BULGARIAN MEDICINE ISSN 1314-3387

Българска медицина

Съдържание

Оригинални статии

Описание на случай

Годишнина

Изисквания към авторите

Българска медицина се реферира
в международната база данни Index Copernicus International

Bulgarian medicine

Content

Original papers

Case report

Anniversary

Author's guidelines

Bulgarian Medicine is included in
Index Copernicus International Journals Master List

A KEY IRON METABOLISM REGULATOR IN CHRONIC KIDNEY DISEASES

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Ключов регулатор на обмяната на желязо при хронично бъбречно заболяване

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РЕЗЮМЕ

ВЪВЕДЕНИЕ

Хепсидин-25 е аминокиселинен пептид, който, представляващ ключов регулатор на системната хомеостаза на желязото. Неговото количествено определяне внася нови виждания по отношение на патогенезата на нарушенията в обмяната на желязото и тяхната терапия.

МЕТОДИ

Използвахме сандвичев ELISA метод за количествено определяне на хепсидин. Бяха Groups контролна група (КГ, n=70) и пациенти с хронично бъбречно заболяване (ХБЗ, n=50). Включващите критерии за КГ бяха липа на нарушена обмяна на желязо, доказана с помощта на клинико-химични показатели.

ABSTRACT

AIM

Hepcidin-25 is an aminoacid cysteine-rich iron regulating peptide, secreted in liver. Its quantification provides new topics for the pathogenesis of iron metabolism and its treatment.

DATA

We use a sandwich ELISA method to quantificate serum hepcidin levels in Bulgarian population. Groups included: healthy control group (CG, n=70) and patients with chronic kidney disease (CKD, n=50). Including criteria for CG was no evidence of iron metabolism disorders, evaluated by clinical parameters for iron status.

РЕЗУЛТАТИ

Установихме сигнификантна разлика между двете групи: 14.9 ± 9.9 μg/L (за КГ) и 92.8 ± 69.9 μg/L (за пациенти с ХБЗ). Сигнификантна положителна корелация се установи между хепсидин и С-реактивен протеин при пациенти от всички стадии на ХБЗ ($r = 0.587$, $p < 0.05$).

ЗАКЛЮЧЕНИЕ

Използването на високо-специфичен ELISA метод за количествено определяне на хепсидин ще допринесе за правилен избор на поведение при терапия на желязо-дефицитна анемия при пациенти с ХБЗ.

Ключови думи: хепсидин, желязо-дефицитна анемия, хронично бъбречно заболяване

RESULTS

We found that serum hepcidin levels correlate significantly between two groups: 14.9 ± 9.9 μg/L (for CG) to 92.8 ± 69.9 μg/L (for CKD). A high significant positive correlation was found between hepcidin and CRP ($r = 0.587$, $p < 0.05$).

CONCLUSIONS

A high specific ELISA method provide a new efforts for therapy management of iron deficiency in CKD.

Key words: hepcidin, iron deficiency anemia, reference ranges, chronic kidney disease

INTRODUCTION

The essential nature of iron for humans is known from XIX century [1].

Recently, it has been found that a key regulator of iron metabolism is hepcidin 25. It is synthesized by hepatocytes as 25-amino acid peptide, which is a biologically active form [2].

Various physiological and pathological processes regulate the synthesis of the hormone hepcidin [3].

Hepcidin acts in duodenal enterocytes and macrofages with ferroportin (an iron intracellular exporter) [4–7].

The introduction of an analytical method with sufficient sensitivity and specificity for accurate quantification of significant concentrations of hepcidin in biological fluids causes a marked interest in its investigation in different biomedical sciences.

Patients with chronic kidney disease are in chronic inflammatory condition. As a result of the synthesis of hepcidin inflammation is mediated by IL-6 induction and coupling of signal transducer and activator of transcription 3 (STAT 3) to the promoter of hepcidin [8]. The level of serum hepcidin in the body is closely associated with the iron, which is due to microinflammatory patients on maintenance hemodialysis and lead to new potential targets for therapy.

AIM

This study describes statistically significant differences in hepcidin serum quantification between control group with no evidence of iron metabolism disorders and patients with chronic kidney disease (CKD) [9].

MATERIALS AND METHODS

Subjects

This study included 70 healthy controls and 50 patients with CKD. The study was approved by the ethics committees of the participating institution. Informed consent was obtained from all healthy controls in accordance with to the Declaration of Helsinki (Directive 2001/20/EO).

70 serum samples from healthy volunteers 35 males (age 41.2 ± 9.2) and 35 females (age 39.9 ± 9.5) were collected. 50 serum samples from patients with CKD 25 males (age 61.3 ± 15.1) and 25 females (age 51.3 ± 11.5) were collected. All samples were collected, stored,

and deidentified to protect patient privacy. CKD patients were separated into disease stage according to eGFR CKD-EPI Creatinine Equation (2009). Samples were stored at −70 °C before analysis of hepcidin levels. CRP, creatinine and transferrin levels were analyzed on Cobas Integra 400 (Roche Diagnostics). For red blood cells and hemoglobin concentration in reticulocytes we use Advia 2120 hematology analyzer (Siemens Healthcare Diagnostics).

DATA ANALYSIS

For statistical significance was used t-test and Pearson correlation.

RESULTS

The established serum hepcidin levels for control group and patients with CKD are showed in Fig. 1. Quantification of serum hepcidin levels in different CKD groups is showed in Fig. 2. The correlation between different CKD groups is shown in Fig. 3.

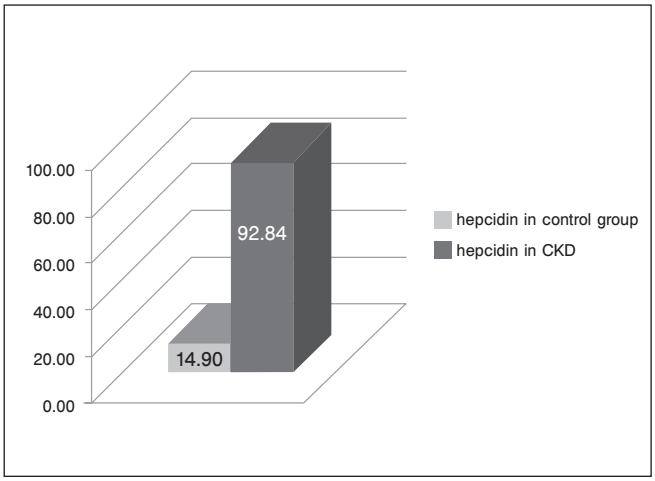

Figure 1. *Serum hepcidin levels in control group and patients with CKD (stages II to V)*

We found that there is a significant difference between serum hepcidin-25 levels in healthy control group compared to all stages of CKD. Values as described: a) for control group 14.9 ± 9.9 µg/l and b) 92.8 ± 69.9 µg/l.

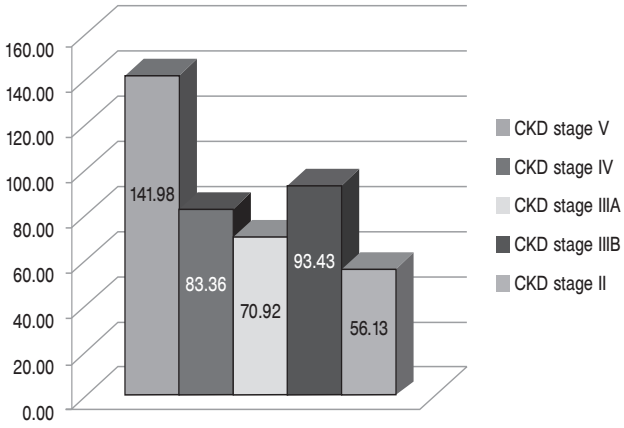

Figure 2. *Hepcidin levels in CKD stages II to V*

We found a difference in serum hepcidin levels between CKD groups. The obtained results are: a) for stage II CKD (eGFR 61 – 90) – 56.13 µg/l; b) for stage IIIA CKD (eGFR 46 – 60) – 70.92 µg/l; c) for stage IIIB CKD (eGFR 31 – 45) – 93.43 µg/l; d) for stage IV CKD (eGFR 16 – 30) – 83.36 µg/l; e) for stage V CKD (eGFR < 15, without dialysis) – 141.98 µg/l.

