

## Neurosyphilis in Women of Reproductive Age

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### Abstract

The research was aimed at examining clinical symptoms of neurosyphilis in women of reproductive age. The diagnoses were based on complaints, anamnestic information, findings of neurological examinations, dermatovenerologist consultations, serological blood and liquor tests. To reveal neurosyphilis-induced cognitive impairments, the patients were neuropsychometrically tested using the following methods: Mini-Mental State Examination (MMSE), "Frontal Assessment Battery", Clinical Dementia Rating scale, Clock drawing test, "Information-Memory-Concentration" test, Mattis Dementia Rating Scale. Nine patients with precocious neurosyphilis (between the ages of 18 to 40) and eight patients with tardy neurosyphilis (between the ages of 28 to 43) were examined. Syphilitic meningitis (six cases), meningovascular neurosyphilis (three cases) were found in patients with precocious neurosyphilis. As for the patients with tardy neurosyphilis, two cases were identified as syphilitic meningitis, two cases as meningovascular neurosyphilis, two cases as progressive paralysis, one case as tabes dorsalis, one case as taboparalysis. Cognitive impairments were revealed in the patients under examination with all stages of neurosyphilis. This article presents a clinical example of a female patient with precocious syphilitic meningitis who gave birth to a baby with congenital syphilis.

**Keywords:** Neurosyphilis; Congenital Syphilis; Cognitive Impairments

### Introduction

Nowadays in Russia, against the backdrop of gradual decrease in the prevalence of syphilis, the number of reported neurosyphilis cases is observed to increase [6]. Due to the subclinical pattern of both precocious and tardy forms of neurosyphilis and the prevalence of meningovascular forms in the pattern of tardy neurosyphilis, neurosyphilis cases, especially at precocious stages of the disease, are rather difficult to be diagnosed [1,2,8,9]. Women of reproductive age who develop neurosyphilis and have not been given appropriate antibacterial therapy are exposed to a risk of giving birth to a baby with congenital syphilis. In recent years, a decrease in the number of cases of congenital syphilis has been observed in Russia and in the countries of Europe and America [3,7]. However, the latest publications describe congenital syphilis cases characterised by serious complications, including intrauterine foetal demise [3,5]. Patients who had syphilis while pregnant are exposed, despite administered antibacterial therapy, to a 2.5 times higher risk of giving stillbirth as compared to healthy women [4].

### Materials and Methods

This research involved studying clinical manifestations of neurosyphilis in patients of reproductive age who were under examination and treatment at the Leningrad Oblast Centre of Specialised Medical Aids and in the St. Petersburg-based Mariinsky Hospital in

2011 through 2014. In Russia, according to the regulation "Protection of employees' reproductive health. Basic terms and concepts"<sup>1</sup>, the reproductive age in women shall be considered to be 15 through 45 years. Neurosyphilis cases were diagnosed based on complaints, anamnestic data, neurological and dermative neurological examination, findings of serological blood and liquor test. Patients were given neuropsychometrical tests such as: the Mini-Mental State Examination (MMSE), the "Frontal Assessment Battery" test, the Clock Drawing Test, the "Information-Memory-Concentration" test, the Mattis Dementia Rating Scale test. To rule out any influence of depressive episodes on the performance of the tasks, depression tests were given, with the CES-D scale and the Montgomery and Asberg Depression Rating Scale being used.

## Results and Discussion

We examined 16 female patients with precocious neurosyphilis and 17 female patients with tardy neurosyphilis. Those with precocious neurosyphilis included 9 female patients of reproductive age (56.25%): aged 18 through 40 years (the median being 29). Those with tardy neurosyphilis included 8 female patients of reproductive age (47.06%): aged 28 through 43 years (the median being 39).

