN: 1312-773X
https://www.journal-imab-bg.org

https://doi.org/10.5272/jimab.2023292.5006
Journal of IMAB. 2023 Apr-Jun;29(2)

Case report

CORTICAL BLINDNESS DUE TO BILATERAL STROKES – A CASE REPORT OF ANTON SYNDROME

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ABSTRACT

Background: Blindness (anopia) is a functional loss of vision, which could be due either to ophthalmological or neurological conditions. Blindness may be congenital or acquired. The main causes of blindness in adults are cataracts, uncorrected ametropia (myopia, astigmatism), glaucoma, macular dystrophy, cortical ischemic strokes, etc. In less than 10% of the patients, the reason for cortical blindness is bilateral occipital strokes, one of them hemorrhagic.

Case Description: In the current case report, we present a 75-year-old patient with complaints of headache and visual loss. The patient has a history of a left PCA (posterior cerebral artery) distal ischemic stroke. The CT scan reveals a hypodense cerebral lesion in the left medial occipital cortex and subcortex (lingual gyri and cuneus) and a hyperdense cerebral lesion in the right medial occipital cortex and subcortex (lingual gyri and cuneus). The neurological examination shows only bilateral visual loss without motor deficits. The patient has visual anosognosia and confabulation in the setting of obvious visual loss and cortical blindness(Anton-Babinski syndrome, also known as ABS or Anton syndrome). However, performing cerebellar tests (dysdiadochokinesis, finger-to-nose test, heel-to-shin test, cerebellar ataxia) was not done because of the visual loss. After being consulted by a neurologist and neurosurgeon with the preliminary diagnosis of brain hemorrhage, the patient was admitted to the Neurology Clinic of UMHAT D-r "Georgi Stranski", Pleven, Bulgaria.

Conclusion: Occipital infarction must be considered in all cases with sudden onset of isolated visual loss. Early diagnosis and treatment of stroke reduce mortality and morbidity. The prognosis depends on the extension of the visual cortex damage.

Keywords: cerebral hemorrhagic stroke, ischemic stroke, cortical blindness, bilateral stroke,

BACKGROUND:

Blindness (anopia) is a functional loss of vision due either to ophthalmological or neurological conditions. Blindness may be congenital or acquired. The main causes of visual loss in adults are cataracts, myopia, astigmatism, glaucoma, macular dystrophy, cortical ischemic strokes, etc. Less than 10% of the cases with cortical blindness are caused by bilateral occipital strokes, one of them hemorrhagic [1]. In the current case report, we present cortical blindness due to bilateral strokes – ischemic and hemorrhagic.

CASE DESCRIPTION:

A 75 years man with a sudden onset of headache and visual loss was admitted to the Neurology Clinic, UMHAT "D-r Georgi Stranski". He had a history of left PCA distal ischemic stroke. The neurological examination showed bilaterally isochoric pupils and normal light reflex but complete visual loss. The other cranial nerves were intact. No motor deficit was found. Cerebellar testing was not performed because of the complete visual loss. The fundoscopy was normal. The patient had visual anosognosia and confabulation in the setting of obvious visual loss and cortical blindness defined as Anton-Babinski syndrome, also known as ABS or Anton syndrome [2,3]. A native CT scan revealed a hypodense cerebral lesion in the left medial occipital cortex and subcortex (lingual gyri and cuneus) and a hyperdense cerebral lesion located in the right medial occipital cortex and subcortex (lingual gyri and cuneus).

B8. Mladenovski, I., Mladenovski, M., **Danovska, M.**, Ovcharov, M., Vasilkova, S. *Ischemic stroke versus glioblastoma occurrence–a case report and review of the literature*. Journal of IMAB, 2023, Jan-Mar, 29(1): 4843-4848; ISSN: 1312-773X; *IF 0,1.*

Journal of IMAB
ISSN: 1312-773X
https://www.journal-imab-bg.org

https://doi.org/10.5272/jimab.2023291.4843
Journal of IMAB. 2023 Jan-Mar;29(1)

Case report

ISCHEMIC STROKE VERSUS GLIOBLASTOMA OCCURRENCE – A CASE REPORT AND REVIEW OF THE LITERATURE

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ABSTRACT

Background: Ischemic stroke and gliomas are pathologies with poor prognosis. Aside from different characteristics and incidences, 10% of ischemic stroke patients will develop glioblastoma in the post-ischemic period. The aim of this study is to present the interplay between cerebral ischemic stroke and glioblastoma in one patient and to review literature data.

Case Description: A 61-year-old patient got sick and became confused and inadequate, incorrectly replacing words and syllables. He complained of a severe headache the whole day. The patient was transported to the Emergency Department of UMHAT "Dr Georgi Stranski", and after a neurological examination and a native CT examination of the brain, the patient was admitted to the Neurology clinic with a diagnosis of MCA ischemic stroke. The neurological examination showed a central lesion of the right VIIth and XIIth cranial nerves, Babinski sign (+) on the right side, sensory loss of the right arm and sensory aphasia. Glasgow-Liege Scale (GLS) =18. National Institutes of Health Stroke Scale (NIHSS) = 6. After 4 days of active medical treatment, the patient was discharged from the clinic with improvement. In 2 months and 10 days, the patient was admitted to the ED again with worsening of the clinical signs. An MRI (with contrast) of the head diagnosed the patient with a brain tumor (glioma), and he was admitted to the Neurosurgery clinic for operative treatment.

Conclusion: Ischemic stroke as an early manifestation of brain cancer is rare. Approximately 10% of patients with ischemic stroke may develop glioblastoma. Exact diagnosis and specific treatment of stroke or glioma is always challenging and requires appropriate MRI or CT protocols to make timely and accurate differentiation.

BACKGROUND:

Glioblastoma, also known as glioblastomamultiforme (GBM), is the most aggressive brain tumor. Usually, the initial signs and symptoms of glioblastoma are nonspecific. They may include headache, personality changes, nausea, and neurological deficit specific to stroke. Symptoms often worsen rapidly and may progress to unconsciousness. Ischemic stroke is a medical condition characterized by impaired blood flow that causes brain cells death. Gliomas and ischemic strokes are pathologies with poor prognosis [1]. Aside from different clinical characteristics and incidences, 10% of ischemic stroke patients will develop glioblastoma in the post-ischemic period. Besides the well-known pathogenesis of post-radiation ischemic stroke in glioblastoma patients, the proper mechanism of developing glioblastomain ischemic stroke patients is still unknown [2, 3]. This study aims to present one patient's interplay between cerebral ischemic stroke and glioblastoma and to review literature data.

CASE DESCRIPTION:

A 61-year-old patient got sick and became confused and inadequate, incorrectly replacing words and syllables. He complained of a severe headache the whole day. The patient was admitted to the Emergency Department (ED) of UMHAT "Dr Georgi Stranski" Pleven. After a neurological examination and a native CT examination of the brain, the patient was admitted to the Neurology clinic with a diagnosis of MCA ischemic stroke. The patient had a history of arterial hypertension (treated) and lumbar degen-

B9. Dimitrov, G., **Danovska, M.**, Marinova, D., Stoev, P., Simeonova, Y. *Gender-Related Differences in Modifiable Risk Factors and Ischemic Stroke Subtype in Young and Middle-aged Patients–a prospective study*. Journal of IMAB, 2023, Jan-Mar, 29(1): 4793-4799; ISSN: 1312-773X; *IF 0,1*.

https://doi.org/10.5272/jimab.2023291.4793

Journal of IMAB
ISSN: 1312-773X
https://www.journal-imab-bg.org

Journal of IMAB. 2023 Jan-Mar;29(1)

Original article

GENDER-RELATED DIFFERENCES IN MODIFIABLE RISK FACTORS AND ISCHEMIC STROKE SUBTYPE IN YOUNG AND MIDDLE-AGED PATIENTS – A PROSPECTIVE STUDY

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ABSTRACT

Background: Male and female patients differ in their risk factors (RFs) and ischemic stroke (IS) subtype. A better understanding of the gender–related differences an important approach to successful prevention strategies for reducing the impact and burden of IS in young adults.