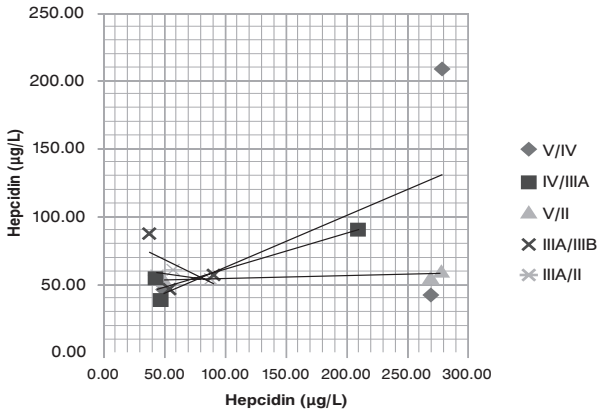

Figure 3. *Hepcidin correlation between CKD stages II to V*

Positive and negative correlation between different CKD stages.

We tried to find a correlation between serum hepcidin levels and measured parameters.

A significant correlation was found between serum hepcidin levels and CRP (Table 1).

Table 1. Correlation of measured parameters between different CKD stages

	hepcidin	
	r	p
CRP	0.587	< o.o5
Crea	0.217	< o.o5
TRSF	-0.252	< o.o5
CHr	-0.306	< o.o5
RBC	-0.387	< o.o5

Significantly high correlation between serum hepcidin levels and CRP and red blood cells was found in all CKD stages ($p < 0.005$). A negative correlation between red blood cells, hemoglobin concentration in reticulocytes and transferrine levels was found.

DISCUSSION

The present study describes a immunological assay for hepcidin quantification in human serum, based on the use of a recombinant hepcidin peptide and a polyclonal antibody.

We found that serum hepcidin levels correlate significantly between two groups 14.9 ± 9.9 µg/L (for control group) to 92.8 ± 69.9 µg/L (in all CKD stages).

High correlation between CRP and hepcidin levels was found, which describes an inflammatory reason for iron-deficiency anemia.

ACKNOWLEDGMENTS

We kindly appreciate help of Medical University – Sofia; Grant № 10/2013.

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Клинична стойност на Лайпцигската точкова система в диагностиката на болестта на Wilson

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Clinical value of the Leipzig scoring system in the diagnosis of Wilson disease

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РЕЗЮМЕ

ЦЕЛ

Болестта на Wilson е рядко, но важно наследствено нарушение на медния метаболизъм, засягащо множество органи. Неговото разпознаване е лесно при класическото клинично представяне. Нетипичните прояви са диагностично предизвикателство и изискват повече изследвания. Целта на това проучване е да се оцени диагностичната стойност на Лайпцигската точкова система при болестта на Wilson.

ABSTRACT

AIM

Wilson disease (WD) is rare but important inherited disorder of copper metabolism involving multiple organs. Its recognition is easy in the classical clinical presentations. Non-typical features are a diagnostic challenge and require more examinations. The objective of this study is to assess the diagnostic value of the Leipzig scoring system in WD.

МАТЕРИАЛ

Анализирани са 65 пациента с болест на Wilson (22 жени и 43 мъже) и контролна група от 26 болни с други хронични чернодробни заболявания. Оценени са клиничните находки и лабораторните показатели, включени в Лайпцигската точкова система.

РЕЗУЛТАТИ

Съгласно тази система, 58 пациента (89,2% от случаите) се представят със скор ≥4 , което потвърждава диагнозата болест на Wilson. Сбор от точки 4 е с най-голям относителен дял сред пациентите с болест на Wilson – 26,2%. Седем болни (10,7%) имат скор 3. При тях бяха изключени други причини за чернодробно заболяване. Само четири пациента от контролната група се представят със скор 3, докато останалите 22 (84,6%) имат скор ≤ 2. Установихме диагностична точност на точковата система 87,91%.

ЗАКЛЮЧЕНИЕ

Нашите резултати показват, че параметрите, включени в Лайпцигската точкова система са надеждна комбинация от критерии за точна и сигурна диагноза на болестта на Wilson. Тази система може да бъде полезна за правилната диагноза, особено при пациенти с необяснимо чернодробно заболяване**,** тъй като ранното диагностициране и лечение осигуряват добра прогноза на болестта.

Ключови думи: Болест на Wilson, Лайпцигска точкова система, тест с Д-пеницилламин

METHODS

Sixty-five patients with WD (22 females and 43 males) and control group of 26 patients with other chronic liver diseases (CLD) were analyzed. Clinical findings and laboratory parameters included in Leipzig scoring system were evaluated.

RESULTS

According to this system, 58 patients (89,2% of the cases) present with a score over four that proves the WD diagnosis. Score of four occupies the greatest relative share of our WD patients – 26,2%. Seven patients (10,7%) present with score of three. In them, other causes of liver disease have been excluded. Only four patients of the control group present with score of three while the rest 22 ones (84,6%) have a score that is less or equal to two. The diagnostic accuracy of scoring system was 87,91%.

CONCLUSIONS

Our results demonstrate that the parameters incorporated in the Leipzig scoring system are a reliable combination of criteria for the precise and definite diagnosis of WD. This system can be useful for the correct diagnosis of WD, especially in patients with a unexplained liver disease because early diagnosis and treatment ensure a good prognosis.

Keywords: Wilson disease, Leipzig scoring system, D-penicillamine test

Wilson disease (WD) is an autosomal recessive inherited disorder of hepatic copper metabolism resulting in the accumulation of copper in many organs and tissues. Diagnosis is based on a combination of clinical symptoms, laboratory, histomorphological, imaging and genetic examinations. It is easy in the classical cases of neurological symptoms, presence of Kayser-Fleischer (KF) rings, liver disease and typical abnormal copper metabolism. Clinical challenge is unclear liver disease along with absent neurological symptoms, KF rings, or most frequent disease mutations. Confirming the difficulties in the diagnosis of Wilson's disease and the need for complex assessment, in 2001 in Leipzig, Germany, at the Eight International Conference on Wilson disease and Menkes disease, an expert group on Wilson's disease adopts an integrated scoring system based on a combination of clinical signs and laboratory tests (4, 5). The objective of this study is to assess the clinical value and practical application of the Leipzig scoring system for the diagnosis of WD.

METHODS

The survey includes 65 patients with WD diagnosed and treated at the Clinic of Gastroenterology and Hepatology, St. Marina University Hospital of Varna, Bulgaria, hospitalized from January, 2003 to May, 2013. Patient's assessment period ranged from 3 months to 21 years. The control group included 26 individuals with other chronic liver diseases (CLD) such as chronic viral hepatitis B and C, autoimmune hepatitis, alcoholic and nonalcoholic steatohepatitis, or liver cirrhosis. A descriptive data analysis was used. Parameters of copper metabolism were assessed. Several haematoloogical, ophthalmological and neurological examinations, brain magnetic resonance imaging (MRI), liver biopsy and DNA analysis were performed. WD scoring system was used to establish the diagnosis.

The purpose of the aforementioned scoring system for diagnosis of WD (5) is to provide objective criteria with high specificity and sensitivity for the disease. A combination of clinical and laboratory tests within a score range between zero and four has been elaborated. It includes the following parameters: KF ring, neurological symptoms, serum ceruloplasmin level, Coombs-negative hemolytic anemia, copper concentration in the hepatic tissue or staining for copper with rhodanine in the hepatocytes, spontaneous and/or provoked urinary copper excretion, and mutation analysis. In 2010, we introduced this system in our Clinic of Gastroenterology and Hepatology and subsequently evaluated all the patients with WD and controls according to it. This scoring system is incorporated into the clinical practice guidelines for WD approved by the European Association for Study of the Liver in 2012 (EASL) (3).

RESULTS

We examined 22 female and 43 male WD patients at a mean age of 37,7 ± 12,9 years at the end of study as well as 13 female and 11 male controls at a mean age 47,7 years. The ophthalmological examination identified KF ring in 23 out of 64 WD patients. Another ocular manifestation, a sunflower cataract, was found out in six patients. In one patient, it was simultaneously present with the KF ring, and in two patients it appeared after KF ring disappearance (Table 1).

