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Marker structures in the liquor of patients with destructive processes in brain tissues

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Abstract

The paper presents the results of studies the solid phase structures of liquor 140 patients' with various types of destructive brain diseases (74 - neurosyphilis, 26 - bacterial meningitis, 7 - aneurysms, 9 - malignant tumors, 24 - discogenic radiculitis). The transfer of liquor into the solid phase was carried out by the method of marginal dehydration of biological fluids. This method allows to visualize the structure of metabolites of the liquid phase of liquor. The results of the study showed presence in the patients' liquor marker structures, which could be used to clarify the diagnosis.

Keywords: *liquor, marginal dehydration method, marker structures, diagnostics, neurosyphilis, bacterial meningitis, brain aneurysm, brain tumors, discogenic radiculitis.*

Introduction

One of the functions of liquor is the accumulation of metabolic products of brain tissues, followed by their excretion through the lymphatic and blood vessels. The metabolites contained in liquor carry important information about the state of brain tissue. This information cannot be obtained using routine research methods. To extract this information, the method of marginal dehydration was used (presented in the section materials and methods).

The main attention in this work was paid to the diagnosis of neurosyphilis. In Russia, after the peak of the syphilis epidemic in the 90s of previous century and in the last decade of this century, occurs a significant decrease in the overall incidence of syphilis. At the same time there were changes in the pattern of disease: a decrease in the number of early forms of syphilis with an increase in the share of hidden and late forms of the disease, including neurosyphilis. So, if in 1999 in Russia there were 144 newly diagnosed patients with neurosyphilis, in 2009 - 872, in 2014 - 1163, and this figure continues to grow [1,2].

As a result of uncontrolled use of antibiotics, since the second half of the last century, there has been increase in the number of latent and late forms of neurosyphilis in many countries [3-5]. The immunological reactivity of patients to treponema pallidum has also changed [6,7]. All this caused a significant decrease in the sensitivity of existing laboratory methods for diagnosing neurosyphilis and, accordingly, an increase in erroneous results [8,9]. According to Russian authors, the frequency of diagnostic errors in neurosyphilis is about 30% in relation to the number of registered patients [10]. Often there are situations in which it is impossible to exclude or confirm the invasion of treponema pallidum in the tissue of the central nervous system. Thus, about a third of the results of liquor studies using routine methods for residual manifestations of neurosyphilis are questionable. This does not allow to assert with certainty about the complete sanitation of the patient. In some cases, only the subjective assessment of the clinician is decisive in the diagnosis of neurosyphilis and the appointment of specific therapy [11].

A study of the liquor of patients with other types of destructive brain diseases was carried out to identify the marker structures of the solid phase of the liquorin these patients and compare them with the structures of the liquor of patients with neurosyphilis.

Aim

The aim was to search for new marker structures in liquor of patients with neurosyphilis and other destructive processes in brain tissues using the method of marginal dehydration biological fluids.

Material and methods

The material for the study was the liquor of 140 patients: 92 men aged 21 to 77 years and 48 women aged 26 to 62 years. The patients were represented by five nosological groups (neurosyphilis, bacterial meningitis, cerebral aneurysm, malignant brain tumor, discogenic sciatica).

The main group included 74 patients with neurosyphilis. This group was divided into 3 subgroups. Subgroup A - 19 patients diagnosed with early asymptomatic neurosyphilis. Subgroup B - 34 patients with a diagnosis of late meningovascular neurosyphilis. Diagnoses in patients of these two subgroups were established based on clinical symptoms, positive indicators of treponemal and non-treponemal tests in blood serum and liquor, including the VDRL test (modern version of Wasserman's reaction). Subgroup C - 21 patients with a doubtful diagnosis of neurosyphilis with positive indicators of treponemal and non-treponemal tests in the blood serum, weakly positive indicators of treponemal and non-treponemal tests in the liquor with a negative VDRL test.