Objective: To compare the gender–related differences in the prevalence of modifiable RFs and IS subtypes in young and middle-aged patients.

Material and Methods: In the study were included 80 patients with acute IS, aged 18 – 59 years, admitted to the Neurology Clinic of UMHAT "Dr Georgi Stranski" Pleven. The following RFs were analyzed: arterial hypertension (AH), diabetes mellitus (DM), dyslipidemia, atrial fibrillation (AF), current smoking, number of cigarettes smoked per day, alcohol abuse, low physical activity, body overweight and chronic psychosocial stress. IS subtype was identified according to the Org 10172 Trial of Acute Stroke (TOAST). The statistical analysis was performed with the Statistical Package for Social Sciences, version 26.0 (SPSS).

Results: Of all the 80 patients, 46 (57,5%) were males with a mean age 48,15±7,42 years, and 34 (42,5%) were females with a mean age 47,38±8,56. Male patients had higher rates of AH (80,4%), DM (47.8%), AF (4,3%), current smoking (73,9%), number of cigarettes smoked per day (60,9%), alcohol abuse (41,3%) and chronic psychosocial stress (52,2%), while the female ones showed higher rates of low physical activity (61,8%) and body overweight (38,2%). A statistical significance was found only for AH (p=0,004), DM (p=0,026), current smoking (p=0,007), number of cigarettes smoked per day (p=0,025) and alcohol abuse (p=0,031). The most common subtype of IS in males was large artery atherosclerosis (47,8%) and small vessel occlusion (28,3%). The female patients demonstrated a higher frequency of IS with other determined etiology (38,2%) and undetermined etiology (26,5%).

Conclusion: Our data contribute to a better understanding of the gender–related differences of modifiable RFs and IS subtype in young and middle-aged patients with acute IS. The above findings definitely imply the necessity of developing additional specific therapeutic strategies for the effective control of modifiable RFs and lifestyle improvement in order to reduce the incidence of the most common subtypes of IS.

Keywords: Ischemic stroke, risk factors, gender-related differences, subtype ischemic stroke, young and middle – age patients.

INTRODUCTION:

Stroke is a leading cause of long–term disability and the second cause of death worldwide [1]. More than 11 million people suffer from IS each year. Half of these cerebrovascular events occur in low and middle-income countries. About 10%-20% of IS occur in young adult patients (usually defined as 18-55 years) [2, 3]. Bulgaria ranks third in the incidence of stroke and 9,2% of all strokes occur in young and middle-aged patients with a predominance of males [4].

In the general population IS are more common in males, than in females. According to recently published data, the incidence of IS in young adult males is 30,6 per 100 000, while in females it is 19,1 per 100 000 [5]. Nowadays, the increasing incidence of IS in young adults is associated with a higher prevalence of modifiable RFs. [6].

The INTERSTROKE study proves the major role of the following RFs for IS: AH, DM, dyslipidemia, cardiac disease, current smoking, alcohol abuse, low physical activity and others [7].

Male and female patients differ in their RFs for IS. Some modifiable RFs, such as oral contraceptive use, pregnancy, postpartum period, migraine with aura, and postmenopausal hormone replacement therapy, are female-specific [8]. On the other hand, most of the modifiable RFs are shared and occur in both male and female patients, but have a higher incidence in one of the sexes. This trend emphasizes the need for a better understanding of sex-related differences in modifiable RFs, which are important determinants of the incidence and IS etiologic subtype in young and middle-aged patients [9].

Early identification and control of potentially modifiable RFs for IS are important approaches for primary and secondary prevention strategies in reducing the impact and burden of IS in young adults. [1, 2, 3, 7].

In the present study, we aimed to compare the gender–related differences in the prevalence of modifiable RFs and IS subtypes in young and middle-aged patients.

B10. Yanakieva M., **Danovska M.**, Ovcharova E., Marinova D. *Neurofilaments as a potential biomarker in patients with multiple sclerosis: a review of literature*. Journal of IMAB, 2024, Apr-Jun, 30(2): 5527-5532; ISSN: 1312-773X; *IF 0,1*.

Journal of IMAB
ISSN: 1312-773X
https://www.journal-imab-bg.org

https://doi.org/10.5272/jimab.2024302.5527

Journal of IMAB. 2024 Apr-Jun;30(2)

Review article

NEUROFILAMENTS AS A POTENTIAL BIOMARKER IN PATIENTS WITH MULTIPLE SCLEROSIS: A REVIEW OF LITERATURE

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ABSTRACT

Background: Multiple sclerosis (MS) is a chronic inflammatory neurodegenerative disease of the central nervous system (CNS) characterized by demyelination, axonal damage and loss of neurons. Its growing incidence has determined the need for more intensive research towards effective models for managing disease progression and evaluation of treatment response. Finding clinically relevant biomarkers has been a significant challenge.

Purpose: This review aims to summarize the findings from current relevant literature sources on neurofilaments as a potential biomarker of diagnostic and prognostic value in patients with MS.

Results: Recently, neurofilaments have been identified as the most promising and informative biomarkers of axonal damage and loss. Neurofilament concentration demonstrates a strong association with the disease course, activity and progression, disability accumulation and response to disease-modifying treatment. A significant correlation with future relapse rates, symptom worsening and risk of conversion from clinically isolated syndrome (CIS) to definite MS has also been established. Several MS therapies have demonstrated a substantial reduction in neurofilament levels upon treatment initiation.

Conclusion: The results available from real-world studies and clinical trials regarding neurofilaments as a reliable predictor and indicator of MS disease course are encouraging. They have consistently proven to be of utility if integrated into the diagnostic and therapeutic algorithm of MS patients. This review encompasses undeniable data confirming the considerable potential of neurofilaments for becoming the first globally verified biomarker for MS. The accessibility, safety, low cost and possibility for serial evaluation make the neurofilaments the perfect component to be implemented in routine clinical tests for MS.

Keywords: multiple sclerosis, biomarkers, neurofilaments, disease progression, disability, disease-modifying treatment,

BACKGROUND

Multiple sclerosis (MS) is a chronic inflammatory neurodegenerative disease of the central nervous system (CNS) characterized by demyelination, axonal damage and loss of neurons [1,2]. In the last decades, studies of MS immunopathology have grown remarkably. Our current knowledge of this mysterious disease is as great as it has never been before, and yet, it is still incredibly difficult to predict long-term clinical disease progression and prevent lasting disability.

Currently, modern diagnostic and prognostic strategies rest mainly on the clinical and neuroimaging features of MS patients [3]. Although the immunopathogenesis of MS is well-studied, there are still some crucial differences among individual patients with MS. The clinical course, progression and response to disease-modifying treatment (DMT) still vary widely among the MS population [4]. Some patients could stay relapse-free for years, also known as benign MS, and others would present with a very aggressive and rapidly progressing disease trajectory. It is still unclear what differentiates one group from the other and which factors impact the disease course exactly [5].

Current concepts indicate neurodegeneration and neuronal death as the main cause of disease progression and accumulation of disability. Nevertheless, axonal loss is an irreversible process, which highlights the imminent need for people with MS to be diagnosed as early as possible in the disease course [6]. The existing framework for the clinical management of MS patients relies predominantly on radiological markers (magnetic resonance imaging, MRI) and immunological evidence of inflammation (oligoclonal bands, OCBs). As essential as these tools are in MS diagnosis, they have not proven to be as useful and reliable in long-term monitoring and prediction of relapse rate, disease progression and treatment response [7]. Moreover, they have limited sensitivity when it comes to the so-called "smoldering" MS. Ultimately, the current knowledge emphasizes a growing need for alternative pre-

Г7. Публикации и доклади, публикувани в научни издания, реферирани и индексирани в световноизвестни бази данни с научна информация:

Г7.1 Alexandrova, M., **Danovska, M.** *Cognitive impairment one year after ischemic stroke: Predictors and dynamics of significant determinants*. Turkish Journal of Medical Sciences, 2016, 46(5): 1366-1373; ISSN:1300-0144; *IF 1,2*; *SJR 0,26*.

