CLINICAL CASE

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DIFFICULTIES IN DIAGNOSING MULTISYSTEM ATROPHY AT EARLY STAGES (CLINICAL OBSERVATIONS)

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Multisystem atrophy (MCA) is a rare neurodegenerative disease characterized by a predominant lesion of the basal ganglia, nuclei of the brain stem, cerebellar systems, autonomic neurons of the trunk and spinal cord. Clinically, the disease is manifested by a combination of parkinsonism with autonomic failure, cerebellar and pyramidal disorders.

The late age of onset of the disease and the early development of autonomic insufficiency should alert physicians and neurologists with respect to MSA, since this rare disease has a rapidly progressive course and leads to death. In turn, early diagnosis of the disease contributes to the timely correction of autonomic and motor disorders and, ultimately, to an increase in the quality and life expectancy of patients. The article presents its own observations of patients with various forms of MSA, examines its clinical features and provides modern diagnostic criteria for this disease.

Key words: multisystem atrophy, autonomic insufficiency, parkinsonism, ataxia, movement disorders, pyramidal insufficiency.

Introduction. Multisystem atrophy (MSA) is a rare neurodegenerative disease characterized by progressive autonomic failure (AF), parkinsonism, cerebellar and pyramidal syndromes in various combinations with a fatal outcome. The incidence is registered on average 0.6-0.7 cases per 100 thousand population a year, however, it increases with age and reaches till 3 cases per 100 thousands people a year among the population over 50 years old [10, 11]. MSA with the same indicator affects both sexes, most often there is increase in mortality within 5-7 years [9, 12, 14].

In MSA, in 20–75% of cases, motor manifestations of the disease are preceded by a prodromal stage, which may be characterized by the development of orthostatic hypotension, neurogenic urination disorders, inspiratory stridor, erectile dysfunction, as well as behavioral disturbances in the sleep phase with rapid eye movements (REM sleep disturbance) [10]. The disease is characterized by rapid and steady progression and 5 years after the first manifestations of the disease, 60% of patients find themselves in a wheelchair, and after 6–8 years most of them become bedridden [10]. The factors of poor prognosis include late age at the time of debut and early development of severe autonomic failure [8, 9, 14, 15, 16]. The most common causes of death in patients with MSA are sudden death during sleep of unclear etiology, aspiration pneumonia due to swallowing disorders, orthostatic hypotension, and other causes [13].

Patients with MSA have a wide range of disorders of the autonomic nervous system, but the most characteristic is the lesion of the genitourinary and cardiovascular systems [11]. More often, patients with the development of these symptoms do not always seek medical help, reducing their complaints to age-related changes in the body. However, it is the disorders of the autonomic system that are most significant for patients with the prodromal stage of MSA.

Description of clinical cases of MCA. *Clinical case No. 1.* Patient I., 71 years old, from the age of 61 began to notice pronounced fluctuations in blood pressure from 60/40 mm Hg up to 230/120 mm Hg. He did not take antihypertensive drugs regularly, he was observed with the diagnosis of hypertension by a local therapist. At the age of 65, urinary incontinence appeared, but did not pay special attention to urinary disorders. A noticeable deterioration in the 7th year of the disease at the age of 68: due to urinary incontinence, he began to wear diapers, slowed down in movements, unsteadiness when walking with periodic falls. The patient was also worried about severe general weakness and non-systemic dizziness, which regressed in the supine position.

By the specialized appointment of a neurologist-parkinsonologist of the Center for Extrapyramidal Disorders and Botulinum Therapy of the Clinic of the M.K. Ammosov North-Eastern Federal University he underwent a medical examination for the 8th year of his illness. The examination revealed symmetric akinetic-rigid syndrome, signs of cerebellar ataxia. The test for orthostatic hypotension revealed a decrease in blood pressure from 130/80 mm Hg. Art. (in prone position) up to 90/60 mm Hg (after 3 minutes in upright position). Cognitive function tests: within normal limits except for a slight decrease in phonetic speech activity. HADS - 5/5 (normal).

The patient for further examination was hospitalized in the Center for Neurodegenerative Diseases of the Yakutsk Scientific Center for Complex Medical Problems (YSC KMP).

The daily monitoring of blood pressure revealed episodes of blood pressure decrease in the morning and afternoon hours with a minimum value of up to 75/53 mm Hg and nocturnal hypertension up to 210/103 mm Hg. MRI of the brain revealed diffuse atrophy of the cerebral cortex, cerebellum.

Taking into account the patient's autonomic insufficiency, akinetic-rigid syndrome, cerebellar signs and characteristic changes on the MRI of the brain, 'Multisystem atrophy, Shai-Dreiger syndrome' was diagnosed.

