

КЛІНІЧНИЙ ВИПАДОК

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SPECIAL ASPECTS OF THE COURSE AND DIAGNOSIS OF NEUROSYPHILIS ON THE EXAMPLE OF A CLINICAL CASE

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Summary. Neurosyphilis is an infectious disease caused by *Treponema pallidum* and characterized by damage of the central nervous system. This disease may be asymptomatic or have an atypical clinical course, which leads to late diagnosis. The most informative diagnostic methods for this disease are specific serological reactions to syphilis, MRI of the brain and cerebrospinal fluid analysis. **Aim.** To show the features of the course, treatment and diagnosis of neurosyphilis using the example of a clinical case. **Materials and methods.** Patient S., born in 1963, complained about significant memory impairment, difficulties with orientation in time and space, mood swings, verbosity and exaggeration, and was hospitalized at the State Institution "Institute of Neurology, Psychiatry and Narcology of the National Academy of Medical Sciences of Ukraine". Neurological status: eye slits and pupils were uniform. The movements of the eyeballs were painless. Insufficiency of the act of convergence was found. Corneal reactions were reduced. The patient felt pain after the palpation of supra- and infraorbital points. There was an asymmetry in the facial innervation. The tongue was on the midline, swollen, with tooth imprints. There were no pathological signs, sensitive violations. Shaking movements were noticed during the Romberg test. During the examination of the cognitive function using the Mini-Mental State Examination (MMSE) scale, the patient scored 21 points, which corresponds to mild dementia. **Results.** 1. According to the results of MRI examination of the brain, there was an MR-picture of areas of cystic-gliosis transformation of the poles of the temporal lobes and structural changes of the hippocampal gyrus (most likely, caused by the chronic inflammatory process); vascular foci of the brain as manifestations of dyscirculatory changes, moderate external hydrocephalus. 2. A serological examination for the presence of the antigen of the *Treponema pallidum* pathogen was performed, the result was positive. 3. Cerebrospinal fluid analysis revealed the following results. Cytosis was $1 \times 10^6/l$, protein was 0.21 g/l, glucose 3.4 mmol/l, Pandy test positivity. Based on the obtained data, the patient was diagnosed with neurosyphilis. The patient underwent etiopathogenetic treatment with benzylpenicillin sodium. After treatment the patient's condition gradually improved. **Conclusions.** Specific serological reactions to syphilis, MRI of the brain and cerebrospinal fluid analysis are mandatory tests for the diagnosis of neurosyphilis. Early detection of *Treponema pallidum* and rational therapy can prevent the development of severe consequences and improve the patient's condition. Syphilis is a multidisciplinary problem today and needs the attention of general practitioners, dermatologists and neurologists.

Key words: neurosyphilis, cognitive impairments, dementia, diagnosis, benzylpenicillin

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Introduction

Syphilis is a chronic multisystem disease caused by *Treponema pallidum*. Today, syphilis is a common sexually transmitted disease in developing countries [1].

According to official state statistical reports, the epidemiological situation regarding the prevalence of syphilis in Ukrainian population is generally characterized by a gradual decline (in 2014 - 3674

cases (8.6 per 100 000 population) in 2015 - 3228 cases (7.6 per 100 000) [2]. According to statistics, the prevalence of syphilis was 3220 cases or 7.6 per 100 000 population in 2016. The incidence has decreased significantly in ten years, but the structure of syphilis is changing - there is a tendency to more severe clinical manifestations [3]. Neurosyphilis is a socially significant problem

of the modern time. 97.1% of patients with neurosyphilis are of working age [4].

Treponema pallidum affects tissues of the nervous system and causes the development of Neurosyphilis. In the initial stages of the disease, hematogenous dissemination predominates: a few hours after infection, the pathogen enters the blood and is fixed in the endothelial cells of blood vessels, and then enters the lymphatic capillaries, perineural spaces, nerve sheaths, subdural and subarachnoid space. The lymphogenic dissemination starts later and more slowly, the pathogen from the lymph nodes enters the perineural area of peripheral nerves, spinal roots, subdural and subarachnoid space [5, 6].