TÜBİTAK

Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2016) 46: 1366-1373
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doi:10.3906/sag-1403-29

Cognitive impairment one year after ischemic stroke: predictors and dynamics of significant determinants

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Received: 06.03.2014 • **Accepted/Published Online:** 18.12.2015 • **Final Version:** 17.11.2016

Background/aim: Evidence suggests that the risk for dementia increases after stroke. This study investigated the dynamics of the neurological and cognitive status of patients with no baseline dementia over a 1-year period after ischemic stroke.

Materials and methods: We examined 47 ischemic stroke patients admitted within 48 h of ictus. Their neurological and cognitive statuses, blood biochemical parameters, and microalbuminuria levels were prospectively evaluated over a 1-year period post-stroke.

Results: A more severe neurological deficit was found in the cognitively impaired patients (P = 0.003). The NIHSS score over a 1-year follow-up period improved only in patients with normal cognition (P = 0.000). Time-varying dynamics of the MMSE score were observed in both patient groups (P = 0.000). Age (P = 0.000), education (P = 0.004), sex (P = 0.041), history of diabetes (P = 0.045), and serum high sensitive C-reactive protein (hs-CRP) on admission (P = 0.003) were significant determinants of cognitive decline 1 year after a stroke. The albumin-to-creatinine ratio was high during the whole follow-up period in the cognitively impaired group after adjusting for sex and age (P = 0.010). Binary logistic regression showed that hs-CRP (P = 0.013) and age (P = 0.010) were independent predictors of patients' cognitive status 1 year after stroke.

Conclusion: The level of inflammatory markers could be considered as an additional criterion of long-term cognitive impairment.

Key words: Cognitive impairment, hs-CRP, ischemic stroke, long-term prognosis, endothelial dysfunction

Г7.2 **Danovska, M.**, Marinova, D., Mladenovski, I., Ovcharova, E., Ivancheva, V., Totsev, N., Tzankov, L. *Extensive intracranial calcification with neurological and ophthalmological complications in a patient with idiopathic hypoparathyroidism: a case report.* Journal of IMAB, 2018, Apr-Jun, 24(2): 1991-1994; ISSN: 1312-773X; *SJR 0,108*.

Journal of IMAB
ISSN: 1312-773X
https://www.journal-imab-bg.org

https://doi.org/10.5272/jimab.2018242.1991

Journal of IMAB - *Annual Proceeding (Scientific Papers).* 2018 Apr-Jun;24(2)

Case report

EXTENSIVE INTRACRANIAL CALCIFICATION WITH NEUROLOGICAL AND OPHTHALMOLOGICAL COMPLICATIONS IN A PATIENT WITH IDIOPATHIC HYPOPARATHYROIDISM: A CASE REPORT.

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ABSTRACT

Background: Idiopathic hypoparathyroidism is a rare endocrine disorder caused by the deficiency of parathyroid hormone. It typically has a progressive course and is characterized by accumulations of calcium deposits in the basal ganglia bilaterally. In untreated patients, the intracranial calcification may also affect the thalamus, dentate nuclei, cerebral cortex, grey-white junctions and the cerebellum. Different locations can mimic multiple neurological diseases making the diagnosis of that rare disease a challenge.

Purpose: To present a clinical case with untreated idiopathic hypoparathyroidism, extensive intracranial calcifications and neurological and ophthalmological complications.

Material and methods: We present a 50-year-old man with untreated idiopathic hypoparathyroidism who was diagnosed in 2015 with massive intracranial calcifications located in the basal ganglia and outside the extrapyramidal structures. The neurological examination showed involuntary choreoathetotic movements of the right arm, progressive severe cognitive decline, generalized tonic-clonic seizures, gait imbalance and visual disorders. Abnormalities in the calcium-phosphorus metabolism and renal function tests were found. CT scans demonstrated extensive brain calcifications. The ophthalmological examination showed diminished visual acuity and mature cataract. The histopathological result did not demonstrate ragged red fibres. Some differential diagnostic opportunities like Fahr's disease or Kearn Sayre's syndrome were also consicered.

Results: The patient was diagnosed with untreated childhood idiopathic hypoparathyroidism with extensive intracranial calcifications and neurological and ophthalmological complications – a rare clinical case. This was confirmed by his medical history, general, neurological and ophthalmological examinations, laboratory, histopathological and neuroimaging investigations.

Conclusion: The CT findings demonstrating extensive intracranial calcifications in the basal ganglia and the extrapyramidal structures make the presented clinical case a diagnostic challenge.

Keywords: Idiopathic hypoparathyroidism, brain calcifications, Kearn Sayre's syndrome.

BACKGROUND

Idiopathic hypoparathyroidism is a rare endocrine disorder associated with deficiency of parathyroid hormone causing decreased blood levels of calcium and higher phosphorus [1, 2]. Basal ganglia calcification was first described by Eaton in 1939 as part of chronic hypoparathyroidism [3]. It is a progressive disorder despite the maintenance of normal calcium levels [3]. Repeated CT scans show the accumulation of calcium deposits by detecting new and increased volume of old calcification sites. Brain calcifications are frequently spread in the basal ganglia bilaterally: the lentiform (putamen and globus pallidus) and the caudate nuclei [2]. Calcifications are rarely spread over the dentate nucleus, corona radiata, subcortical white matter and thalamus [2]. Up to 1.5% of the patients with hypoparathyroidism have calcifications in the thalamus, dentate nuclei, cerebral cortex, gray-white junctions and the cerebellum [3]. The exact mechanism of extensive intracranial calcification has not been clarified yet. It could stem from lower PTH level, but also from the hypocalcaemia and hyperphosphatemia duration [4]. Scientific research shows that hyperphosphatemia is important for the ectopic brain calcifications and the superoxide production of mitochondria in patients with idiopathic hypoparathyroidism and intracranial calcifications [4]. Bilateral symmetrical calcification is typical for Fahr's disease, however, the patient's biochemical profile is normal [2].

Г7.3 Marinova, D., **Danovska, M.** *The non-motor symptoms–challenge in diagnosis of Parkinson's Disease*. Journal of IMAB, 2020, Oct-Dec, 26(4): 3469-3474; ISSN: 1312-773X; *SJR 0,225.*

Journal of IMAB
ISSN: 1312-773X
https://www.journal-imab-bg.org

https://doi.org/10.5272/jimab.2020264.3469

Journal of IMAB - *Annual Proceeding (Scientific Papers).* 2020 Oct-Dec;26(4)

Review article

THE NON-MOTOR SYMPTOMS–CHALLENGE IN DIAGNOSIS OF PARKINSON'S DISEASE

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ABSTRACT

Parkinson's disease (PD) is the second most common neurodegenerative disorder after the dementia of Alzheimer. The clinical presentation of PD is dominated by typical motor symptoms as resting tremor, cogwheel rigidity, bradykinesia, and postural instability. Non-motor symptoms (NMS) of Parkinson's disease are common but are often under-recognized in clinical practice either due to the lack of spontaneous complaints by the patients or to the absence of systematic questioning by healthcare professionals. In contrast to motor dysfunctions, non-motor symptoms frequently remain unreported. Recently, a self-completed NMS questionnaire and NMS scale for identification and evaluation of these symptoms have been validated. An international survey has shown that up to 62% of NMS in PD remain undeclared to healthcare professionals because patients are unaware that NMS symptoms are linked to PD. Based on both clinical and neuropathological data, PD, traditionally accepted as a dopaminergic motor disorder, now can be characterized as a multisystem neurodegenerative disease that involves many neurotransmitter systems and affects not only motor but non-motor functions, too.