All patients with neurosyphilis had previously received specific treatment. When examining patients, various serological studies (treponemal and non-treponemal) of blood serum and liquor were carried out: passive hemagglutination reaction, immunofluorescence reaction, enzyme-linked immunosorbent assay with the determination of different classes of immunoglobulins, etc. Liquor analysis also included determination of the total protein concentration and the number of cells.

The following comparison groups were taken: 26 patients with bacterial meningitis and 16 patients with volumetric brain formations (malignant tumors - 9, aneurysms - 7). Due to the lack of possibility to obtain liquor in a healthy person, 24 patients with discogenic radiculitis who had normal indicators of routine laboratory liquor tests were taken as a group of conditional norm.

The main method of research was the method of marginal dehydration of biological fluids developed by us [12]. The method was set up on glass test cards with special markings in the form of windows. A drop of liquor was applied to each window of the test card and covered with a cover glass – an analytical cell was created. Four analytical cells were prepared for each liquor sample. The test card was positioned strictly horizontally. Dehydration was performed under standard conditions: temperature 20-25°C, relative humidity 55-60%. Water evaporation occurred through the gap between the surface of test card window and cover glass for five days. Slow evaporation created conditions for local self-organization of the liquor. As a result, special anisotropic formations - "morphons" were formed in the analytical cells. Morphones were represented by normal structures (spherulites) and sundry structures characteristic of various types of pathology. Morphones were studied using a Leica DM2500 polarizing microscope. All figures in the article are shown in polarized light. .

Result

Investigation of the structures of the liquor solid phase made it possible to identify a number of different morphones specific to the groups of patients under consideration. It should be noted that in addition to the main morphones in the analytical cells of all examined patients, background structures were determined in the form of anisotropic formations of various sizes and shapes.

Morphons in the liquor of patients with discogenic radiculitis were represented by clusters of spherulites (Figure 1). These morphons were taken as conditional structures of the norm. It should be noted that such structures were present in small amounts in liquor of all examined patients.

Certain types of morphons were detected in the liquor of patients with neurosyphilis. All 19 patients with early asymptomatic neurosyphilis (subgroup A) had morphons in the form of ovals of various sizes with an isotropic shell and an anisotropic center. Some of these structures were embedded in the spherulites (Figure 2a), and some were scattered around them (Figure 2b).

Thirty-four patients with meningovascular neurosyphilis (subgroup B) contained many morphons in the form of balls filled with small grainy structures. These balls were located separately (Figure 3a) or were embedded in spherulites (Figure 3b).

Liquor morphons in 3 out of 21 patients with a dubious diagnosis of late meningovascular neurosyphilis (subgroup C) did not differ from the picture of liquor morphons patients of subgroup B. In the liquor of remaining 18 patients of subgroup C, spherulites with multiple isotropic inclusions (Figure 4a), with a crystalline coating on the periphery (Figure 4b), with single round isotropic inserts (Figure 4c) were determined. These structures in their form approached the picture of the norm.

The morphones of all 26 patients with bacterial meningitis were represented by balls of small granular structures, similar to those of patients with late meningovascular neurosyphilis (subgroup B).

In the liquor of 7 patients with cerebral aneurysm, separately lying balls from granular structures (Figure 5a) or granulations included in spherulite (Figure 5b) were determined.

In the liquor of 9 patients with malignant brain tumors, special morphons - conglomerates of spherulites and balls of small granular structures (Figure 6) were identified.

Table 1 shows the distribution of liquor marker structures in the examined patients.

Table 1 shows that marker morphons are necessarily present in the liquor of all patients in certain groups. Moreover, two groups of patients (with late meningovascular neurosyphilis and bacterial meningitis) had similar markers.