Neurosyphilis is divided into early and late stages. At the beginning of syphilis, the cerebrospinal fluid, meninges and blood vessels are primarily affected. At this stage, it can clinically manifest as asymptomatic meningitis, symptomatic meningitis and meningovascular disease. Later, the parenchyma of the brain and spinal cord is affected [6].

Neurosyphilis may be asymptomatic or have an atypical clinical picture, therefore, a careful differential diagnosis is needed. Late stages of syphilis with damage of the nervous system can be formed on the basis of latent syphilitic infection; the timely diagnosis of it depends on the effectiveness of laboratory methods [7].

Multiple organ neurological disorders and mental disorders predominate among the clinical forms of neurosyphilis. Vascular forms of neurosyphilis are more often recorded (our clinical case can serve as an example of such a form), in contrast to the destructive-parenchymal forms, this is due to the pathogenesis of the disease in modern conditions of the development of medicine. Nowadays the number of erased, low-symptom, atypical forms has increased, which leads to the complication of the diagnosis of neurosyphilis. Syphilitic damage to the nervous system can be suspected in almost all patients with acute cerebrovascular accidents and progressive decline in cognitive functions against the background of chronic cerebrovascular insufficiency according to a number of authors [4].

The most informative of the additional diagnostic research methods for this disease are MRI and cerebrospinal fluid analysis [8].

Also, it is important to organize effective cooperation between general practitioners, dermatologists and neurologists to diagnose Neurosyphilis in the early stage and prevent complications.

Clinical case

Patient S., 58 years old, resident of Kharkiv.

Complaints

Patient S., born in 1963, complained about significant memory impairment for current events, difficulties with orientation in time and space, mood swings, verbosity, tendency to exaggerate, and was hospitalized at the State Institution "Institute of Neurology, Psychiatry and Narcology of the National Academy of Medical Sciences of Ukraine" to the Department of Vascular Pathology of the Brain.

Anamnesis morbi

The patient considers himself ill since 2018 when relatives began to notice memory impairment, he began to repeat the same thing several times, there were difficulties with orientation in space. In January 2019 his colleagues noticed that the patient had a memory impairment, he was not able to remember the current date and month. He was hospitalized at the neurological department of the city hospital, he was treated from 22.01 to 31.01.19. The patient was diagnosed with transient global amnesia, right pyramidal insufficiency.

MRI examination of the brain was performed (22.01.19). The MR picture of structural changes of the pole of the left temporal region of the left hippocampus 45x15 mm was found - post-contusion, foci of the white matter of the brain of a dyscirculatory nature.

The patient was examined by a psychiatrist, no pathological symptoms were found. The patient was discharged with improvement, memory was restored within 2 days. Memantine and donepezil were prescribed.

Memory impairment resumed six months after the treatment. MRI examination was performed (21.08.19): areas of cystic-gliosis transformation of the poles of the temporal lobes, structural changes of the hippocampal gyrus, focal lesions of the white matter of the brain, probably manifestations of the chronic remitting inflammatory process were found. A diffuse

atrophic process of the cerebral cortex (GSA-1) was detected. The patient had a progressive course of the disease - memory impairment increases, the patient stopped performing his professional duties, began to get confused in previously familiar places, and therefore in May 2020 he was forced to resign.

2 weeks before the hospitalization in the State Institution "Institute of Neurology, Psychiatry and Narcology of the National Academy of Medical Sciences of Ukraine" the patient and his wife noticed significant memory impairments, problems with orientation in time and space, mood swings, and due to this deterioration of the course of the disease he was hospitalized for further examination and treatment.

Anamnesis vitae

In 1980, he was diagnosed with hepatitis A. He experienced a head injury in 1980. No allergies. Blood transfusions were not performed. Negative family history. According to the patient, he did not contact patients with infectious diseases.