Keywords: Parkinson's disease (PD), Non-motor symptoms (NMS), quality of life,

lation suffer from PD. The prevalence of PD tends to increase with ageing, and approximately 1% of the population above 60 years is affected by PD [3]. According to the epidemiological study of Van Den Eeden SK et al., the incidence of PDrapidly increases over the age of 60 years, with only 4% of the cases being under the age of 50 years.[4]. In Bulgaria, no official data concerning the incidence of PD have been published. Taking into consideration that the population of Bulgaria is about 7.500.000, the indicative number of patients with PD must be about 12.000-13.000 [5].

NON – MOTOR SYMPTOMS OF PD (NMSPD)

Non–motor symptoms (NMS) of Parkinson's disease (PD) are common, but are often underrecognized in clinical practice because of the lack of spontaneous complaints by the patients, or by the absence of systematic questioning from the healthcare professionals [6]. In contrast to the evident motor dysfunctions, the non–motor symptoms, frequently remain unreported and hidden for the examiner. Recently, a self-completed NMS questionnaire and NMS scale for identification and evaluation of NMS in PD have been validated. An international survey has shown that up to 62% of NMS in PD may remain undeclared to healthcare professionals because patients may be unaware that the symptoms are linked to PD [7]. NMSs in PD were system-

Г7.4 Ovcharova, E., **Danovska, M.**, Marinova, D., Pendicheva, D., Tonchev, P., Shepherd, N. *Role of diet and supplementation with omega-3 polyunsaturated fatty acids for managing chronic fatigue in patients with relapsing-remitting multiple sclerosis*. Journal of Biomedical and Clinical Research, 2022, 15(2): 99-104; ISSN: 1313-6917;

sciendo

J Biomed Clin Res Volume 15 Number 2, 2022

DOI:10.2478/jbcr-2022-0013

Review

ROLE OF DIET AND SUPPLEMENTATION WITH OMEGA-3 POLYUNSATURATED FATTY ACIDS FOR MANAGING CHRONIC FATIGUE IN PATIENTS WITH RELAPSING-REMITTING MULTIPLE SCLEROSIS

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Summary

Multiple sclerosis (MS) is a chronic autoimmune demyelinating disease of the central nervous system (CNS) with unclear and multifactorial etiology, variable clinical symptoms with different severity, and treatment with limited efficacy. Authors conclude that the immune system has a role in pathogenesis, and many modern therapies target the immune system. Among clinicians, it is accepted that not every patient will progress in the same way, and there is high variability between clinical courses of MS in different patients.

Modern therapies have shown to reduce new lesions and clinical relapses but lack effectiveness at halting underlying neurodegeneration at lesions, the localized inflammation on a small scale, chronic demyelination, and axonal and neuronal damage. Dietary metabolites have far-reaching and systemic effects. It has been suggested that diet can play an essential role in helping to modify immune system function to promote regulation as opposed to inflammation. Polyunsaturated fatty acids decrease inflammation through conversion into anti-inflammatory prostaglandins E1 and E2, which affect cytokine production, leukocyte migration, and other immune system components. The Mediterranean style diet is a diet low in saturated fats, high in polyunsaturated and monounsaturated fats, rich in fruits and vegetables, and low in processed foods (low salt content). Eating a Mediterranean-style diet can help reduce fatigue (as reported by patients) and change the clinical course favorably.

Keywords: relapsing-remitting multiple sclerosis, Mediterranean diet, chronic fatigue, polyunsaturated fatty acids, interleukin 17

Г7.5 Marinova, D., **Danovska, M.**, Todorova, Y., Obreshkova, T. *Depression in Parkinson's Disease–Profile and Assessment*. Journal of Biomedical and Clinical Research, 2023, 16(2): 91-95; ISSN: 1313-6917;

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J Biomed Clin Res Volume 16 Number 2, 2023

DOI:10.2478/jbcr-2023-0012

Review

DEPRESSION IN PARKINSON`S DISEASE – PROFILE AND ASSESSMENT

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Summary

Depression and anxiety are the most common nonmotor symptoms in Parkinson`s disease-NMSPD in the department of the neuropsychiatric disorders. Depression is present in all stages of PD - early and advanced even in premorbid stage of PD. The incidence of depression in PD varies in large limits according of used methods and criterions. Some somatic symptoms are part of the depression syndrome. At the presence no consensus exists about the etiology of depression in PD. The concomitant occurrence of depression and PD and the overlapping symptomatology of PD and depression usually lead to the terminological discussion and discrepancy. To explain the high prevalence of depression in PD some hypotheses have been proposed. Many scales were used for assessment of depression in PD. The properties and critique of nine scales was discussed.

Keywords: Parkinson`s Disease (PD, nonmotor symptoms in Parkinson`s Disease (NMSPD), health related factors quality-of-life (HRQL)

Г7.6 Vasileva, V., Stoev, P., **Danovska, M.**, Mladenovski, I., Ovcharova, E., Simeonov, E. *Painless Neuralgic Amyotrophy (Parsonage-Turner syndrome)–a case report*. Journal of IMAB, 2024, Jan-Mar, 30(1): 5346-5349; ISSN: 1312-773X; *IF 0,1*.

Journal of IMAB
ISSN: 1312-773X
https://www.journal-imab-bg.org

https://doi.org/10.5272/jimab.2024301.5346

Journal of IMAB. 2024 Jan-Mar;30(1)

Case report

PAINLESS NEURALGIC AMYOTROPHY (PARSONAGE-TURNER SYNDROME) – A CASE REPORT

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ABSTRACT:

Background: Neuralgic amyotrophy (NA) is a rare disorder typically characterized by an abrupt onset of upper extremity pain followed by progressive muscle weakness, atrophy and occasional sensory loss. Although NA has been hypothesized to be an autoimmune-mediated disorder. It is considered a primarily clinical diagnosis, electrodiagnostic evaluation is essential for the diagnosis confirmation and can exclude other etiologies. Electrodiagnostic findings can reveal patchy damage to any nerve within the brachial plexus.

Case Description: In the current case report, we are presenting a 43-years-old man admitted to the Neurology Department of "UMHAT Dr. Georgi Stranski" in Pleven, Bulgaria, with decreased muscle strength and limited active movements in the left upper shoulder for approximately 3 weeks. The patient denied feeling any pain during the onset and afterwards. He had no previous infections, vaccinations and history of other diseases. The detailed neurological examination showed the left upper extremity decreased antigravity strength in the deltoid and infraspinatus muscles with marked atrophy of the same. Hyporeflexia of the left biceps and brachioradialis deep tendon reflexes was present. Electromyography findings showed denervation of the deltoid and infraspinatus muscles. Initial reinnervation of supraspinatus and cervical paraspinal muscles was present. The diagnosis of NA was confirmed by both the neurological examination and the electrophysiological findings.

Conclusion: We are presenting a clinical case of idiopathic neuralgic amyotrophy with atypical painless presentation and discussing the most significant aspects of the disorder with regards to the difficulties in approaching the correct diagnosis. A better understanding of the NA clinical symptoms and signs variability improves the diagnostic and therapeutic approach.

