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Anti-MOG syndrome: two case reports

The paper describes two cases of adolescent-onset anti-MOG (myelin oligodendrocyte glycoprotein) syndrome. One case had an onset of optic neuritis, followed by myelitis; a recurrence of the syndrome occurred during interferon-β therapy. In the other case the syndrome also began with optic neuritis; and after a long latent period it was manifested as unilateral encephalitis with contralateral hemiparesis and rare epileptic seizures.
Detection of anti-MOG syndrome is of great importance, because its management tactics is different from that for multiple sclerosis; furthermore, the laboratory diagnosis of this syndrome can be made in our country now.

Keywords: *anti-MOG syndrome; optic neuritis; myelitis; encephalitis.*
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The last decades were marked by dramatic progress in understanding of the pathogenesis, diagnostics and treatment of demyelinating diseases. This interest is due to the important social role of multiple sclerosis, which is one of the most common causes of persistent disability of working age people. As our understanding of the pathogenesis of demyelinating diseases increases, it becomes apparent that they are a combination of various pathological processes, often overlapping. Examples include the opticospinal form of multiple sclerosis and neuromyelitis optica (Devic's disease) [1], the latter, however, in recent years has been regarded as a part of "neuromyelitis optica spectrum disorders" (NMOSD) [2]. In patients with optic neuritis and / or myelitis who do not have antibodies to aquaporin-4 (as well as people with other clinical manifestations of demyelinating diseases), the disease can be caused by the presence of antibodies to myelin oligodendrocyte glycoprotein (MOG), which can be phenotypically manifested in a number of conditions, including acute disseminated encephalomyelitis (ADEM), optic neuritis, myelitis (including severe transverse myelitis with a pronounced longitudinal lesion of the spinal cord [**L**ongitudinally **E**xtensive **T**ransverse **M**yelitis, LETM]), and encephalitis [3].

Thus, in a large study by S. Mariotto et al. [4] involving 425 patients with demyelinating diseases, antibodies to MOG were detected in 22 subjects. In Russia, the research of anti-MOG syndrome was hampered by the fact that none of large laboratories performed tests for these antibodies as a routine practice, and only recently there has appeared an opportunity of their research at the Scientific Center of Neurology in patients over 18 years old, using ELISA type Sandwich method with reagents of Cloud-Clone Corp (USA).

We present a description of two clinical observations of anti-MOG syndrome.

Male patient X.*, born in 1999, in 2014 after an acute respiratory viral infection presented with pain during the left eyeball movement and a sharp vision loss in the left eye. The history of this patient in the period of 2014–2015 was described in an earlier publication [5]. Following the left-sided optic neuritis, the patient developed myelitis, which did not meet the LETM criteria (Fig. 1, 2), and the analysis for antibodies to aquaporin-4 turned out to be negative.*

The diagnosis of multiple sclerosis was established, and interferon beta ($IFN_β$) was prescribed. With repeated MRI, performed at the age of 17, negative dynamics was observed in the form of the appearance of demyelination foci that did not accumulate a contrast agent in the white matter of the brain hemispheres (Fig. 3).

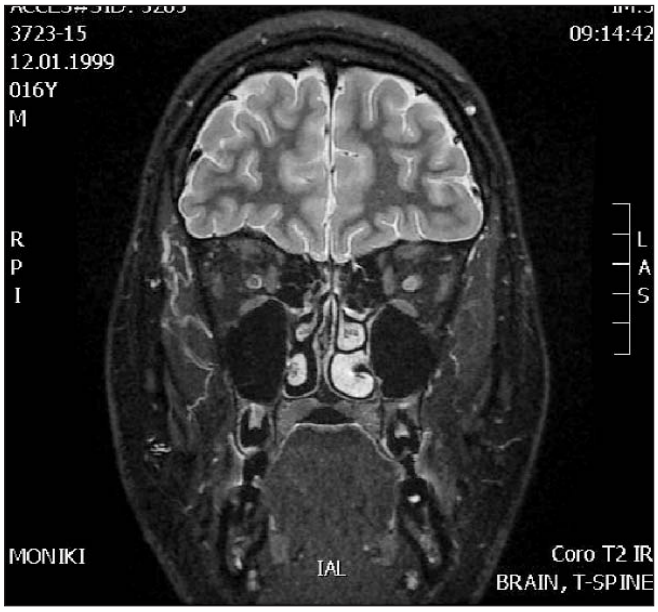

Fig. 1. *Patient X., 16 years old. MRI of the brain. In T2-WI[1] mode, a thickening of the left optic nerve is determined – a sign of optic neuritis. In the structure of the left optic nerve throughout its intraorbital length, at the level of the bony funnel of the orbit, a focus of increased intensity with a length of about 35 mm, and up to 3 mm in the cross section is visualized, not accumulating a contrast agent.*

[1]T2-WI – T2-weighted images.