Objective status

The general condition was satisfactory. Peripheral lymph nodes were not enlarged. Vesicular respiration was examined above the lungs. The thyroid gland was not enlarged. Body mass index was 25 kg/m². Heart tones were pure, rhythmic. Blood pressure was 105/70 mmHg, pulse 64-70 beats per minute. The abdomen was soft and painless. The liver, spleen were not enlarged. There was no peripheral edema.

Neurological status: eye slits and pupils were uniform. Photoreactions were lively. The movements of the eyeballs were painless. There was a lack of convergence. Corneal reactions were reduced. Pain after the palpation of supra- and infraorbital points. Nystagmus was not observed. Facial asymmetry in facial innervation was found. The tongue was on the midline, swollen, with tooth impressions. Muscle strength was sufficient. Muscle tone was not changed. There were no pathological signs, sensitive violations. Shaking movements were noticed during the Romberg test. Pain on palpation of paravertebral points, especially in the lumbar spine. Vegetative, emotional lability. During the Mini-Mental State Examination (MMSE) scale, the patient scored 21 points, which corresponds to mild dementia.

Results of the examinations

A serological examination was performed for the presence of the antigen of the *Treponema pallidum* pathogen, the result was positive.

EEG was performed (09.07.2020), the epileptic activity was observed mainly in S temporal canals.

According to the results of MRI examination of the brain (09.07.2020), there was an MR-picture of areas of cystic-gliosis transformation of the poles of the temporal lobes and structural changes of the hippocampal gyrus (most likely, caused by the chronic inflammatory process); vascular foci of the brain as manifestations of dyscirculatory changes, moderate external hydrocephalus, malnutrition of the cerebral cortex. Compared with the data of MRI examination from 21.08.2019 - without negative dynamics.

Cerebrospinal fluid analysis revealed the following results. Cytosis was $1 \times 10^6/l$, protein was 0.21 g/l, glucose 3.4 mmol/l, Pandy test positivity.

Recommended drug therapy

The patient was discharged with significant improvement. Observation of the neurologist at the place of residence is recommended. The patient was referred to the Institute of Dermatology and Venereology of the National Academy of Medical Sciences of Ukraine for further treatment and observation.

The patient underwent etiopathogenetic treatment with benzylpenicillin sodium. During treatment, the concentration of benzylpenicillin sodium in the blood was constantly maintained at the treponemocidal level. It is known from the follow-up that the patient's condition gradually improved - memory improved, he was able to visit the store on his own; became critical to his condition. During the Mini-Mental State Examination (MMSE) after 1 month, the patient scored 24 points.

Discussion

This clinical case confirms that a correctly collected anamnesis and examination of a patient, as well as correctly selected methods of further instrumental diagnostics, are fundamentally important for establishing a diagnosis and successful treatment in the future. First of all, to establish a definitive diagnosis in patients, it is necessary to confirm (serologically or microscopically) the fact of *T. pallidum* infection.

The gold standard for the diagnosis of neurosyphilis is lumbar puncture and subsequent analysis of cerebrospinal fluid. In recent years, a significant number of cases of neurosyphilis were asymptomatic and may manifest in the distant future with various forms of CNS damage, in which case the final diagnosis of neurosyphilis can be established only by analysis of cerebrospinal fluid [6]. In our case cerebrospinal fluid analysis of the patient's revealed the following results: cytosis was $1 \times 10^6/l$, protein was 0.21 g/l, glucose 3.4 mmol/l, Pandy test positivity.

Absolute indications for lumbar puncture in patients with any form of syphilis are neurological symptoms, pathology of vision and hearing; mental disorders, the dissonance between the clinical picture and MRI neuroimaging data (inflammatory changes in the temporal areas, as in our case). Relative indications include malignant syphilis even without neurological symptoms; patients with late stages and latent syphilis; patients with serological resistance [9].

It is important to perform MRI of the brain for diagnostic purposes, it is useful for the specialist's understanding of the differentiation of meningeal manifestations against the background of neurosyphilis from other brain pathologies.