Keywords: Neuralgic amyotrophy, Personage-Turner syndrome, painless,

BACKGROUND

Neuralgic amyotrophy (NA), also known as Parsonage–Turner syndrome (PTS) and idiopathic brachial neuritis, is a rare disorder typically characterized by an abrupt onset of upper extremity pain followed by progressive muscle weakness, atrophy and occasionally sensory loss. Although PTS has been hypothesized to be an autoimmune-mediated disorder, its etiology is still unknown. NA is considered a primarily clinical diagnosis, electrodiagnostic evaluation is essential for the diagnosis confirmation and can exclude other etiologies. [1, 2, 3, 4] Electrodiagnostic findings can reveal patchy damage to any nerve within the brachial plexus. NA is often misdiagnosed as cervical radiculopathy, spinal cord compression, adhesive capsulitis, rotator cuff impingement, labral tear, glenohumeral osteoarthritis, malignancy and even amyotrophic lateral sclerosis. [5]

CASE DESCRIPTION

We present a 43-year-old man, admitted to the Neurology Department of "UMHAT Dr. Georgi Stranski" Pleven, with decreased muscle strength and limited active movements in the left upper shoulder for about 3 weeks. He reported that his complaints started the following morning after heavy physical activity related to his job. The patient denied any feeling of pain at the onset and afterwards. He had no previous infections, vaccination and history of other diseases. The detailed neurological examination showed that the left upper extremity decreased antigravity strength (2/5) in the deltoid and infraspinatus muscles with marked atrophy of the same. Hyporeflexia of the left biceps and brachioradialis deep tendon reflexes was present. The left arm exteroceptive sensation was normal. Normal strength, sensation, and reflexes were present in the right upper extremity without increased tone, fasciculations, or atrophy. Provocative tests for radiculopathy, musculoskeletal shoulder pathology, and peripheral nerve entrapment were negative. The initial laboratory workup was completely unremarkable. (image 1) (image 2) Photos of the

Г7.7 **Danovska M.** *Tabes dorsalis: is the diagnosis a challenge nowadays?* Journal of IMAB, 2024, Jul-Sep, 30(3): 5642-5644; ISSN: 1312-773X; *IF 0,1.*

https://doi.org/10.5272/jimab.2024302.5642

Journal of IMAB. 2024 Jul-Sep;30(3)

Journal of IMAB
ISSN: 1312-773X
https://www.journal-imab-bg.org

Case report

TABES DORSALIS: IS THE DIAGNOSIS A CHALLENGE NOWADAYS?

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ABSTRACT

Purpose: To present a rare case of neurosyphilis, the tertiary form of syphilitic infection, following adequate but belated treatment and manifesting with a variety of clinical signs and further progression to tabetic neurosyphilis. Known as the "great imitator", neurosyphilis is often misdiagnosed and underestimated.

Materials/methods: A 48-year-old male patient was admitted to the Neurology clinic of UMHAT "Dr Georgi Stranski" Pleven, Bulgaria, with progressive neurological deficit including numbness in the lower limbs, imbalance and wide-based gait. The T2W- MRI showed abnormally high longitudinal signals at Th12-L1 level, consistent with transverse myelitis. CSF analysis revealed leucocytic pleocytosis, elevated proteins and normal glucose. The nerve conduction studies confirmed sensory motor polyneuropathy.

Results: After treatment with intravenous aqueous crystalline (IV) penicillin, 2 million intravenously every 4 hours for 20 days, the sensory symptoms reduced. The coordination disturbances persisted, but the gate showed moderate improvement.

Conclusions: The diagnosis of syphilitic myelitis, known as tabes dorsalis, is always complex, not only because of its rarity but because of its unique clinical presentation with multiple clinical symptoms, mimicking other more common neurological disorders. Though confirmation of the diagnosis needs a lot of laboratory and neuroimaging studies, the option of effective specific treatment is worth all the efforts.

Keywords: neurosyphilis, tabes dorsalis, syphilis, sensory ataxia,

INTRODUCTION

Syphilis is a sexually transmitted infection caused by a spirochete, Treponema pallidum. Neurosyphilis, the tertiary form of syphilitic infection occurring most often due to inadequate treatment or lack thereof, can manifest either with early symptoms or with further progression as late neurosyphilis. Tabes dorsalis, also called tabetic neurosyphilis, affects the posterior columns of the spinal cord and the dorsal roots. Its clinical presentation includes sensory ataxia, neuropathic pain and less commonly, paresthesia and gastrointestinal disturbances [1].

In the 21st century, with the availability of various antimicrobials and prompt diagnosis and treatment, the progression of syphilis to its secondary and tertiary forms is rarely seen. Since the introduction of penicillin during the 1940s, the incidence of neurosyphilis has declined profoundly. However, with the increasing number of HIV cases, there has been a surge in the cases of neurosyphilis. Worldwide, approximately 30% of the total syphilis cases have a complication with late neurosyphilis, with one-third suffering from tabes dorsalis [2]. Due to the wide spread use of antibiotics, its typical forms have been replaced by atypical ones, making the diagnosis challenging [3, 4]. The incidence of neurosyphilis has been ranging between 0.47 and 2.1 cases per 100,000 [5]. In the early stages of the infection, frequent manifestations include asymptomatic or symptomatic meningitis, gumma and meningovascular syphilis. Late symptomatic neurosyphilis (dementia paralytica and tabes dorsalis) occurs in 10 to 20% of all untreated cases, developing decades after the primary infection [6]. In the modern era, late symptomatic neurosyphilis has been significantly less reported in developed countries, most often observed in untreated patients or in patients with HIV coinfection [7].

Г7.8 Dimitrov G., **Danovska M.**, Mineva E.. *A Prospective Study of Age-Related Differences in Modifiable Risk Factors, Stroke Subtype and Functional Outcome in Young and Middle-Aged Patients with First-Ever Ischemic Stroke* Journal of Biomedical and Clinical Research, 2024, ISSN: 1313-6917;

JBCR Journal of Biomedical & Clinical Research
Journal of Medical University of Pleven

Journal of Biomedical and Clinical Research 17(2): 157–166 (2024)
DOI: 10.3897/jbcr.e132202

Research Article

A prospective study of age-related differences in modifiable risk factors, stroke subtype, and functional outcome in young and middle-aged patients with first-ever ischemic stroke

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Summary

The objective of our study was to compare the age-related differences in the prevalence of modifiable risk factors (RF), stroke subtype and functional outcome at hospital discharge in young and middle-aged patients with first-ever ischemic stroke (IS). The study included 120 patients with acute first-ever IS, aged 18–59 years, admitted to the Neurology Clinic of Dr. Georgi Stranski University Hospital, Pleven. Of these, 41 (34.2%) were in the young-age group and 79 (65.8%) were middle-aged. The middle-aged patients had higher rates of arterial hypertension (81.0%), diabetes mellitus (45.6%), dyslipidemia (83.5%), low levels of HDL cholesterol (68.4%), high levels of LDL cholesterol (72.2%) and arterial fibrillation (7.6%). The most common subtype of IS in middle-aged patients was large artery atherosclerosis (40.5%), small vessel occlusion (29.1%) and cardioembolism (6.3%). In comparison, we found a higher incidence of IS in the young patients with other determined (34.1%) and undetermined aetiology (34.1%). Our data on functional outcomes at hospital discharge confirm age-related differences in the prevalence of modifiable RFs and stroke subtype in young and middle-aged patients with first-ever IS. These findings highlight the need to develop specific therapeutic approaches for early identification and effective control of health- and lifestyle-related RFs to reduce the incidence of the most common subtypes of IS.

Key words: functional outcome, ischemic stroke, lifestyle-related risk factors, middle-aged patients, young patients

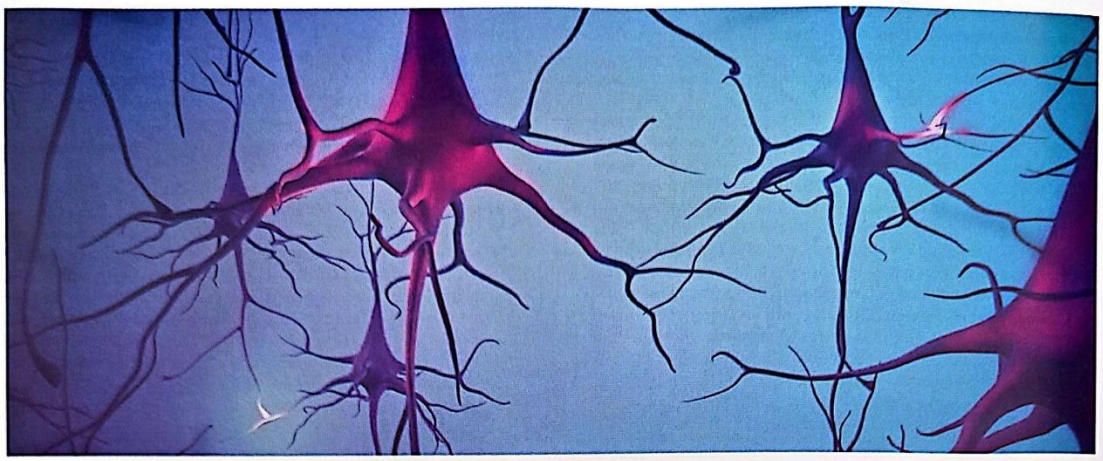
OPEN ACCESS

Academic editor: Galya Stavreva
Received: 21 November 2023
Accepted: 19 April 2024
Published: 7 August 2024