We established neurological symptoms in 35 patients. Of them, 32 patients presented with a mixed hepatic and neurological form and the rest three did with solely neurological manifestations. The most common symptoms were tremor of the extremities, incoordination

Table 1.
Clinical findings according to the Leipzig diagnostic criteria

Таблица 1.
Клинични находки съгласно Лайпцигските диагностични критерии

Typical clinical findings	n
KF rings	23/64
Sunflower cataract	6/64
Neurological symptoms	35/65
Brain MRI abnormalities	15/25
Serum ceruloplasmin <0.2 g/L	55/65
Coombs-negative hemolytic anemia	7/65

Other tests	*n*
Liver biopsy	23/65
Rhodanine-positive staining	10/19
Urinary copper	
normal	10/65
>2x ULN*	37/62
after D-penicillamine:	
> 5x ULN	38/43
> 10x ULN	32/43
Mutations detected	26/54

* ULN – upper limit of normal

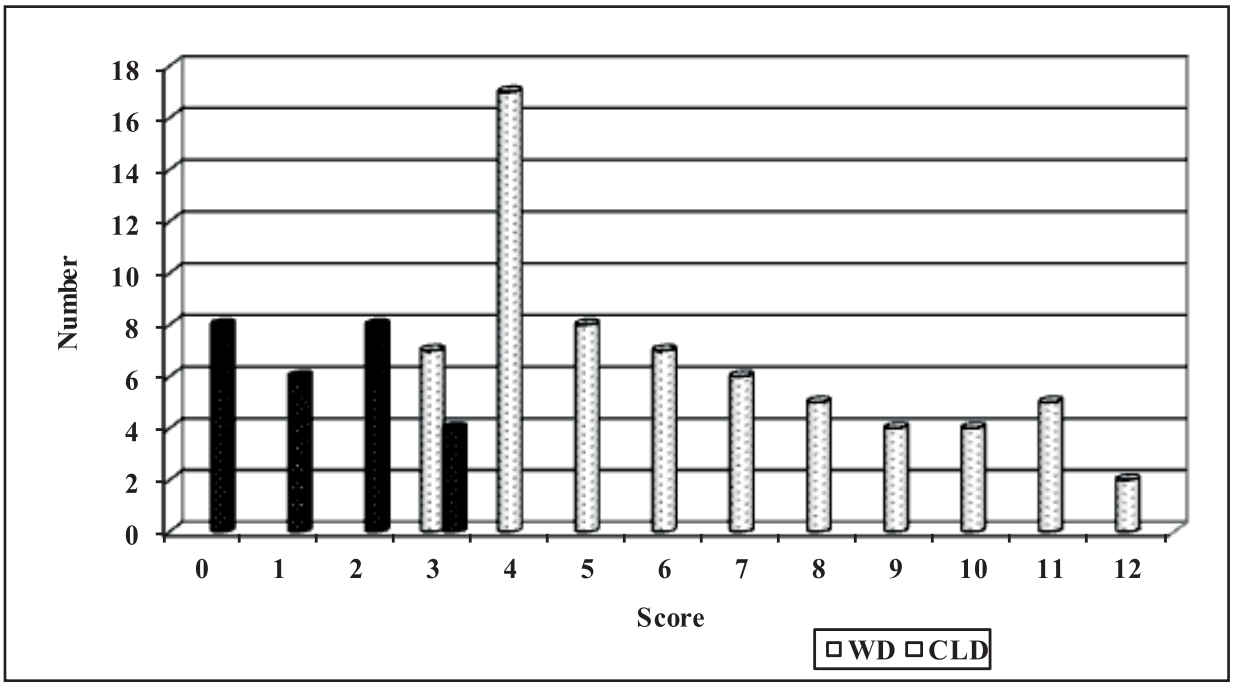

Fig. 1.
Patients' distribution according to the Leipzig scoring system

Фиг. 1.
Разпределение на пациентите съгласно Лайпцигската точкова система

(intention tremor and dysmetria), dysgraphia, and dysarthria.

Brain MRI was performed in 25 patients and proved abnormalities in 15 of them.

In 55 WD patients (84,6% of the cases), the value of serum ceruloplasmin remains below the reference limits, while in 10 ones (15,4% of the cases), it is within the normal range. Coombs-negative hemolytic anemia was proved in seven patients. DNA analysis was accomplished in 56 patients and revealed ATP7B gene mutations in 26 of them (46,4% of the cases).

Twenty-three patients (35,4% of the cases) underwent percutaneous aspiration liver biopsy. A histochemical examination with rhodanine for copper detection was carried out in 19 patients. A positive result for rhodanine was obtained in 10 patients (52,6% of the cases).

Basal urinary copper excretion was measured in 62 WD patients and was by two times higher than ULN in 59,7% of the cases. D-penicillamine challenge test was performed in 43 patients. There is a five-fold increase of D-penicillamine test over the normal range in 38 WD patients as well as a ten-fold one in 10 of them.

The distribution of the patients with WD and with other CLD according to the criteria of Leipzig scoring system is demonstrated on Fig. 1.

According to this system, 58 patients (89,2% of the cases) present with a score sum over four that proves the diagnosis of WD. Score of four occupies the greatest relative share of WD patients – 26,2%. The relative share of the patients with score of five is 12,3% and with score of six is 10,8%. The relative share of 7,7% is equal for the patients with scores of 8 and 11 as well. Seven patients (10,7%) present with score of three. Only four patients with other CLD present with score of three while the rest 22 ones (84,6%) do with a score that is less or equal to two.

DISCUSSION

WD is inherited, but treatable disorder of copper metabolism. The diagnosis is usually estab-

lished by biochemical testing following clinical suspicion. The symptoms may be non-specific and might not be easily recognized. There is no single diagnostic test that can exclude or confirm WD with certainty. To overcome the diagnostic difficulties, the working group propose scoring system in Leipzig, 2001.

We found a small number of reports of other authors who have used this score in adults (1, 7, 8), may be due to low prevalence of the disease (1:30000). There are no data available comparing results with other CLD in this age group. Dhawan reported results of a large retrospective study, using this scoring system for WD diagnosis in children. He compared fifty-four WD patients with 88 non-WD group. This system provided a good combination of sensitivity and specificity (both higher 96%) for WD diagnosis (2).

Serum ceruloplasmin estimation is a useful diagnostic test. Our data are similar to the results reported elsewhere and indicate the usefulness of this diagnostic parameter (1, 7). We found sensitivity and specificity of this test 84,62% and 65,38% respectively. The number of our WD patients with a normal serum ceruloplasmin level is close to that reported by other authors (8). This fact should not be ignored and ceruloplasmin can be used mainly in combination with the rest parameters in such cases. The diagnosis of the disease could not be excluded.

KF ring is one of the clinical criteria for the diagnosis of WD. Although this is considered a strong pathognomonic sign, only 23 of our patients (35,4%) present with KF ring. Of them, 17 present with neurological symptoms. It is assumed that KF ring can rarely be found out in other chronic cholestatic diseases (3, 13). In our evaluation, sunflower cataract also carries points like KF ring.

Establishing the diagnosis of WD may be problematic in atypical cases because any neurological findings or KF rings may be absent and because there is no single reliable biochemical test. WD diagnostic scoring system is helpful in these cases (15). Basal urine copper measurement can provide useful diagnostic information. D-penicillamine-induced cupriuria, i. e. D-penicillamine challenge test, is an important and valuable additional diagnostic test, which has been re-evaluated by several study groups (6, 9, 10, 12). The elevation of copper excretion in comparison with its initial level by more than five times in WD patients is of importance, too. The sensitivity and specificity of this measurement were 95,35% and 69,23% respectively. This fact enables us to consider this non-invasive test useful, necessary and applicable diagnostic parameter, especially in the cases of inexplicable hepatomegaly, vague liver disease, elements of hemolysis or unspecified neurological disease.

According to Leipzig criteria, 58 patients of ours (89,2% of the cases) present with a score over four that proves WD diagnosis. Seven patients (10,7%) present with score of three. In them, the viral, autoimmune and toxic reasons for a CLD have been excluded. Clinical observation and favourable therapeutic influence on the laboratory parameters has confirmed the diagnosis in these patients. Most individuals with CLD have scores less or equal to two. We note that our control group is small and more extensive clinical observations are needed to validate this score. Nevertheless, these results demonstrate that the parameters incorporated in the Leipzig scoring system are a reliable combination of criteria for the precise and definite diagnosis of WD. The diagnostic accuracy was 87,91% and sensitivity 89,23%. It is noteworthy that there does not exist any unique parameter for this diagnosis at all. On the other hand, it is not correct to accept that all the parameters should obligatorily be abnormal. In this respect, the complex evaluation, clinical observation and, in some cases, the therapeutic test with D-penicillamine could help the correct diagnosis (11, 13, 14).