The patients of reproductive age with precocious neurosyphilis were diagnosed with the following clinical forms of the disease: six cases (66,67%) were diagnosed as syphilitic meningitis and three cases (33,33%) were diagnosed as meningovascular neurosyphilis. As for the pattern of syphilitic meningitis, five cases (83.33%) were diagnosed as basal meningitis, only one case (16.67%) being diagnosed as latent meningitis. The gynecologic history of the female patients with syphilitic meningitis tells that three of them were in labour some years prior to being diagnosed with syphilis and in two patients, the first time their serological blood test for syphilis was found positive was in maternity hospital. Typical of the female patients with basal meningitis were complaints of a headache, giddiness, shaky walk, reduction in vision. It is significant that none of the patients had previously consulted doctors about the above-stated complaints. The first time their serological blood test for syphilis was found positive was while being under therapeutical or gynecological examination and treatment as inpatients or while being under examination at the Leningrad Oblast Centre of Specialised Medical Aids as sexual partners of patients with newly diagnosed syphilis. Neurologically, detected in the said patients were impaired pupillary innervation in the form of anisocoria and/or reduced photoreaction. The direct Argyll Robertson symptom (the pupils unresponsive to light while keeping on being responsive to convergence and accommodation), pathognomonic for neurosyphilis, was identified only in two cases. None of the patients of the said group showed any meningeal symptoms (nuchal rigidity; Kernig's sign; Brudzinski's signs upper, middle or lower). Specific skin and mucous membrane lesions in the form of papular eruption over the tongue, the torso, the palms and plantae, cicatricial changes of the perianal region were found only in two cases.

Results of psychometric testing in the patients with precocious syphilitic meningitis.

Test name	Composite score	Result
MMSE	25 to 30 (the median being 27)	Moderate cognitive impairments
Frontal Assessment Battery	16 to 18 (the median being 16)	Moderate cognitive impairments
Clock Drawing	8 to 10 (the median being 9)	Mild cognitive impairments
Information-Memory-Concentration	28 to 30 (the median being 30)	Mild cognitive impairments
Mattis Dementia Rating Scale	77 to 83 (the median being 79)	Moderate cognitive impairments

Table 1

<sup>1</sup>Order of the Ministry of Public Healthcare "Protection of employees' reproductive health - Basic terms and concepts" (approved by the Ministry of Public Healthcare of the Russian Federation on Oct. 02, 2003, No. 11-8/13-09).

Depression in patients of the said group was not revealed either on the CES-D scale or on the Montgomery and Asberg Depression Rating Scale.

Asymptomatic meningitis was diagnosed only in one female patient, aged 26 years. The specific feature of the clinical pattern in the said patient was that she had no complaints nor neurological signs. The first time her serological blood test for syphilis was found positive was as she had a physical examination at work, previously the patient was screened for syphilis about one year back. For further examination the patient was referred to the Leningrad Oblast Centre of Specialised Medical Aids. As she was initially undergoing dermatovenerologic inspection, no specific manifestations of syphilis on the skin or mucous membranes were detected. Due to the duration of the disease being more than one month, to rule out a specific affection of the nervous system, the patient was made a lumbar puncture followed by a general liquor test and a serological liquor test for syphilis. The findings of the general liquor test are: lymphocytic cytolysis  $5.67 \times 10^6/l$ , protein 0.8 g/l. The findings of the serological liquor test are: RW with cardiolipin antigen (-), RW with treponemal antigen 4+, Microprecipitation test (-), TPI (-), IFA abs. 4+. Therefore, based on the serological liquor test, the patient was diagnosed as having: "Precocious neurosyphilis. Asymptomatic meningitis".

Among the female patients with precocious meningovascular neurosyphilis, there was only one having been in labour some years prior to syphilis being detected. At admission, the patients of the said group complained of undue fatigability, a headache, giddiness, reduction in vision, shaky walk. Neurologically, detected were symptoms of impaired pupillary innervation, a direct Argyll Robertson symptom found only in one case, also detected were facial asymmetry, tongue deviation, symptoms of oral automatism, anisoreflexia, pathological plantar signs, unilateral or bilateral cerebellar symptoms and signs. In one patient meningovascular neurosyphilis manifested itself as a past acute cerebrovascular accident (CVA) on the left carotid basin. At admission, the patient presented complaints of restraint of movements in the right extremities. Neurologically, detected were impairments of pupillary innervation in the form of anisocoria, facial asymmetry due to the right nasolabial fold being effaced, right-sided hemiparesis up to 3.5 points. The patient had hepatitis C, B-23, used to be a heroin addict.

Results of psychometric testing in the patient with precocious meningovascular neurosyphilis.

Test name	Composite score	Result
MMSE	23	Dementia of mild intensity
Frontal Assessment Battery	13	Moderate cognitive impairments
Clock Drawing	5	Severe cognitive impairments
Information-Memory-Concentration	20	Severe cognitive impairments
Mattis Dementia Rating Scale	67	Severe cognitive impairments

Table 2

No depressive episodes were revealed in the said patient.