Citation: Dimitrov G, Danovska M, Mineva-Dimitrova E (2024) A

Г8. Публикации и доклади, публикувани в нереферирани списания с научно рецензиране или в редактирани колективни томове:

Г8.9 **М. Дановска**, Д. Маринова-Трифонова, Е. Овчарова. *Когнитивни нарушения при мозъчно стареене*. Медикарт, 2018, бр. 4, стр. 38-42; ISSN: 1312-9384



Когнитивни нарушения при мозъчно стареене

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Постиженията на съвременната медицина осигуряват все по-дълга средна продължителност на живот. Уникалната възможност, която се предоставя на възрастните хора да живеят пълноценно и независимо, често е компрометирана от настъпващи когнитивни дисфункции. Нормалното стареене е свързано с известен когнитивен упадък, включващ нарушения предимно в епизодичната памет и екзекутивните функции. Почти 40% от хората над 65 години имат някаква форма на паметови нарушения (1). Липсата на медицински установена причина за отслабване на паметта се дефинира като „свързано с възрастта когнитивно нарушение", представляващо естествена част от процеса на нормалното мозъчно стареене (2).

В световен мащаб е налице тенденция за застаряване на населението. Делът на възрастовата група над 85 години нараства с най-бързи темпове, а броят на населението над 65 години се очаква да се удвои в следващите 40 години (3). Нормалното стареене е съпроводено от редица когнитивни промени, повлияващи ежедневието и функционалната независимост на възрастните, и тяхното добро познаване позволява своевременното разграничаване на нормалното остаряване от патологични състояния като леки когнитивни нарушения и деменция.

Когнитивните промени като част от нормалния процес на стареене са добре документирани в научната литература (4). Някои когнитивни способности като езиковите умения остават гъвкави при стареещия мозък, дори биха могли да се подобрят с годините. Други като памет, концептуално разсъждение и скорост на обработка на информацията постепенно намаляват с напредване на възрастта.

Невропсихологични аспекти на нормалното стареене

Концепцията за „кристализирана" и „флуидна" интелигентност се прилага при описание на моделите на когнитивни промени през целия живот. Кристализирата интелигентност включва познания, възможности и умения на базата на дългосрочната памет. Тя се оценява с тестове за езикови познания и професионална експертност (2). Кристализираните умения и способности остават стабилни или постепенно се подобряват през 6-ата и 7-ата декада на живота (1). Тъй като кристализираната интелигентност се дължи на натрупаната в практиката информация, възрастните изпълняват по-добре определени задачи, изискващи този тип интелигентност, в сравнение с по-младите хора. Флуидната интелигентност касае способности, участващи при решаването на проблеми и разсъждения за по-малко познати и независими от заучените неща. Флуидната когниция се основава на краткосрочната памет и включва персоналната, присъща на човека възможност да обработва и заучава нова информация, да решава проблеми, да присъства и манипулира обкръжението си (5). Екзекутивните функции, скоростта на обработване, паметта и психомоторните възможности са флуидни когнитивни домейни. Психомоторните умения и скоростта на обработка достигат своя пик през третото десетилетие от живота, след което постепенно намаляват (2).

Когнитивните възможности обединяват: скорост на обработка, внимание, памет, език, зрително-пространствени възможности и екзекутивни функции.

Скоростната обработка представлява скоростта, с която се осъществяват когнитивните активности и съответните моторни отговори. Тази флуидна способност започва да намалява през третата декада на живота (1). В резултат на забавена скорост на обработване негативно се повлияват невропсихологичните тестове, оценяващи другите когнитивни домейни.

Вниманието се определя като възможност за концентриране и фокусиране върху отделни стимули. Възрастово обусловеният ефект е отчетен при изпълнение на по-сложни задачи за внимание като селективно и разпределено внимание (1). Възрастните се справят по-лошо със задачи, изискващи включване на работната памет, като например подреждане на поредица от букви и числа в правилна буквено-цифрова последователност.

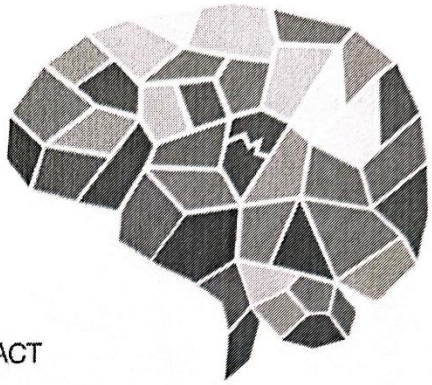
Едно от най-често срещаните субективни оплаквания при възрастни пациенти е промяна в паметта, индикатор не само за когнитивно влошаване, но и за съпътстваща депресия (таблица 1). Паметовите нарушения при нормално стареене могат да бъдат обяснени с намалена скорост на обработка (6), редуцирана възможност за игнориране

Г8.10 Дановска М., Маринова-Трифонова Д., Овчарова Е., Димитров Г. *Рискови фактори за мозъчен инсулт специфични за млада възраст*. MED Post, 2019, бр. 31, стр. 60-64; ISSN: 2367-6469

НЕВРОЛОГИЯ

Рискови фактори за МОЗЪЧЕН ИНСУЛТ

СПЕЦИФИЧНИ ЗА МЛАДА ВЪЗРАСТ



Доц. Мая Дановска, дм, д-р Д. Маринова-Трифонова, д-р Е. Овчарова, д-р Г. Димитров
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Мозъчният инсулт е спешно състояние в неврологията с нарастваща медицинска и социална значимост. Според актуални статистически данни мозъчният инсулт е втората водеща причина за смъртност в световен мащаб като понастоящем около 5,7 милиона души загиват от инсулт и се прогнозира техният брой да нарастне до 7,8 милиона през 2030 година (1). Очертаващите се тенденции за застаряване на населението и подмладяване на инсултите превръщат в сериозно предизвикателство задълбоченото познаване на съдовия рисков профил на пациентите и прилагане на ефективни превантивни мерки за намаляване заболяемостта и смъртността от мозъчен инсулт, особено при млади хора. Колкото и непредвидим да е мозъчният инсулт като заболяване и непредсказуем като резидуален неврологичен дефицит, безспорно доброто познаване и ефективният контрол на рисковите фактори за мозъчен инсулт се оказва най-ефективната терапевтична стратегия на лекаря в аспект на първична и вторична профилактика.

Приблизително 5% от пациентите с исхемичен мозъчен инсулт са на възраст до 45 години, а 10% са по-млади от 50 години. В литературата съществуват различни дефиниции за мозъчен инсулт в млада възраст (между 40-55 години) поради различията в етиологията и рисковите фактори между младите и по-възрастни пациенти. При възрастните пациенти с исхемичен мозъчен инсулт основната съпътстваща патология е представена от атеросклероза на магистрални съдове, абсолютна аритмия от предсърдно мъждене и оклузия на малки съдове. Най-важните рискови фактори, засягащи съществено кардиоваскуларната система, като хипертония, захарен диабет и дислипидемия не са обичайни за младите пациенти, при които водещите рискови фактори са различни и подлежат на допълнителни проучвания.

Друга особеност, отличаваща младите от възрастни пациенти с исхемичен мозъчен инсулт е, че дори след задълбочено клинично и лабораторно изследване при повечето от тях етиологията на мозъчносъдовия инцидент остава недефинирана, без да бъде доказан добре документиран рисков фактор. При много от тези пациенти остават неидентифицирани дори рискови фактори за исхемичен мозъчен инсулт като алкохолна злоупотреба, обструктивна сънна апнея или нарушения в кръвосъсирването.