In conclusion, our modest experience gained with the application of the Leipzig scoring system indicates that this is reliable combination of clinical, laboratory, genetic and mor-

phological parameters. It can be helpful for the precise diagnosis of WD, especially in the patients with a subclinical liver damage with a view to the timely treatment and prevention of the complications of this potentially curable hereditary disease.

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KINESITHERAPEUTICAL BEHAVIOUR IN IMPINGEMENT SYNDROME

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КИНЕЗИТЕРАПЕВТИЧНО ПОВЕДЕНИЕ ПРИ IMPINGEMENT SYNDROME

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РЕЗЮМЕ

Структурите, които най-често се засягат при това притискане са сухожилията на m. supraspinatus, m. infraspinatus, burssasubdeltoidea и m. bicepsbrachii-caputlongum.

Синдром на субакромиалното притискане (impingementsyndrome) се характеризира с раменна болка и слабост при елевация на мишницата.

Целта на кинезитерапията е функционално възстановяване и възвръщане на трудоспособността на болния.

Функционалното лечението протича в три фази. Максимално-протективна фаза в която средствата на кинезитерапията включват лед, компресия, елевация, масаж, покой, ортеза, стягаща превръзка, нежни мануални ставно-мобилизационни техники за всички стави на раменния пояс с малка амплитуда, от безболезнена позиция на ставата.

Във втората умерено протективна фаза, средства на кинезитерапята се състоят в защита – ортези и тейпинг. За намаляване на ефек-

ABSTRACT

The structures which are most commonly affected in this nip are the tendons of m. supraspinatus, m. infraspinatus, burssa subdeltoidea and m. biceps brachii-caput longum.

Subacromial compression syndrome (impingement syndrome) is characterized by shoulder pain and weakness in arm elevation.

The purpose of kinesitherapy is to reach functional recovery and restore the patient's ability to work.

The disease occurs in three phases,so the tasks and resources to achieve the objective are different in the different stages of treatment.

The functional treatment is performed in three phases. The first is the maximal – protective phase in which the means of kinesitherapy include ice, compression, elevation, massage, rest, orthoses, firming dressing, chiropractitioners' gentle joint mobilization techniques for all joints of the shoulder girdle with a small amplitude of painless position of the joint.

In the second phase, moderately protective, the kinesitherapeutic means consist in protection – or-

та от формиране на контрактури и постепенно увеличаване на мобилността на меките тъкани и обема на движение в ставите се прилагат пасивни ставно-мобилизационни техникии

В третата фаза на лечението-минимално протективна фаза, средства на кинезитерапията включват стречинг на ограничаващите структури. За увеличаване на мекотъканната, мускулната и ставната мобилност се прилагат стречинг техники и автостречинг, тренировката за издръжливост и обучаване на пациентът в безопасно прогресиране както и профилактика на рецидиви.

Ключови думи*:* тестове, синдром на субакромиално притискане, кинезитерапия.

thoses and taping. To reduce the effect of the formation of contractures and gradually increase the mobility of the soft tissues and the amount of movement in the joints passive joint mobilization techniques are applied.

In the third phase of treatment –the minimal-protective phase, the means of kinesitherapy include stretching of the restraint structures. To increase soft tissue, muscle and joint mobility various stretching techniques, autostretching and endurance training are appliedwith the patient being trained in a safe progression,so as to ensure recurrence prevention.

Key words: tests, impingement syndrome, kinesitherapy.

INTRODUCTION

Subacromial compression syndrome (impingement syndrome) is characterized by shoulder pain and weakness in arm elevation. The state is the consequence of repeated compression and deposition of salts in the tissue located between the head of the humerus and the caudal surface of the acromion and the coracoacromial ligament. The structures which are most commonly affected in this nip are the tendons of m. supraspinatus, m. infraspinatus, burssa subdeltoidea and m. biceps brachii-caput longum (4).

The tests of Neer, Hawkins and Yocum are applied for executing a precise topography of the lesioned tendons of the rotator cuff. The Jobe test objectifiesthe pinched tendon of m.suprascapularis;the Pattetest objectifiesthe tendonlesion of m. infraspinatus;the lift-off test proves the involvement of the tendon of m. subscapularis and the palm-up test objectifies the lesioned tendon m. biceps brachii-caput longum (11).

The reasons for the occurrence of this condition can be various inflammatory diseases, stressing of the joint, degenerative diseases, infections.

The condition of the shoulder joint is evidenced by X-ray.

CLINICAL EXAMINATION OF THE SHOULDER.

Patients complain of nocturnal pain and sleep disturbances during the acute symptoms such as pain on movement and frequently while being at rest during the acute symptoms. A reduced joint play and range of motion is observed, with a common external rotation and abduction and slight constraint of internal rotation and flexion.

The possible outcomes include vicious postural compensations with prolonged and forwardshifted scapula, prolonged, elevated and rounded shoulders, and impaired coordination of arm movements while walking. There is a general weakness and poor muscle endurance in the shoulder with straining of scapular muscles, leading to pain in the dorsal cervical muscles and m.trapezius.

The scapula-humeral rhythm is damaged, leading to limited movement in the shoulder joint and increased elevation of the shoulder and scapular motion (3.1).

The medical check-up consists of four stages. The first is a brief inspection, involving,in particular, assessment of trophics of m. deltoideus. Well developed, this muscle can often compensate for or conceal existing lesions of

the tendons of the muscles of the rotator cuff (5).

It is necessary to investigate the presence of a static deformation of the spine. Palpation ofthe acromio-clavicular jointis performed to establish the painful symptoms (9).

The third stage is the most important one and refers to the study of active and passive mobility in the joint. The comparison between them will help to clarify the diagnosis and treatment. A 90˚ removal mobilizesthe glenohumeral joint, the state over 90˚ engagesthe scapula-thoracic joint with activation of trapezius muscle,while placing under tension theacromio-clavicular-joint(5). A limited alignment of the shoulder joint reveals lesion of m. pectortalis major, most often of post-traumatic nature. In capsulitis, the flexion is preserved but limited in the case of intra-articular lesions such as arthrosis or arthritis of the glenohumeral joint. By performing external rotation, m. supraspinatus and m. infraspinatusare tested, while internal rotation is estimated by m. subscapularis (11).

The purpose of performing kinesitherapeutic treatment is to achieve functional recovery and restore the patient‘s ability to work.

The disease occurs in three phases, so the tasks and resources to achieve the objectives are different in the different stages of treatment and are especially important for improving the functionality of the upper limb gestures.

PHASES OF FUNCTIONAL TREATMENT

The first phase is the maximal-protective phase of kinesitherapy.

The kinesitherapeutic tasks in this phase are limited to establishing pain control of the swelling and spasm of muscles, maintaining mobility of the soft tissues and joints, keepingthe function of thehealthy adjacent parts, training the patient to avoid contraindicated movements.

The kinesitherapeutic means in this phase include ice, compression, elevation, massage, rest, orthoses, firming patch (10), tender chiro-practitioner’s joint mobilization techniques to all the joints of the shoulder girdle with a small amplitude (I degree) from painless position of „a position of the capsule-ligament relaxation of the joint. In some patients in the first 2 days after trauma these healing techniquesmay be inapplicable. They are applied cautiously and only if they reduce the pain symptoms (6).

To maintain the mobility of the soft tissues and joints, controlled passive exercises for motion range in any direction, passive joint traction and sliding movements from painless position are applied. A series of light isometric muscle contractions are also applied for all muscles of the shoulder complex and elbow due to their relationship with movements in the shoulder joint (7).

To maintain the function of the healthy adjacent parts,active exercises are performed (with help, free, against resistance, etc.), arm exercises (squeezing of a little ball,a small ring or other soft object). If any swelling is found, the upper limb is kept in drainposition above the level of the heart whenever treatment is possible in this posture. The patient is instructed to keep the joints, distal to the injury, most active and mobile. He/she is informed about the expected time of recovery, how to spare the damaged part and how to maintain functional activity without provoking the recurrence of symptoms (6).

The recommended exercises, contraindicated during this period of active treatment,are active ones for range of motion of the shoulder joint, for stretching the muscles of the shoulder joint, exercises against resistance for traumatized area. In overdose, pain increases,as well as the symptoms of inflammation.