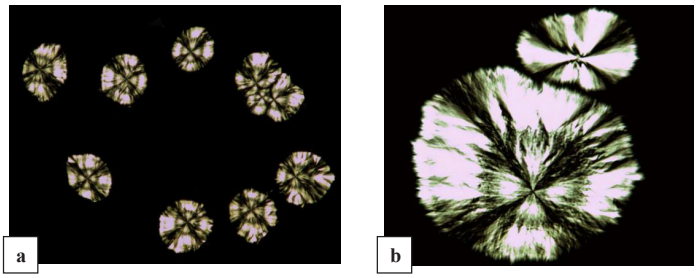

Figure 1.*Morphones of liquor patient's with discogenic radiculitis: a - x200; b - x630*

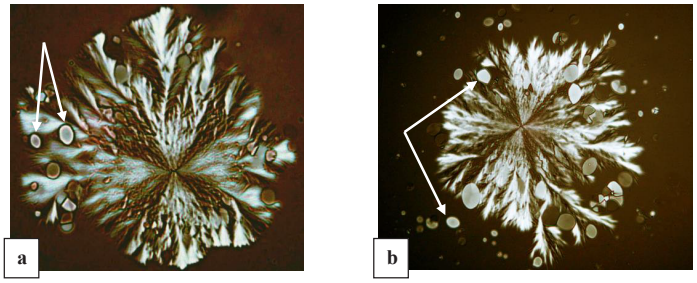

Figure 2.*Morphones of liquor in patients with early asymptomatic neurosyphilis: a - ovals inside spherulites (arrows); b - ovals outside the spherulite (arrows). x400*

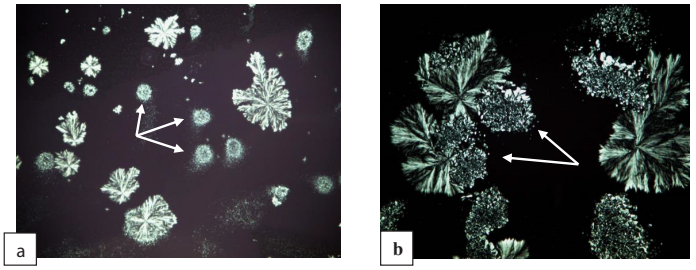

Figure 3.*Morphones of liquor of patients with late meningovascular neurosyphilis in the form of balls of small grainy structures (arrows): a - balls on the background of spherulites and dendrites, x50; b - balls in the structure of spherulites. x200*

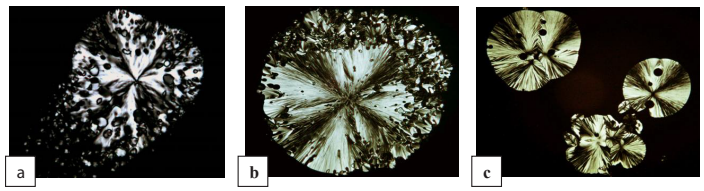

Figure 4.*Morphones of liquor of patients with a doubtful diagnosis of late meningovascular neurosyphilis: a - spherulite with multiple isotropic inclusions, x200; b - spherulite with crystal structures along the periphery, x200; c - spherulite with single round isotropic inserts, x100*

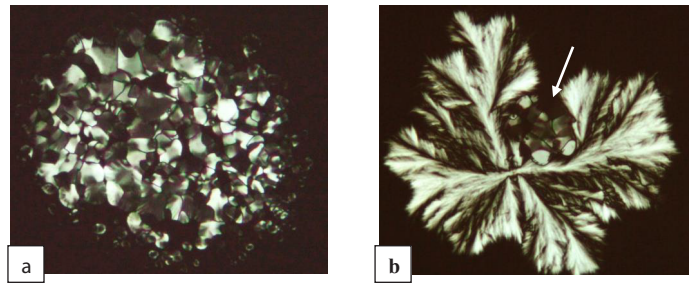

Figure 5.*Morphones of liquor in patients with cerebral aneurysms: a - ball of granular structures, x400; b - spherulite with the inclusion of granular structures (arrow), x400*