В групата от рискови фактори, определяни като специфични за възникване на мозъчен инсулт в млада възраст, се включват генетична или придобита тромбофилия, употреба на неразрешени наркотични вещества, мигрена с аура, сърдечни предсърдни аномалии, злоупотреба с алкохол, възпаление и инфекции, сърповидноклетъчна анемия, а при жените специално внимание се отделя на употреба на орални контрацептиви, бременност и постпартален период. Въпреки че много от тези рискови фактори могат да причинят инсулт и при по-възрастни пациенти, основания да бъдат определяни като възрастово специфични дават следните факти:

А) факторите са налични само в млада възраст (свързани са с репродуктивното здраве),

Б) факторите се откриват във всички възрастни, но връзката им е статистически по-достоверна в млада възраст (мигрена с аура, отворен форамен овале, инфекции),

В) факторите са свързани със специфично поведение, по-често наблюдавано в млада възраст (злоупотреба с алкохол, алкохолно опиянение, злоупотреба с неподозволени наркотични средства, пушене, запълстяване).

Г8.11 Янакиева М, Овчарова-Духленска Е, Маринова-Трифонова Д, **Дановска-Младенова М**. *Метадон-свързана миелопатия при пациент със спастична долна параплегия: клиничен случай*. Юбилейна научна конференция с международно участие, 1-3 ноември 2024г. Сборник доклади “50 години Медицинско образование и наука в Плевен”, стр. 39-42; ISBN: 978-954-756-346-9

METHADONE-RELATED MYELOPATHY IN A PATIENT WITH SPASTIC PARAPLEGIA: A CASE REPORT

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Introduction. Though presenting with similar clinical, neurophysiological and neuroimaging characteristics, myelopathies are associated with a wide spectrum of underlying factors, thus evoking a diagnostic challenge. Methadone-related myelopathy is one of the less common types with rising occurrence due to the emerging incidence of drug addiction.
Objective. To increase awareness and emphasise a rare side effect of methadone toxicity.
Materials/methods. A 36-year-old female patient was admitted to the Neurology Department of Dr Georgi Stranski University Hospital in Pleven, Bulgaria, with a subacute onset of back pain and weakness in the lower limbs following intravenous exposure to methadone. She had a history of chronic hepatitis C and opioid abuse since she was 18 years old. On examination, a spastic paraplegia with sensory loss at the level of Th8-Th9 was found. Spinal cord MRI revealed thoracic myelopathy with extensive T2-weighted hyperintensity from Th3 to Th6 segments.
Results. A wide diagnostic panel was performed to identify the aetiology of the myelopathy. CSF analysis showed hyperproteinorrhachia. The patient was treated with high-dosage Methylprednisolone intravenously without a significant response. Physiotherapy was initiated with moderate clinical improvement.
Conclusion. This case report highlights the long-term neurotoxic impact of methadone abuse on the central nervous system.
Keywords: myelopathy, methadone, neurotoxicity

Г8.12 Маринова-Трифонова Д, **Дановска-Младенова М**, Янакиева М., Овчарова-Духленска Е, Василева В, Стоев П. *Влияние на метаболитния синдром върху краткосрочния изход при пациенти с остър некардиоемболичен исхемичен инсулт*. Юбилейна научна конференция с международно участие, 1-3 ноември 2024т., Сборник доклади “50 години Медицинско образование и наука в Плевен”, стр. 866-871; ISBN: 978-954-756-346-9

THE IMPACT OF METABOLIC SYNDROME ON THE SHORT-TERM OUTCOME OF PATIENTS WITH ACUTE NON-CARDIOEMBOLIC ISCHEMIC STROKE

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Background. The metabolic syndrome (MetS) is associated with an increased risk of cerebrovascular disease and ischemic stroke (IS).
Purpose. To assess the impact of MetS multiple components on the short-term prognosis of patients with acute non-cardioembolic IS.
Methods. A prospective study of 100 acute IS patients admitted to the Neurology Clinic of Dr Georgi Stranski University Hospital in Pleven was conducted from Jan 2020 to Jan 2021. The Patients were divided into two groups - with and without MetS.
Results. Stroke patients with MetS (n=50) showed demographic and gender differences with a prevalence in the age group 61-70 years and female gender. Despite the preexisting therapy with antidiabetics, antihypertensives and statins, the patients with MetS showed a worse risk profile in comparison with the controls: arterial hypertension (78%), diabetes mellitus (100%) and dyslipidemia (64%). In the control group (n=50), arterial hypertension was prevalent (24%) in males and hypercholesterolemia (20%) in females. The evaluation with the National Institute of Health and Stroke Scale (NIHSS) on discharge demonstrated predominantly moderate stroke in controls, while 20% of the MetS group had severe strokes with 2.5-fold poorer outcomes.
Conclusions. Patients with MetS are at higher risk of IS, especially females. The multiple components of MetS significantly impact the short-term outcome of IS, but their control and treatment still remain a therapeutic challenge.
Keywords: ischemic stroke, metabolic syndrome, risk factors

Г8.13 **Дановска М**., Овчарова Е., Янакиева М. *Съвременни аспекти на терапевтичния подход при пациенти с пристъпно-ремитентна форма на множествена склероза*. GP Medic, бр.4/2024г.; **in press**, ISSN: 2603-4719

MEDIC PRINT
МЕДИЦИНСКО ИЗДАТЕЛСТВО

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Съвременни аспекти на терапевтичния подход при пациенти с пристъпно-ремитентна форма на множествена склероза

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Резюме: Множествената склероза (МС) е демиелинизиращо автоимунно заболяване, с генетично предразположение, чиято клинична картина е изключително многообразна. Прогресивният ход и болестните прояви на МС значително влошават качеството на живот на пациентите. Въпреки широката гама от терапевтични възможности, изборът за персонализиран подход към конкретния пациент остава труден. През 2021 год. с одобреното от ЕМА първо моноклонално антитяло за подкожно приложение веднъж месечно при пациенти с пристъпмно-ремитентна МС – ofatumumab, настъпва нов пробив в лечението на МС.

Ключови думи: множествена склероза, болест-модифицираща терапия, персонализирана медицина, офатумумаб

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Под редакцията
на акад. проф. д-р Иван Миланов, д.м.н.