The second phase is the phase of controlled movements or moderate-protective phase.

The kinesitherapeutic tasks in this phase include controlling of pain, swelling and joint effusion and stimulating the regeneration of the traumatized tissue. Another task involves reducing the effect of formation of contractures and gradually increasing the mobility of the soft tissues, muscles, and the amount of motion in

the joints. Also, the focus is on continuously increasing the muscle strength, improving the function of the strong neighboring parts, training the patient in an appropriate home rehabilitation.

The kinesitherapeutic means consist in protection – orthoses and taping (10).

To reduce the effect of the formation of contractures and gradually increase the mobility of the soft tissues and the amount of movement in the joints,passive joint mobilization techniques are applied (8).

Withpain reduction and at plateau status in the potential range of motion, mobilization techniques progress, as the shoulder joint is placed at the maximum possible final range of motion and in this positionsome sliding in the appropriate direction is applied.

Pendural exercises are used, which are in factautomobilisation techniques,utilizing the effect of gravity for distraction of the humerus relative to glenoid fossa. They help to reduce pain by gentle traction and oscillating movements-II level and provide early movements of the articular structures and synovial fluid (1). Initially,weights are not used. When a patient tolerates stretching,weight is added in the hand or through a wrist cuff, to reach grade III distraction. For precise targeting of the distraction towards the glenohumeral joint,the blade is fixed manually or through a belt (2).

Distractions may be applied only whenstretching of the joint capsule is evidentin the minimal-protective phase. What is needed is a good fixation of the scapula to target the distraction to a glenohumeral joint and avoidance of excessive stretching of the soft tissues in the scapula-thoracic complex.

Pendural exercises are not appropriate if, after their application,there is observedpain increase and reduction of the potential range of motion (12).

To increase the range of motion and mobility of affected tissues a progressive transfer is made from passive to active exercises. Initially, active exercises to feeling pain are applied,including all the movements of the shoulder and scapula. Highly recommended exercisesinclude self-help with theother, healthy hand, using an overhead hoist or a gymnastic stick (13).

To gradually increase muscle strength the focus is laid on the control of muscle spasticity and improvement ofthe stabilizingfunction of the muscles of the rotator cuff. A recovery of the caudate sliding head humerus is necessary before the execution of any other exercises for the shoulder joint consisting of caudate sliding retention, which helps the repositioning of the humeral head in the glenoid fossa (8).

Exercises with a closed kinematic chain with mild burden (eg push-ups against a wall or on a table by standing) promote co-contraction of the rotator cuff and scapular stabilizers. If there are no contraindications, the implementation of a slight displacement of the body back and forth on the left-right stimulates the muscles to control movement.

A slight burdening with the body weight leads to compression in the joint and is appliedrelative to tolerance.

Training of external rotators helps the depression of the humeral head in the abduction of the armpit. The patient is trained in an active conscious depression of the humeral head in the following way: he/she is made to try to move the ailing arm caudally. We give him/her a slight resistance in the region of the elbow for proprioceptive feedback. A mild depression of the blade is permissible in this movement. The patient is verbally encouragedto properly execute the exercise with a caudal glide of the humerus (13).

The process goes through training of the patient to perform abductionto his armpit, keeping the caudate sliding of the humerus. Multiangular isometric exercises are applied against average resistance force. With the increase inthe range of motion, normalization of joint play and advance in the recovery process isotonic exercises are included in the complex against the increasing resistance.

To improve the function of the healthy neighboring parts, progressive strength and stabilization exercises and light activities are performed, involving the shoulder joint (2).

The methodological guidelines relate to compliance with the signs of overdose – pain at rest, fatigue, increased weakness and muscle spasm. Proper dosage and careful progression of exercises exclude reoccurrence of the above-mentioned symptoms.

The third phase is the phase of treatment to functional recovery or minimal-protective phase.

The kinesitherapeutic tasks during this phase are to reduce pain from contractures or adhesions. It involves an increase in soft tissue, muscle and joint mobility; correction of impaired joint mechanics and impaired posture;enhancement of muscle strength and balance; endurance training;growing in functional independence; training the patient to actively participate in the recovery process.

The kinesitherapeutic means include stretching of the restraint structures.

To increase soft tissue, muscle and joint mobility,various stretching techniques and autostretching are applied. Autostretching is performed when the reaction of the joint becomes predictable and the patient can tolerate stretching (7).

The patient is trained in automobilisation techniques for homeshoulder rehabilitation treatment consisting of:

- Caudal mobilization – the patient sits on a hard surface and grabs its edge with the ailing arm. Then tiltsthe body in the opposite direction;
- Ventral mobilization – the patient lies down on a hard surface and put his/her hands behind the body. Then, propped on them and by weight of the body, carries mobilization-
- Dorsal mobilization – the patient takes the starting position of leg support on his/her elbows. Releasing the body weight on the hands he/she performs mobilization (1).

For correction of impaired joint mechanics and impaired posture, stretching of hypertensive and strengthening of weakened muscles are applied.

If the joint constraint is long-standing, the patient usually offsets the impairment by an increased mobility of the scapula. In this case, exercises for stabilization and control of the blade are applied. By progressively increasing resistance from concentric to eccentric,the exercises are applied initially in open and later in closed kinematic chains (6, 1).

Endurance training is accomplished by progressively increasing the time of exercise at a low rate, involving more complex exercises for a longer time, application of exercises with a faster rate for a longer time (7).

The patient is trained in safe progression relative to his/her self-estimate of his/her condition and,also, to prevent recurrence.

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PLEXIFORM FIBROMYXOMA OF THE STOMACH: A CASE REPORT

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ПЛЕКСИФОРМЕН ФИБРОМИКСОМ НА СТОМАХА: ОПИСАНИЕ НА СЛУЧАЙ

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РЕЗЮМЕ

Плексиформеният фибромиксом на стомаха е рядък бенигнен мезенхимен тумор определен като отделен на скоро като самостоятелна неоплазма. В достъпната литература са публикувани само 24 случаи. Ние описваме пълвия случай на този тип тумор в България. Препарати от 51 годишна жена с първична диагноза ГИСТ на стомаха бяха изпратени за второ мнение и имунохистохимично изследване. В антралната част на стомаха близо до лигавица, която е интактна е намерен не добре отграничен тумор с размери 2,5х2 см.Хистологично се установява мултинодуларна неоплазма, разделяща мускулните влакна, съставена от мезенхимни клетки разположени в миксоиден алцианофилен матрикс. Диагнозата е базирана на имунохистохимичната констелация от негативност на туморните клетки за СД117, СД34 и S100, и силна позитивна реакция за гладко-мускулен актин. Няма данни за рецидив или метастази 1 година след секторалната резекция на стомаха. Представеният случай на плексиформен фибромиксом разширява спектъра на мезенхимни стомашни тумори и този тумор трябва да се включи в тяхната диференциална диагноза.

ABSTRACT

Plexiform fibromyxoma of the stomach is a rare benign mesenchymal tumor, determined as a distinctive neoplastic entity recently.Only 24 cases were publicated in the available literature.We describe the first case of this type of tumor in Bulgaria. The specimen of 51-yr old woman with diagnosis GIST of the stomach w ere sent for second opinion and immunohistochemical approvement. The ill-defined firm tumor which measured 2.5/2 cm. has been found in stomach wall near to intact mucosa. The histological structure presented multinodular neoplasm discerning the muscle fibres,composed of mesenchymal cells situated in a myxoid alcianophilic matrix. The diagnosis was based on Immunohistochemical constellation of negativity of the tumor cells for CD117,CD34 and S-100, but strong positive reaction for smooth muscle actin.There is no data of recurrence or metastases one year after sectoral resection of the stomach.The presented case of plexiform fibromyxoma widens the spectrum of the mesenchymal gastric tumors and this tumor has to be included in their differential diagnosis .