Manifestations of syphilis on the skin and mucous membranes within the group of patients with precocious meningovascular neurosyphilis were detected only in one patient in the form of a cicatrix in the vaginal region.

In female patients with tardy neurosyphilis, the following clinical forms of the disease were detected: syphilitic basal meningitis was diagnosed in two cases; meningovascular neurosyphilis was diagnosed in two cases; progressive paralysis, in two cases, tabes dorsalis, in one case and taboparesis, in one case.

One of the patients with tardy syphilitic meningitis was in labour some years prior to being diagnosed with syphilis. The two patients as well as patients with precocious syphilitic meningitis complained of a headache and reduction in vision. Neurologically, detected in

the patients of the said group were impairments of pupillary innervation, a direct Argyll Robertson symptom found only in one case; also found in one of the patients was peripheric paresis of muscles of facial expression.

Results of psychometric testing in the patients with tardy syphilitic meningitis.

Test name	Composite score	Result
MMSE	24 and 30	Moderate cognitive impairments and normal
Frontal Assessment Battery	13 and 17	Moderate cognitive impairments and normal
Clock Drawing	8 and 10	Moderate cognitive impairments and normal
Information-Memory- Concentration	30 and 32	Mild cognitive impairments and normal
Mattis Dementia Rating Scale	77 and 83	Moderate cognitive impairments and normal

Table 3

The results of all the psychometric tests suggested that the patients of the said group had no depression.

One of the patients with tardy meningovascular neurosyphilis was in labour twice some years prior to being diagnosed with syphilis. At admission, the patients complained of a headache, giddiness, shaky walk. Neurologically, a direct Argyll Robertson symptom, facial asymmetry, tongue deviation, symptoms of oral automatism, anisoreflexia, pathological plantar signs were detected. One of the patients was long time drugged up on haloperidol. Neurologically, at admission, detected in the said patient was quadriparesis and muscular hypertonicity predominantly extrapyramidally.

Results of psychometric testing in the patient with tardy meningovascular neurosyphilis.

Test name	Composite score	Result
MMSE	12	Moderate dementia
Frontal Assessment Battery	2	Frontal-type dementia
Information-Memory-Concentration	10	Severe cognitive impairments

Table 4

The results of all the psychometric tests suggested that the patient had no depressive episodes.

Neither of the two patients with progressive paralysis had any previous history of gravidity. The patients complained of general weakness, undue fatigability and reduction in vision. One of the patients was a month prior to admission to the Leningrad Oblast Centre of Specialised Medical Aids under treatment in an mental hospital for a hallucinatory syndrome. Neurologically, detected in the patients were impairments of pupillary innervation in the form of anisocoria, facial asymmetry, tongue deviation, symptoms of oral automatism, anisoreflexia, pathological plantar signs, bilateral cerebellar symptoms and signs.

Results of psychometric testing in the patients with progressive paralysis.

Test name	Composite score	Result
MMSE	25	Moderate cognitive impairments and normal
Frontal Assessment Battery	10 and 11	Frontal-type dementia
Clock Drawing	10 and 9	Normal and mild cognitive impairments
Information-Memory-Concentration	23 and 25	Moderate cognitive impairments
Mattis Dementia Rating Scale	75	Moderate cognitive impairments

Table 5

Depression in patients of the said group was not revealed either on the CES-D scale or on the Montgomery and Asberg Depression Rating Scale.

The patient with *tabes dorsalis* had no previous history of gravidity. At admission, the patient complained of shaky walk, especially in the dark and going up and down stairs. Neurologically, detected in the patient was hypotension in the muscles of the lower extremities, absence of knee-jerk reflexes, impaired deep sensibility in the toes, "stamping" gait.

Results of psychometric testing in the patients with *tabes dorsalis*.

Test name	Composite score	Result
MMSE	28	Normal
Frontal Assessment Battery	17	Normal
Clock Drawing	7	Moderate cognitive impairments
Information-Memory-Concentration	28	Moderate cognitive impairments
Mattis Dementia Rating Scale	78	Moderate cognitive impairments

Table 6

The depression tests suggested that the patient had no depressive episodes.