The differential diagnosis of neurosyphilis should be made with meningitis of other etiology (tuberculous meningoencephalitis, cytomegalovirus meningoencephalitis, toxoplasmosis of the brain, cryptococcal meningoencephalitis, bacterial meningoencephalitis) and brucellosis, sarcoidosis, and tumors of the brain and spinal cord. Patients with HIV infection are vulnerable to cerebrovascular diseases due to various etiological factors. Meningovascular form of neurosyphilis may be the initial manifestation of syphilis in both HIV-positive and HIV-negative individuals. Due to the increased incidence of syphilis, as well as co-infection with HIV, it is recommended to examine young patients with a stroke of unknown etiology in case of undetermined neurological symptoms and changes in the cerebrospinal fluid for HIV and syphilis. Clinical manifestations of neurovascular syphilis tend to be regressed in the course of specific antibiotic therapy [10].

Establishment of the final diagnosis became possible due to a comprehensive examination of

the patient, namely: symptoms of CNS damage, data from instrumental methods of examination, as well as data from blood and cerebrospinal fluid analysis.

Conclusion

This clinical case illustrates the clinical diversity of neurosyphilis, which occurs against the background of latent syphilitic infection, and the complexity of its diagnosis. This confirms that syphilis is a multidisciplinary problem today and it needs the attention of general practitioners, dermatologists and neurologists.

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ОСОБЛИВОСТІ ПЕРЕБІГУ ТА ДІАГНОСТИКИ НЕЙРОСИФІЛІСУ НА ПРИКЛАДІ КЛІНІЧНОГО ВИПАДКУ

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Резюме. *Нейросифіліс — інфекційне захворювання, яке характеризується ураженням центральної нервової системи в результаті проникнення в неї збудника сифілісу *Treponema pallidum*. Дане захворювання може протікати малосимптомно або мати атипичну клінічну картину, що призводить до пізнього діагностування. Найінформативнішими діагностичними методами при даному захворюванні є специфічні серологічні реакції на сифіліс, МРТ головного мозку та дослідження ліквору. **Мета роботи.** На прикладі клінічного випадку показати особливості перебігу, лікування та діагностики нейросифілісу. **Матеріали та методи.** Хворий С., 1963 року народження, звернувся до ДУ “Інститут неврології, психіатрії та наркології НАМН України” зі скаргами на значне порушення пам’яті на поточні події, труднощі з орієнтацією в часі та просторі, перепади настрою, гарний піднесений позитивний настрій, багатомовність, схильність до перебільшення. Неврологічний статус: очні щілини і зіниці рівномірні. Рухи очних яблук безболісні. Недостатність акту конвергенції. Корнеальні реакції знижені. Біль при пальпації супра- та інфраорбітальних точок. Наявна мімічна асиметрія в лицьовій іннервації. Язик по середній лінії, набряклий, з відбитками зубів. Патологічних знаків, чутливих порушень немає. Координаторні проби виконує задовільно. Похитування в пробі Ромберга. Вегетативна, емоційна лабільність. Спостерігаються порушення пам’яті. При обстеженні когнітивних функцій за допомогою шкали Mini-Mental State Examination (MMSE) пацієнт набрав 21 бал, що відповідає деменції легкого ступеню. **Результати.** 1. За даними МРТ-обстеження головного мозку: виявлено ділянки кістозно-гліозних трансформацій полюсів скроневих долей та структурні зміни гіпокомпальних звивин, найбільш вірогідно, хронічного запального процесу, судинні вогнища головного мозку, як прояви дисциркуляторних змін, помірна зовнішня гідроцефалія, гіпотрофія кори головного мозку 2. Було виконано серологічне дослідження на наявність антигену збудника сифілісу *Treponema pallidum*, результат позитивний. 3. Виконано аналіз спинномозкової рідини (20.07.2020): цитоз 1×10^6 /л, білок 0,21 г/л, цукор 3,4 мМоль/л, реакція Панді позитивна. На основі отриманих даних було встановлено діагноз: нейросифіліс. Пацієнт пройшов етіопатогенетичне лікування бензилпеніциліном натрію. Після лікування стан пацієнта поступово покращувався. **Висновки.** Специфічні серологічні реакції на сифіліс, МРТ головного мозку та дослідження ліквору є обов’язковим дослідженнями для постановки діагнозу нейросифілісу. Раннє виявлення *Treponema pallidum* та раціональна терапія, попереджає розвиток важких наслідків і покращує стан хворого. Сифіліс є мультидисциплінарною проблемою повсякденності та вимагає прицільного уваги лікарів загальної практики, дерматовенерологів і неврологів.*