The plexiform fibromyxoma is a rare benign mesenchymal tumor of the stomach, determined as tumor entity by M.Miettinen et al.(4). This tumor has been described as gastric myxoma or fibromyxoma in the older literature but now is known with alternative names "plexiform angiomyxoid myofibroblastic tumor"(PAMT), (2,8,9) or "gastric plexiform fibromyxoma" (GPF), (1). It is most frequently localized in the antrum of the stomach. Until now there are about 24 cases reported (2,3). The tumor measured between 3 and 15cm, localized predominantely in the muscularis propria of the gastric antrum. Microscopically it is characterized by multinodular intramural plexiforme growth pattern of spindle cells scattered in fibromyxoid stroma with rich arborizing capillary network. The histological feature was similar to gastrointestinak stromal tumor (GIST), but the tumor demonstrated an immunophenotype, different from GIST: it was negative for CD 117,CD34 and S-100 protein.Tumor cells were diffusely positive for small muscle actin (SMA) consistent with myofibroblastic differentiation. Now we would like to present a new case of plexiforme fibromyxoma of gastric antrum.

CASE DESCRIPTION

A biopsy of a 51 yrs old woman (M.A.D BN4588 /13) was sent to our department for second opinion after sectoral resection of the stomach. Previously was taken a gastroscopic biopsy which showed an intramucosal signet-ring gastric carcinoma. Despite the very careful sectioning of the surgical resection, the mucosa is found to be intact, both macro- and microscopically. The tumor was described as relatively well-defined, with firm consistency, size 2,5x2cm, histologically composed of fibroblast-like cells, dissecting the muscle fibers. Clinically and pathomorphologically the tumor has been suspected for GIST and further examination was needed.

Microscopically the tumor showed plexiform growth pattern discerning the fascicles of the muscle layer (fig.1).

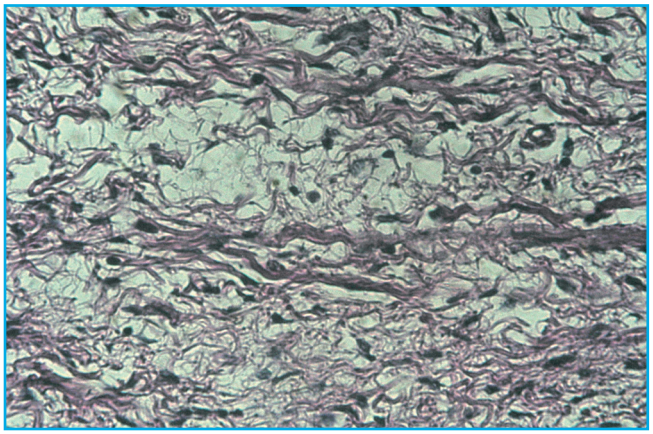

Fig 1. Nodules of spindle tumor cells discern muscles fascicles (horizontal in the middle HE staining

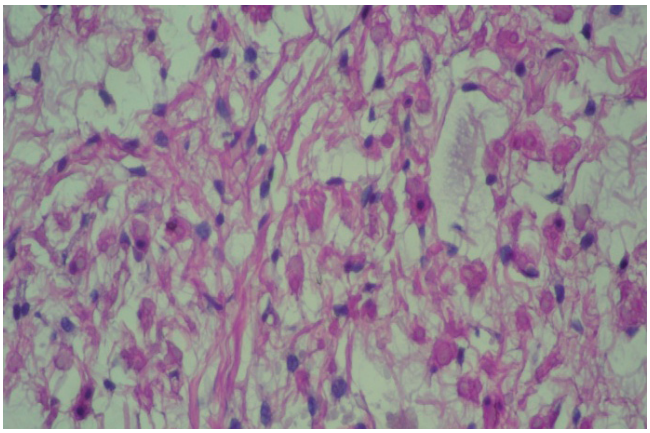

Fig 2. The stroma is myxoid with pool of alcianopfille mucin. HE staining

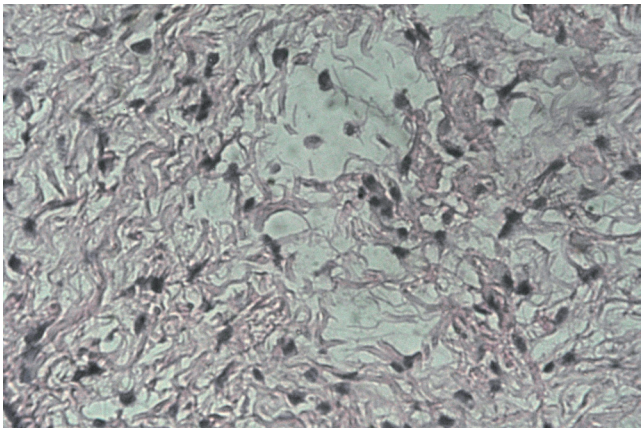

Fig 3. The epitheloid feature of tumor cell in some zone of the tumor. HE staining

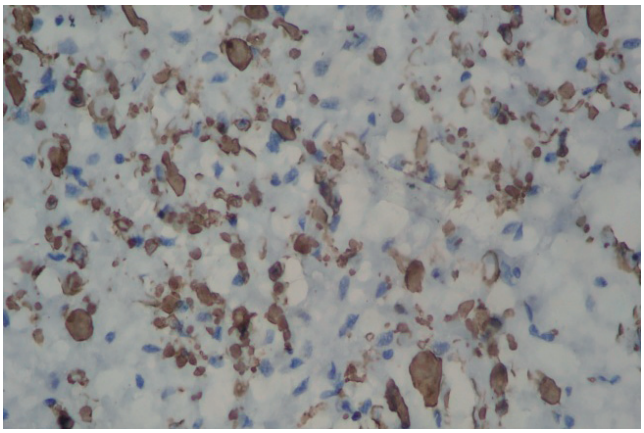

Fig.4. The tumor cells are immunopositive for SMA (smooth muscle actin).

The tumor cells are fusiforme or oval without significant atypia or mitotic activity. In some areas the cells have epitheloid feature (fig.2) .They are situated in myxoid or hyalinised matrix. (fig.3). The vascular stroma is presented as moderately proliferated capillary network. There is no necrosis, cysts formation nor calcificates. Histochemical staining with PAS and alcian blue showed negative PAS reaction and alcianophillia of the myxoid stroma. Immunohistochemically the tumor cells were diffusely positive for SMA (fig.4), focally positive (under 25%) for desmin and CD10; negative for CD 117 (Kit), CD34 and S-100 protein. Antibody MAB1 (Ki 67) showed low proliferative activity- only 1% of tumor cells were with nuclear immunopositivity.

The histochemical and especially immunohistochemical results permitted to make differential diagnosis of mesenchymal tumor of the stomach which includes the following entities: GIST – myxoid variant,gastric plexiform fibromyxoma (G.P.F.), Inflammatory fibroid polyp (I.F.P), plexiform neurobifroma, (P.N.), Myxoid leiomyoma (ML) and Fibromatosis(F). The main immunohistochemical characteristics are shown in table N1.

The tests which were carried out, allowed the establishment of the diagnosis – plexiform fibromyxoma of the stomach, based on the published until now criteria for this tumor, according to the Department of pathology, Stanford University School of Medicine,2011 (1). One year later the patient was doing well without objective data of recurrence.

DISCUSSION

The plexiform fibromyxoma of the stomach is a very rare tumor. M.Miettinen et al (4,5) found that P.F. was less than 1/150 compared with that of gastric GIST. Analysing all reported 24 cases A.Kim et al (2) showed that the age of the patients varied from 7 to 75 yr and that males and females were involved equally. All of the tumors are localized in the antral mucose and have multinodular way of growth as in our case. The tumors involved muscularis propria-frequently they caused ulcerations of the gastric mucosa (2), or propagation to subserosa (1) and very rarely showed transmural involvement with fistulating abscessus (3). The cytological characteristic and mucoid matrix of the observed case were other features similar to the previous publicated cases.

The immunohistochemical results were the basis of making a differential diagnosis with other mesenchymal gastric tumorsm (5,6,7). The most important among them were a positivity of SMA and negativity of CD117 , GOT-1 and CD34. Some discussion arose about the in-

Table1

Tumor / Antibody	G.P.F.	GIST	I.F.P.	P.N.	M.L.	F.
CD 117	—	+	—	—	—	—
S- 100	—	—	—	+	—	—
SMA	+	—	—	—	+	—
Desmin	—	—	—	—	+	—

terpretation of the focal positivity of desmin, protein consistent with smooth muscle differentiation and SMA – consistent with myofibroblastic differentiation. The dominating results of positivity of SMA in these tumors was the argument to accept myofibroblastic histogenesis and thus support PAMT as the correct terminology to be used (2).Y. Sing et al.(7) considered that plexiform fibromyxoma and PAMT are related, but different tumors – *immunohistochemically* by focal positivity of desmin and caldesmon in PAMT and *clinically* with larger size, vascular invasion and extragastric propagation of plexiform fibromyxoma.Having in mind that every tumor might be variable and the rarity of the gastric plexiform fibromyxoma this discussion would continue while more cases would be reported.