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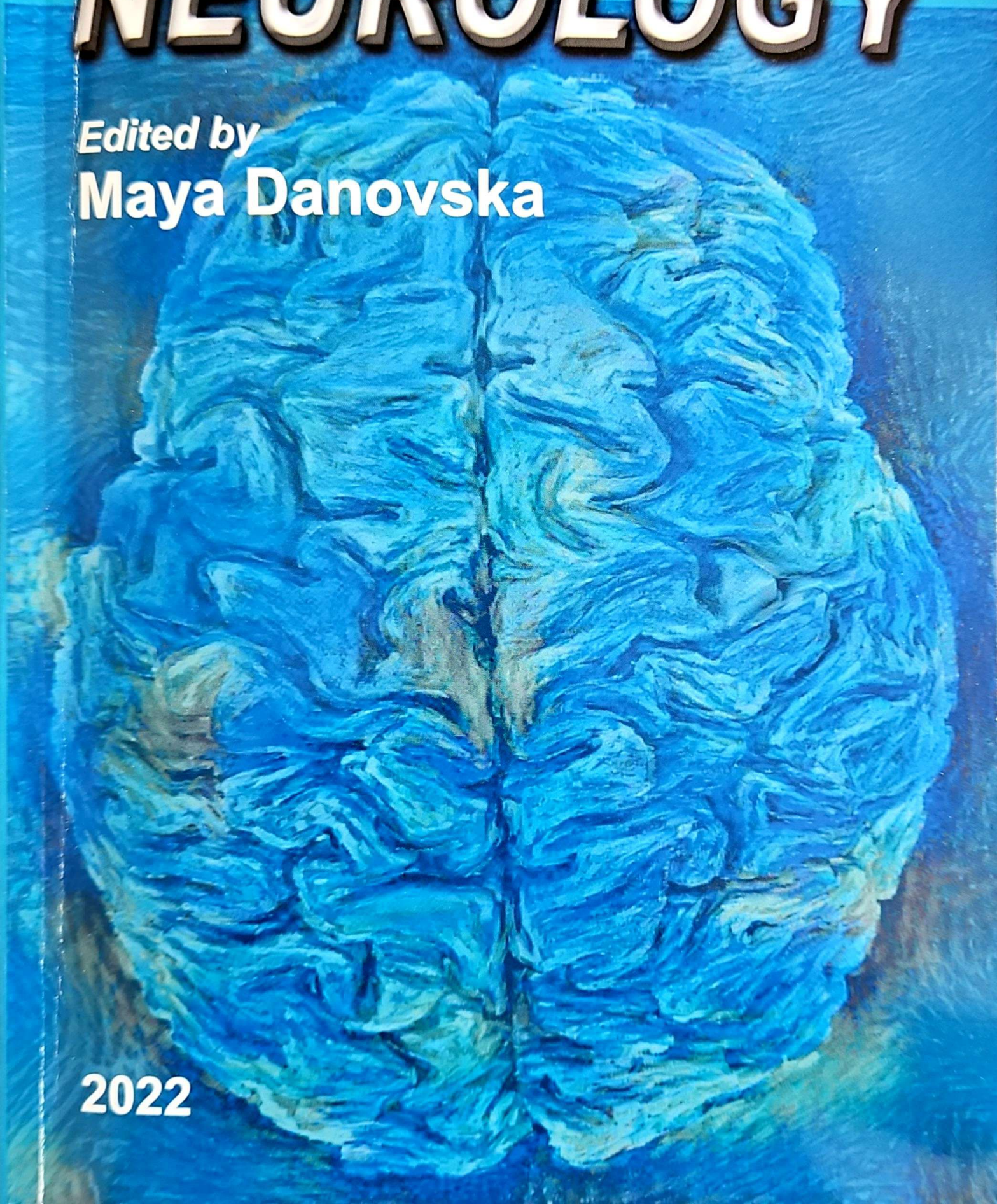
ISBN 978-619-241-135-0

NEUROLOGY

Edited by

Maya Danovska



2022

NEUROLOGY

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Viewers: Kaprelyan A., MD, PhD, DSci

© Publishing Center, Medical University – Pleven, Bulgaria
Print: „EA" AD
1st Edition, Pleven, 2022
ISBN 978-954-756-286-8

Maya Danovska

NEUROLOGY TESTS

2023

Edited by Maya Danovska

Medical University -Pleven, Bulgaria

NEUROLOGY TESTS

Edited By:

Maya Danovska, MD, PhD

Publishing Centre

Medical University Pleven

2023

Neurology Tests

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Bulgarian, First Edition
Pleven, 2023

Print: "EA" - AD

ISBN: 978-954-756-336-0

НЕВРОЛОГИЯ

ПОД РЕДАКЦИЯТА НА

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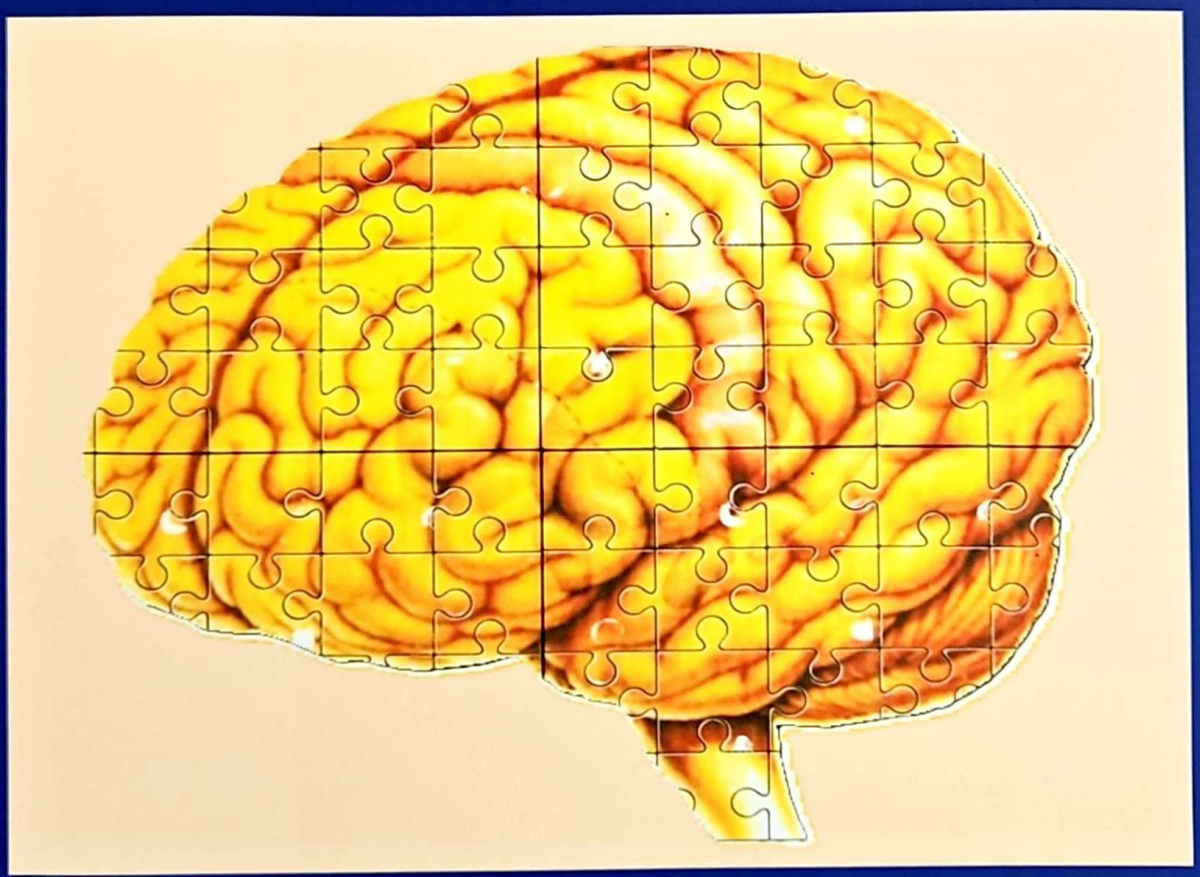

Медицинско издателство
АРСО

СОФИЯ 2024

НЕВРОЛОГИЯ

ПОД РЕДАКЦИЯТА НА
Проф. Д-р ПЕНКО ШОТЕКОВ

ТРЕТО ПРЕРАБОТЕНО ИЗДАНИЕ

Учебник за студенти по медицина

Изданието съдържа:
260 фигури
88 таблици

НАСТОЯЩЕТО ИЗДАНИЕ СЕ ПОСВЕЩАВА НА
100 ГОДИНИ
БЪЛГАРСКА НЕВРОЛОГИЯ
(1922 – 2022)

Медицинско издателство АРСО

Медицинско издателство АРСО
2024

Тази книга е написана със съдействието на следните фармацевтичните компании:

AbbVie Ltd	Novartis Pharma GmbH
Chemax Pharma	Roche
Gerot&Lannach	Sopharma AD
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Medochemie Ltd	Wörvag Pharma

НЕВРОЛОГИЯ
Под редакцията на проф. П. Шотеков, дмн
Трето преработено издание 2024
Второ преработено издание 2010
Първо издание 2004

NEUROLOGY
Edited by Penko Shotekov, M.D., Sc.D.
Professor of Neurology
Third edition 2024
Second edition 2010
First published 2004

Медицински редактори: д-р В. Гълъбова, д-р Б. Йошинов, д-р К. Михаилова

© Медицинско издателство "АРСО" – АРСО-КП ЕООД, гр. София,
ул. Здраве 9 (книжарница) тел.: 0899 139 816
Фирмена книжарница – на същия адрес.

© Medical publishing house "APCO", 1439 Sofia, Bulgaria

ISBN: 978 - 619 - 197 - 093 - 3