Ключові слова: нейросифіліс, когнітивні розлади, деменція, діагностика, бензилпеніцилін

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ОСОБЕННОСТИ ТЕЧЕНИЯ И ДИАГНОСТИКИ НЕЙРОСИФИЛИСА НА ПРИМЕРЕ КЛИНИЧЕСКОГО СЛУЧАЯ

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Резюме. *Нейросифилис — инфекционное заболевание, которое характеризуется поражением центральной нервной системы в результате проникновения в нее возбудителя сифилиса *Treponema**

pallidum. Данное заболевание может протекать малосимптомно или иметь атипичную клиническую картину, что приводит к поздней диагностике. Наиболее информативными диагностическими методами при данном заболевании являются специфические серологические реакции на сифилис, МРТ головного мозга и исследование ликвора. **Цель работы.** На примере клинического случая показать особенности течения, лечения и диагностики нейросифилиса. **Материалы и методы.** Больной С., 1963 года рождения, обратился в ДУ «Институт неврологии, психиатрии и наркологии НАМН Украины», с жалобами на значительное нарушение памяти на текущие события трудности с ориентацией во времени и пространстве, перепады настроения, хорошее вознесенное позитивное настроение, многоречив, склонность к преувеличению. Неврологический статус: глазные щели и зрачки равномерны. Движения глазных яблок безболезненны. Недостаточность акта конвергенции. Корнеальные реакции снижены. Боль при пальпации супра- и инфраорбитальных точек. Имеется мимическая асимметрия в лицевой иннервации. Язык по средней линии, отекий, с отпечатками зубов. Патологических знаков, чувствительных нарушений нет. Координаторные пробы выполняет удовлетворительно. Шаткость в пробе Ромберга. Вегетативная эмоциональная лабильность. Наблюдаются нарушения памяти. При обследовании когнитивных функций при помощи шкалы Mini-Mental State Examination (MMSE) пациент набрал 21 бал, что соответствует деменции легкой степени. **Результаты.** 1. По данным МРТ-обследования головного мозга: выявлено участки костно-глиозных трансформаций полюсов височных долей и структурные изменения гиппокампальных извилин, наиболее вероятно, хронического воспалительного процесса, сосудистые очаги головного мозга, как проявления дисциркуляторных изменений, умеренная внешняя гидроцефалия, гипотрофия коры головного мозга. 2. Было выполнено серологическое исследование на наличие антигена возбудителя сифилиса *Treponema pallidum*, результат положительный. 3. Выполнено анализ спинномозговой жидкости (20.07.2020): цитоз 1×10^6 /л, белок 0,21 г/л, сахар 3,4 ммоль/л, реакция Панди положительная. На основе полученных данных было установлено диагноз: нейросифилис. Пациент прошел этиопатогенетическое лечения бензилпенициллином натрия. После лечения состояние пациента постепенно улучшалось. **Выводы.** Специфические серологические реакции на сифилис, МРТ головного мозга и исследования ликвора является обязательным исследованием для постановки диагноза нейросифилиса. Раннее выявление *Treponema pallidum* и рациональная терапия, предупреждает развитие тяжелых последствий и улучшает состояние больного. Сифилис является мультидисциплинарной проблемой повседневности и требует прицельного внимания врачей общей практики, дерматовенерологов и неврологов.

Ключевые слова: нейросифилис, когнитивные расстройства, деменция, диагностика, бензилпенициллин

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