The prognosis of all reported cases had been good, coinciding with the "calm" histological feature and low proliferative index (below 2%).

To the best of our knowledge this is the first case of plexiform fibromyxoma of the stomach in Bulgaria. The presented case widens the differential diagnosis of the mesenchymal tumors of the stomach and enriches the diagnostic practice of the pathologist.

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50 YEARS OF GERONTOLOGY RESEARCH: THE SOFIA CENTRE OF GERONTOLOGY AND GERIATRICS

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50 ГОДИНИ ГЕРОНТОЛОГИЧНИ ИЗСЛЕДВАНИЯ: БЪЛГАРСКИЯТ ЦЕНТЪР ПО ГЕРОНТОЛОГИЯ И ГЕРИАТРИЯ

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РЕЗЮМЕ

Българският Център по геронтология и гериатрия в София (ЦГГ) бе основан на 10 юли 1963 год. към тогавашното Министерство на народното здраве и социалните грижи. От 1964 год. той разгърна обхватна научно-изследователска работа под ръководството на първия си директор чл. кор. професор д-р Драгомир Матеев (1902–1971). В ЦГГ се изградиха седем секции: ***физиология на стареенето; психология и психопатология на стареенето; биохимия; морфология; физическа активност и стареене; гериатрия; социална геронтология.*** Основан като научно-изследователски център, ЦГГ развви в следващите години и преподавателска (следдипломни курсове по геронтология и гериатрия); клинична гериатрична и методична дейност. В статията са обобщени основните приноси на ЦГГ, публикувани в 9 тома ***Проблеми на геронтологията и гериатрията***, както и в редица книги и научни публикации в страната и в чужбина от 1965 год. и досега. Днес ЦГГ не съществува, а част от подготвените в него геронтолози и гериатри работят при трудни условия в различни институти. Наследник на

ABSTRACT

The Bulgarian Centre of Gerontology and Geriatrics (CGG) was founded on the 10th July 1963 in Sofia at the Ministry of Health and Social Cares. Since 1964 CGG carried out a comprehensive research activity. The first director of CGG was the eminent Bulgarian physiologist and gerontologist Professor Dragomir Mateeff (1902–1971). In the CGG have been developed seven sections: of ***Physiology of Ageing***; ***Psychology and Psychopathology of Ageing***; ***Biochemistry***; ***Morphology***; ***Physical Activity and Ageing***; ***Social Gerontology***; and ***Geriatrics***. Beginning as a research centre, CGG carried out during the next years also educational (postgraduate), clinical and methodical activities. In that paper we summarize the main contributions of CGG for 50 years, published in 9 volumes of ***Problems of Gerontology and Geriatrics*** as well as in numerous books and publications from 1965 up to now. Today a part of the Bulgarian gerontologists and geriatricians, qualified in the former CGG, worked at various institutes. A successor of CGG is the Clinical centre of endocrinology and gerontology at the Sofia Medical University.

ЦГГ е Клиничният център по ендокринология и геронтология при Медицинския университет, София. Посрещайки 50-годишнината на българския Център по геронтология и гериатрия, ние всички имаме мисията да продължим неговата разностранна и изключително важна за нацията дейност.

Welcoming the 50th anniversary of CGG we have the mission to continue the gerontology research in Bulgaria and to take pains to restore the full range of activities in our multidisciplinary and unique science. The imperatives of nowadays Bulgarian society oblige all us.

On 10 July 1963 – by order of the then Bulgarian Minister of Health and Social Cares Dr. Kiril Ignatov – was founded a Research Centre of Gerontology and Geriatrics (CGG). From its beginning the CGG was based for the next 20 years on the Old People's Home No 11 in Sofia, a new built social home designed for older people. The first Director of CGG was the eminent Bulgarian physiologist and gerontologist Professor Dragomir Mateeff (1902–1971). He skillfully grounded extensive research in the main directions of gerontology and geriatrics. The full range of research activity began at February 1964 with the appointment of the first researchers of the CGG: Liudmila Venova, Luben

Valnarov, Sofia Todorova, Enio Boyadjiev, Ignat Petrov. Beginning as a research centre, CGG carried out during the next years also educational, clinical and methodical activities. In the CGG have been developed seven sections: ***Physiology of Ageing*** (headed by Luben Valnarov, and later by Maria Guncheva); ***Psychology and Psychopathology of Ageing*** (head Ignat Petrov); ***Biochemistry*** (head Pavlina Angelova, later Otto Zlatarev; Atanas Kiriakov); ***Morphology*** (Georgi Chavrakov and Marta Hristova); ***Physical Activity and Ageing*** (head Enio Boyadjiev); ***Social Gerontology*** (head Georgi Stoynev); and ***Geriatrics*** (head Vladimir Denev, later Georgi Angarov; Velichko Golemanov; Ignat Petrov). The main contributions of CGG in its first 8–9 years were published in 8 volumes of Problems of Gerontology and Geriatrics, edited by Meditsina i Fizkultura 1965–1972, as well as in numerous books, chapters of books and scientific papers in Bulgaria and abroad. One of the main topics of Mateeff and his colleagues from 1964 to 1971 were the longitudinal studies about the effects of physical and mental activity on the health and well-being of older people. They were published in volumes IV and V of Problems of Gerontology and Geriatrics. Valuable personal studies of Mateeff on the biological nature and theory of ageing were published in the last year of his life (1971) in prestigious international journals as well in the volume VI of Problems of Gerontology and Geriatrics. Another studies of Ignat Petrov (one part of them in collaboration with Konstantin Konstantinov) – on the role of mental and physical activity for the mental health in ageing. Other important studies in that period have been on morbidity and death rates in different ages, longevity, Bulgarian centenarians (Georgi Stoynev and coll.). Further gerontological population studies were carried on: a homogeneous representative sample of rural people from 46 Shopp villages (initiated by Georgi Stoynev and continued by Ignat Petrov as a longitudinal and cross-sectional assessment on mental health and ageing); the mental health problems also of an elderly population sample of Sofia City (Konstantin Konstantinov); the dyslipoproteinaemias in the population (Atanas Kiriakov et coll.). Many other contributions of CGG are valuable, among them on: energy aspects of metabolism in ageing (Pavlina Angelova); hearing and ageing (Velichko Golemanov, Kiril Popov); ageing and vision (Vladimir Denev; Emilia Peicheva); anthropometric evaluation of ageing (Velislav Todorov); ventilation and lung functions in ageing (Maria Guncheva); ageing and arterial hy-

pertension (Sabina Zacharieva); other geriatric aspects of internal medicine (Milka Bagrenska; Stoyan Vizev; Diana Brinikova; Ivancho Ivanov; Ilija Popiliev et al.); ageing and different aspects of atherosclerosis (Professor Mihail Rashev and his research group including Nevena Pelova and Athanas Kiriakov); also epidemiology of atherosclerosis (Stoyan Vizev); ageing, health and illness in general (Georgi Stoynev and coll.); ageing and psyche; ageing and depression (Ignat Petrov); culture therapy in old people's home (Ignat Petrov and Lilia Vlahlijska); social integration of the elderly people (Lilia Vlahlijska); two consecutive Bulgarian-Hungarian psychogerontological transcultural studies (Ignat Petrov and Nadia Dumeva in collaboration with Bela Kolozsi, Laszlo Ivan and Janos Bartok); ageing and blood coagulation (Georgi Angarov; Dimitar Tharaktchiev); the effects of regular physical exercises on ageing people (Enio Boyadjiev, Liudmila Venova, Ivan Tulilov, Ivan Petkov, Bagra Delcheva etc.); the effects of physical activity in older people in good health and after illness, including after myocardial infarction (Ivan Petkov), and with lung diseases (Bagra Delcheva); longitudinal assessment of physically active older people (Ivan Petkov); socio-economic state of people over the age of retirement (Zvetana Arnaudova); other aspects of social gerontology (Sylvia Maksimova; Lubomir Tomov); the health of the participants in the communist movement (R. Kermova; Lubomir Tomov); the long lived people (Stoyan Vizev, Raisa Yatzemirska and colleagues).