The patient with *taboparalysis* was in labour twice some years prior to being diagnosed with syphilis. At admission, the patient complained of undue fatigability. Neurologically, detected in the patient were a direct Argyll Robertson symptom, anisoreflexia, absence of knee-jerk reflexes, impaired deep sensibility in the toes, pathological plantar signs, right-sided cerebellar symptoms and signs. When being psychometrically tested, the composite score on the MMSE in the patient was equal to 28, which corresponds to normal, on the "Frontal Assessment Battery" test, 17, which also corresponds to normal. The composite score on the "Clock Drawing" test was equal to 8, which testifies to moderate cognitive impairments. The composite score on the "Information-Memory-Concentration" test was equal to 32, which corresponds to normal, and the composite score on the Mattis Dementia Rating Scale test was equal to 84, which also corresponds to normal.

Results of psychometric testing in the patients with *taboparalysis*.

Test name	Composite score	Result
MMSE	28	Normal
Frontal Assessment Battery	17	Normal
Clock Drawing	8	Moderate cognitive impairments
Information-Memory-Concentration	32	Normal
Mattis Dementia Rating Scale	84	Normal

Table 7

The results of all the psychometric tests suggested that the patient had no depression.

Below is cited one clinical example of a patient with neurosyphilis, whose serological blood test for syphilis was found positive for the first time prior to childbirth.

Patient G., aged 29 years, was admitted to the Leningrad Oblast Centre of Specialised Medical Aids on the 4th day after childbirth, referred by the Tsentralny District Hospital, where she had been in the postnatal unit. About one year back the patient was under medi-

cal examination, the serological blood test for syphilis being found negative. The patient had no record at the maternity welfare center concerning the present pregnancy. At admission to the Tsentralny District Hospital, the patient's serological blood test for syphilis was found positive for the first time. At the gestational age of 32 weeks the patient gave birth to a baby weighing 2 kg with manifestations of precocious congenital syphilis in the form of bullous syphilide. At birth, detected in the child were skin manifestations on the palms and plantae - blisters of 0.5 - 1.0 cm in diameter. The blisters had a dense coat, were located on an infiltrated base, filled with serous fluid. The child was given a course of treatment for congenital syphilis in the maternity hospital. The patient showed no manifestations of syphilis over the skin or mucous membranes. At the Leningrad Oblast Centre of Specialised Medical Aids the patient was examined by a neurologist, detected was an impairment of pupillary innervation in the form of a direct Argyll Robertson symptom, pathognomonic for neurosyphilis: a sluggish pupillary response to light with the responses to convergence and accommodation appearing intact. No other cerebral or focal neurological symptoms were detected. To rule out neurosyphilis, the patient was made a lumbar puncture followed by a general liquor test and a serological liquor test for syphilis. The findings of the general liquor test are: lymphocytic cytolysis 25 x 106/l, protein 0.5 g/l. The findings of the serological liquor test are: RW 4+ with cardiolipin antigen, with treponemal antigen (-), Microprecipitation test (-), TPI (-), IFA abs (-). Based on the anamnesis data, neurological examination and laboratory tests, the patient was diagnosed as having: "Precocious neurosyphilis, specific basal meningitis". A course of antibacterial therapy was administered. Therefore, not only does the presence of syphilis in women of reproductive age involve an affection of their nervous system, but it also brings about development of congenital syphilis in children.

### Conclusion

Because of increase in the number of subclinical neurosyphilis cases, improvement of diagnostics of the said disease is required. It should be noted that characteristic of precocious and tardy forms of neurosyphilis is development of cognitive disorders varying in their degree of manifestation: ranging from moderate cognitive impairments to dementia. The course of meningovascular neurosyphilis can be complicated by acute cerebrovascular accidents. Wherever acute cerebrovascular accidents or encephalopathy of unknown origin are detected in women of reproductive age, there being no evidence of any somatic pathology promoting development of cognitive disorders, testing for neurosyphilis is necessary, including a lumbar puncture followed by a serological liquor test for syphilis. In case of the serological blood test for syphilis being positive in patients who are under treatment in neurology units, dermatovenerologist consultation, a lumbar puncture followed by general and serological liquor tests are necessary. Patients with indeterminate duration or with over one month's duration of syphilis, who seek medical advice as outpatients, should be hospitalised and a lumbar puncture should be performed on them followed by general and serological liquor tests for the infection under review in order to detect a neural affection in good time and assign an appropriate antibacterial therapy. Such an approach promotes early diagnostics of neurosyphilis and prevention of congenital syphilis.

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