At discharge, it is recommended to take α-adrenergic agonist (midodrine) under the supervision of a neurologist in the home area, as well

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as symptomatic therapy was appointed.

Clinical case No. 2. Patient P., 61 years old, was admitted to the Center for Neurodegenerative Diseases of the YSC KMP with complaints of slowness and stiffness in movements, severe anxiety, inability to sleep lying down due to severe anxiety, frequent urination and constipation.

From the anamnesis of the disease it is known that from the age of 58 he began to notice unsteadiness when walking, frequent urination, constipation, non-systemic dizziness and rapid fatigue.

Over the next two years, he was observed by a therapist with chronic constipation and by a neurologist diagnosed with dyscirculatory encephalopathy. The symptoms were slowly increasing. At the age of 61, slowness and stiffness in movements joined, so 'Vascular Parkinsonism' was diagnosed. Pramipexole was prescribed in a daily dose of 0.75 mg / day without effect. Neuropsychological tests: MoCA - 24 points (signs of moderate cognitive impairment), HADS - Anxiety - 6 points, depression - 18 points. Pronounced clinical evidence of depression.

The neurological status revealed a bilateral symmetric akinetic-rigid syndrome, pyramidal insufficiency (in the form of hyperreflexia and pathological extensor signs), mild cerebellar symptoms (intention when performing the fingernasal and knee-heel tests) and pelvic disorders in the form of frequent urination with episodes of incontinence. The orthostatic test did not record a clinically significant decrease in blood pressure.

The MRI of the brain revealed changes characteristic of MCA (Fig. 1).

The patient was prescribed levodopa / carbidopa with titration up to 750 mg + 75 mg / day, against which the manifestations of akinetic-rigid syndrome significantly decreased. In addition, buspirone was prescribed at a dose of 10 mg / day to relieve anxiety.

Thus, taking into account of the prevalence of symmetric akinetic-rigid syndrome, pyramidal insufficiency, early development of symptoms of autonomic failure, a positive response to levodopa therapy, 'Multisystem atrophy, nigrostriatal variant' was diagnosed to the patient.

Clinical case No. 3. Patient N., 59 years old, was admitted to the Center for Neurodegenerative Diseases of the YSC KMP with complaints of speech changes, unsteadiness and instability when walking, choking when eating liquid food, frequent urination with episodes of urinary incontinence, interrupted sleep due to frequent urination.

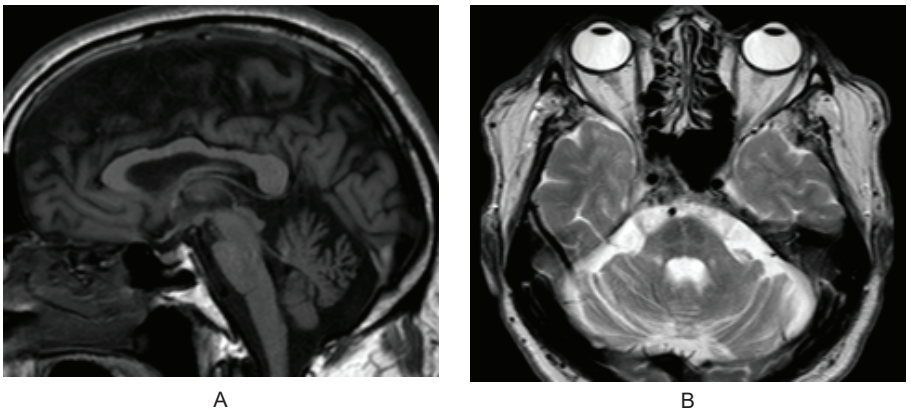
The onset of the disease at the age of 57 with changes in speech, voice, choking when eating and gait instability. At the age of 58, unsteadiness when walking with falls, frequent urination, episodes of urinary incontinence joined. Due to the presence of cerebellar ataxia, the patient was excluded from the diagnosis of type 1 spinocerebellar ataxia.

The neurological status revealed: signs of stato-locomotor ataxia, dysphonia, dysphagia, dysarthria, pelvic incontinence disorders. The orthostatic test did not record a clinically significant decrease in blood pressure.

Neuropsychological tests were conducted: MoCA - 22 points (signs of moderate cognitive impairment), HADS - 6/4 (normal).

MRI of the brain revealed signs of atrophy of the cerebellum and pons with the formation of a "cross" symptom.

Taking into account the prevalence of cerebellar symptoms, the presence of autonomic disorders, characteristic MRI signs, the patient was diagnosed as 'Multisystem atrophy, olivopontocerebellar type'.



A B

Figure: 1. MRI of the patient's head P: atrophy of vermis cerebellum and pons is determined on sagittal sections (A), atrophy of the cerebellar hemispheres with widening of furrows, cavity of the fourth ventricle and atrophy of pons with the formation of a 'cross' symptom (B).