The teaching activity of CGG began in 1969 with regular every year's post-graduate courses in gerontology and geriatrics for physicians, nurses, physiotherapists and other professionals. Also since 1969 the clinical geriatric activity marked out a further development through a co-operation of leading geriatricians of CGG with some University clinics of the Sofia Medical Faculty: so Konstantin Konstantinov and Ignat Petrov worked on the basis of the University Psychiatric Clinic; Vladimir Denev and Emilia Peicheva – in the Ophtalmology; Velichko Golemanov and Kiril Popov – in the Otorhino-laryngology; a number of geriatricians worked in the Clinic of Endocrinology. Many researchers have obtained their PH degree in the CGG, and many of them work now at leading positions in other medical Institutes.

In 1972 Professor Georgi Stoynev was appointed as head of CGG. The same year, with the project of the communist party to form a gigantic Medical Academy, the CGG was merged mechanically in the Institute of Endocrinology. At 1972 CGG had 7 sections and a staff of 86 persons. But the sections of gerontology and geriatrics have been subordinated and gradually assimilated in the new institute. At the official circles there predominated an underestimating of the gerontology with a misunderstanding of its identity and multidisciplinary essence. This negative tendency continued during the 1980s and 1990s. The loss of independence and the further assimilation of the sections of CGG had result in the loss of dozens of educated and motivated gerontologists and geriatricians who were constrained to shift their specialty.

Nowadays a successor of the CGG is the Clinical Centre of Endocrinology and Gerontology (CCEG) at the Medical University of Sofia. Few of the researchers from the former CGG continue to work now in the CCEG, whose function is only in the field of education – but on the basis of one purely endocrinological clinic. Other gerontologists have been transferred to the Faculty of Public Health of the Medical University, whose activity is also purely educational. Within that Faculty there work successfully the researchers-gerontologists Zacharina Savova (social gerontology); Polina Balkanska (psychology) and Zhenia Georgieva (psychotherapy and ageing).

Meanwhile the participation of Bulgarian gerontology in the activity of the powerful International Association of Gerontology and Geriatrics (IAGG) has increased considerably. In 1994 researchers from CGG (a part of them retired) and public figures founded the ***Bulgarian Association on Ageing***, an NGO – member

of IAGG since 1997. Among the contributions in gerontology in the last years are: the book edited in 2009 by Prof. Vodenicharov '***Actual Problems of Ageing and Old Age***', with chapters written by the gerontologists Sylvia Maksimova, Polina Balkanska, Zhenia Georgieva, Jasmine Pavlova, Zaharina Savova et al.; the book of Krasimir Vizev on the biologic age; the publications of Dimitar Tcharaktchiev on gerotechnologies; the study of Ignat Petrov on the feelings and attitudes of older people towards the changes in the period of transition. **The *elderly in a period of transition*** was one of the central topics at the 18th World Congress of Gerontology and Geriatrics in Rio de Janeiro 2005, where Ignat Petrov organized and convened a symposium. That work of Petrov was further published in the Annals of New York Academy of Sciences and in the International Journal of Geriatric Psychiatry (London). Finally, a fruitful collaboration in psychogerontology exists now between our Centre and the group of Professor Peter Coleman, University of Southampton, UK, with a number of publications 2011–2012 and a book on the attitudes and feelings of older people: ***Ageing, Ritual and Social Change*** (eds. Peter Coleman, Daniela Koleva and Joanna Bornat), Farnham, Surrey, Ashgate Publishing, 2013.

Welcoming the 50th anniversary of CGG we have the mission to continue the gerontology research in Bulgaria and to take pains to restore the full range of activities in our multidisciplinary and unique science. The imperatives of nowadays Bulgarian society oblige all us.

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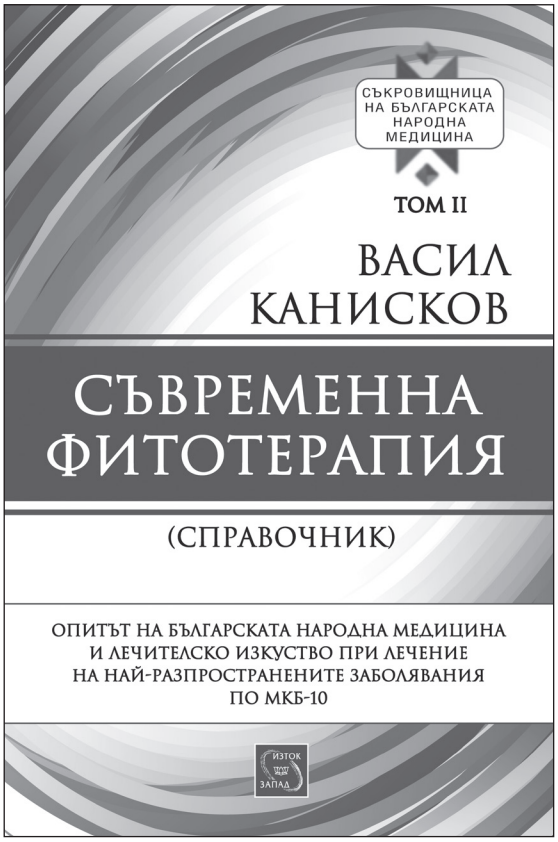
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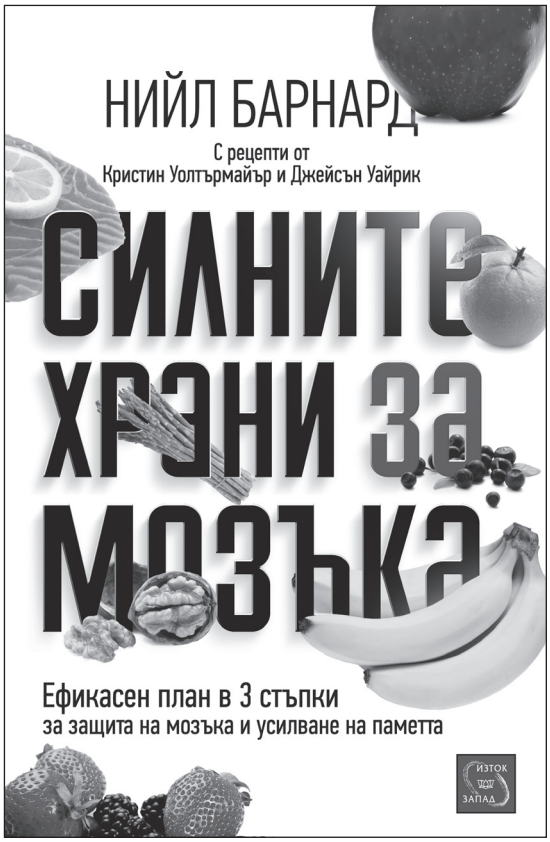
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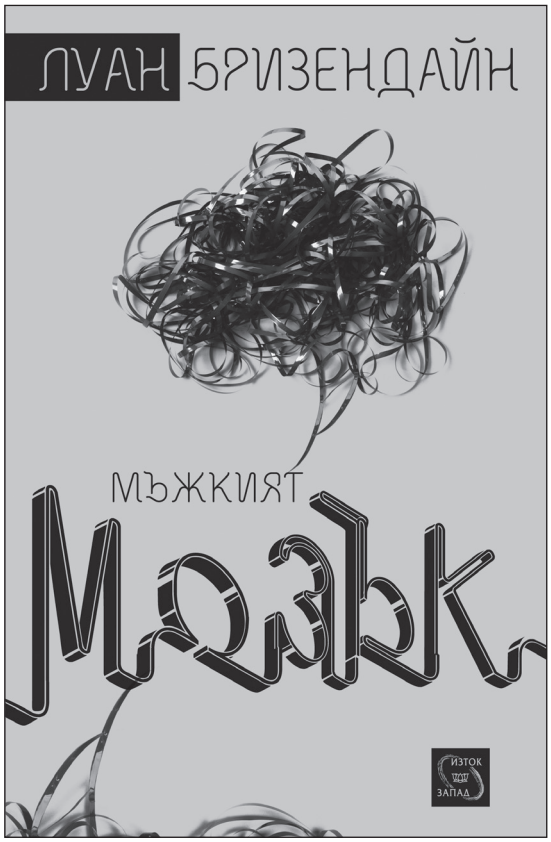
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