Markers / Type of pathology	Oval structures	Balls made of small granular structures	Balls made of granular structures	Conglomerates of spherulites and balls of small granular structures
Early asymptomatic neurosyphilis (n=19)	100%	-	-	-
Late meningovascular neurosyphilis (n=34)	-	100%	-	-
Bacterial meningitis (n=26)	-	100%	-	-
Brain aneurysm (n=7)	-	-	100%	-
Malignant brain tumor (n=9)	-	-	-	100%

Table 1.*Types of anisotropic morphones - marker structures of liquor in patients with destructive brain pathology*

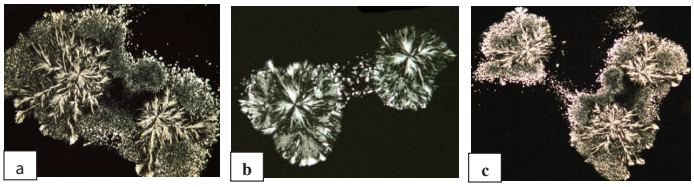

Figure 6.*Morphones of liquor patients with malignant brain tumors: conglomerate of spherulites and granular balls, a - x400; b, c - x200*

Discussion

TThe results of a study using the method of marginal liquor dehydration of patients with various types of brain pathology showed that brain lesions with infectious agents (neurosyphilis and bacterial meningitis) and volume formations (tumor, aneurysm) cause the appearance of decay products in the liquor. When the cerebrospinal fluid passes into a solid phase, these products form special structures - morphones.

Morphones in the form of spherulites without any inclusions were accepted as conditional norm markers. Morphones with a specific structure associated with a specific pathological process were assigned to the corresponding marker structures. Thus, in patients with early asymptomatic neurosyphilis (subgroup A), oval structures of various sizes were found in the liquor. Such morphons were found only in representatives of this subgroup and were assigned to markers of early asymptomatic neurosyphilis.

The liquor of patients with late meningovascular neurosyphilis (subgroup B) and patients with bacterial meningitis contained many morphons in the form of spheres consisting of small grainy structures. These morphons were assigned to marker structures associated with the action of an infectious agent. In this case, the distinctive diagnostic signs of bacterial meningitis were: the corresponding clinical symptoms of meningitis, high content of total protein in liquor (1.5-11.0 g/l) and pleocytosis (500-12000 in 1 µl), which was not observed in patients with late form of neurosyphilis.

The significance of the marker identified in the liquor of patients in group B was shown when examining a group of patients with a doubtful diagnosis of neurosyphilis (subgroup C). In the liquor of three patients, the presence of a marker in the form of spheres of small grainy structures confirmed the diagnosis of neurosyphilis and allowed undoubtedly to prescribe them specific treatment. In the remaining 18 patients of subgroup C, this marker was not detected. In their liquor were identified spherulites with various isotropic inclusions which indicated on the state sanitation of these patients. These patients were taken for further clinical and laboratory control.

Specific morphons were found in the liquor of patients with cerebral aneurysms. They were represented by two types of structures: the first - granular anisotropic particles collected in balls; the second - these particles entering in spherulite. In the liquor of patients with malignant brain tumors, morphons were identified as conglomerates consisting of incomplete spherulites surrounded by a dense ring of balls of small grainy structures. We can only assume that these formations are markers of these pathological conditions. Finding out their specifics requires further research.

It should be noted that the marker structures of the norm (spherulites), are present in small amounts in the liquor of all the examined patients. This is since pathological processes occur simultaneously with physiological processes and both types of metabolites enter the liquor at the same time. Therefore, in pathological conditions, the presence of spherulites should be considered accompanying structures, and not markers of the norm.

Conclusion

The destruction of the brain tissue caused by pathogenic microorganisms or volumetric formations is accompanied by the release of the corresponding metabolites with a specific structure into the liquor. When liquor is transferred to a solid phase by the method of limiting dehydration, tissue metabolites form specific creations (markers) available for visual analysis. These markers had characteristic structural features signs indicating to pathology that caused the destruction of brain tissue. Thus, the study of the structures of the solid phase of liquor made it possible to obtain fundamentally new information that improves the quality of diagnosis of destructive brain diseases.

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