Discussion. Orthostatic hypotension is the most frequent and at the same time severe cardiovascular autonomic disorder, that develops as a result of impaired activation of sympathetic vasoconstrictor neurons [10]. Symptoms can be latent and are expressed by general weakness, tremors in the body, headache, nausea, as well as discomfort in the neck and shoulders when changing from horizontal to vertical. With a more pronounced decrease in blood pressure, syncope and falls are possible. In addition to orthostatic hypotension, cardiovascular disorders in the framework of autonomic insufficiency can be manifested by arterial hypertension in the supine position (especially at night), a fixed pulse, postprandial hypotension (hypotension after a meal) [1].

In MSA, other autonomic disorders can also develop: weakening of gastrointestinal tract motility, impaired pupillary reactions, thermoregulatory disorders, anhidrosis or hyperhidrosis, acrohypothermia [10].

Vegetative disorders are also characteristic of Parkinson's disease, which requires differential diagnosis, especially in the absence of cerebellar and pyramidal signs. At the same time, in MSA, autonomic disorders develop at an early stage, may precede the development of symptoms of parkinsonism, and make a greater contribution to a decrease in the quality of life of patients than motor deficits [2].

The clinical cases described by us demonstrate the necessity of careful observation and examination of patients with autonomic disorders. In all three cases, cardiovascular and pelvic disorders preceded the diagnosis of MCA. At the same time, it should be pointed out that the diagnosis of MSA requires the presence of not only autonomic failure, but also cerebellar ataxia and / or parkinsonism (Table) [10].

Respiratory disorders also play a significant role among the non-motor manifestations of MSA. So, in almost half of cases at the advanced stage of MSA, there is an inspiratory stridor resulting from dystonia of the vocal cords or denervation of the laryngeal muscles, a little less often (in 40% of patients) there are sleep apnea syndromes of both obstructive and central genesis [1].

Cognitive and affective impairments are characteristic of MSA. Despite the fact that dementia is considered an exclusionary symptom in MSA, it should be

Diagnostic criteria for multisystem atrophy (by Fanciulli A., Wenning G., 2015)

Category	Features
Credible ISA	Posthumous detection: 1) numerous a-synuclein; 2) neurodegenerative changes in the strionigral and olivopontocerebral areas;
Probable ISA	A sporadic progressive disease (onset after age 30) characterized by autonomic failure, including urinary incontinence (with erectile dysfunction in men) or orthostatic blood pressure drop of at least 30 mm Hg. systolic or 15 mm Hg. diastolic after 3 minutes of standing plus one of the following: 1) parkinsonism with a poor response to levodopa (subtype MSA-P), 2) cerebellar syndrome (subtype MSA-C);
Supporting criteria	Dystonia of the muscles of the head and neck region; disproportionate antecollis; bent spine (forward, sideways, or both); contractures of the arms or legs; breathing sighs; severe dysphonia; severe dysarthria; new or increased snoring; cold hands and feet; incontinence with emotional reactions (laughing or crying); postural or kinetic tremor;
Not characteristic signs	Rest tremor, pill rolling; clinically significant neuropathy; hallucinations not caused by drugs; onset after 75 years; positive family history; dementia (according to DSM-IV criteria); changes in the white matter of the brain, characteristic of multiple sclerosis.

remembered that in one third of patients there is a moderate decrease in cognitive functions, usually of the frontal type. In later stages, 4.5% of patients may develop dementia [9]. Depression, anxiety and panic attacks are found among emotional disorders in MSA [1].

Treatment for MSA remains symptomatic. Orthostatic hypotension therapy often improves the quality of life of patients with MSA. Non-drug methods include applying compression bandages to the lower limbs, increasing the salt in the diet, raising the head end of the bed. Drug therapy for orthostatic hypotension includes the administration of α-adrenergic agonists (midodrine), mineralocorticoids (fludrocortisone), and acetylcholinesterase inhibitors (pyridostigmine) [4].

Anticholinergics of peripheral action are effective in urinary incontinence, but often induce urinary retention; Desmopressin taken at night provides regression of nocturia. In case of incomplete emptying of the bladder, intermittent catheterization is necessary [6].

Currently, there is no effective treatment for cerebellar disorders of MCA. To reduce the symptoms of parkinsonism, levodopa preparations are used at a dose of up to 1000 mg / day, provided that it is well tolerated [6].

Conclusion. Thus, rapidly progressive and difficult to treat symptoms of autonomic failure may be the initial manifestations of MSA. Unfortunately, the treatment of this disease remains symptomatic, however, the timely initiation of therapy can somewhat improve the quality of life of patients.

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