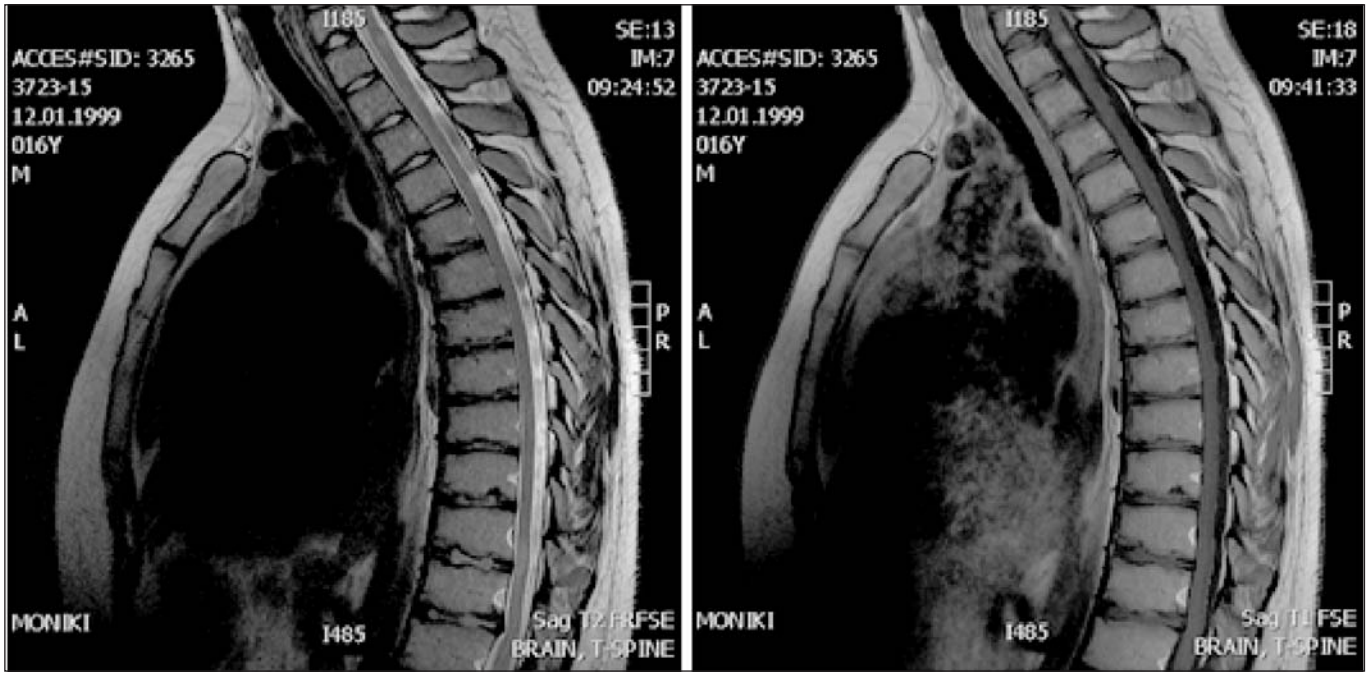

Fig. 2. *Patient X, 16 years old. MRI of the thoracic spine. The figure visualizes foci in the spinal cord with signs of damage to the blood-brain barrier at the TI level. At the level of C_{VII}–L_I bodies, foci 4.5x4.5x6 mm in size accumulating a contrast agent are visualized in the area of the upper half of the TI body; in the area of the disk $T_{IV–V}$ in the left posterior sections, there are foci 2.5x2x5 mm in size, which do not accumulate a contrast agent; in the area of the bodies and disk $T_{XI–XII}$, foci 17x6x3 mm in size, also without signs of contrast enhancement are visualized.*

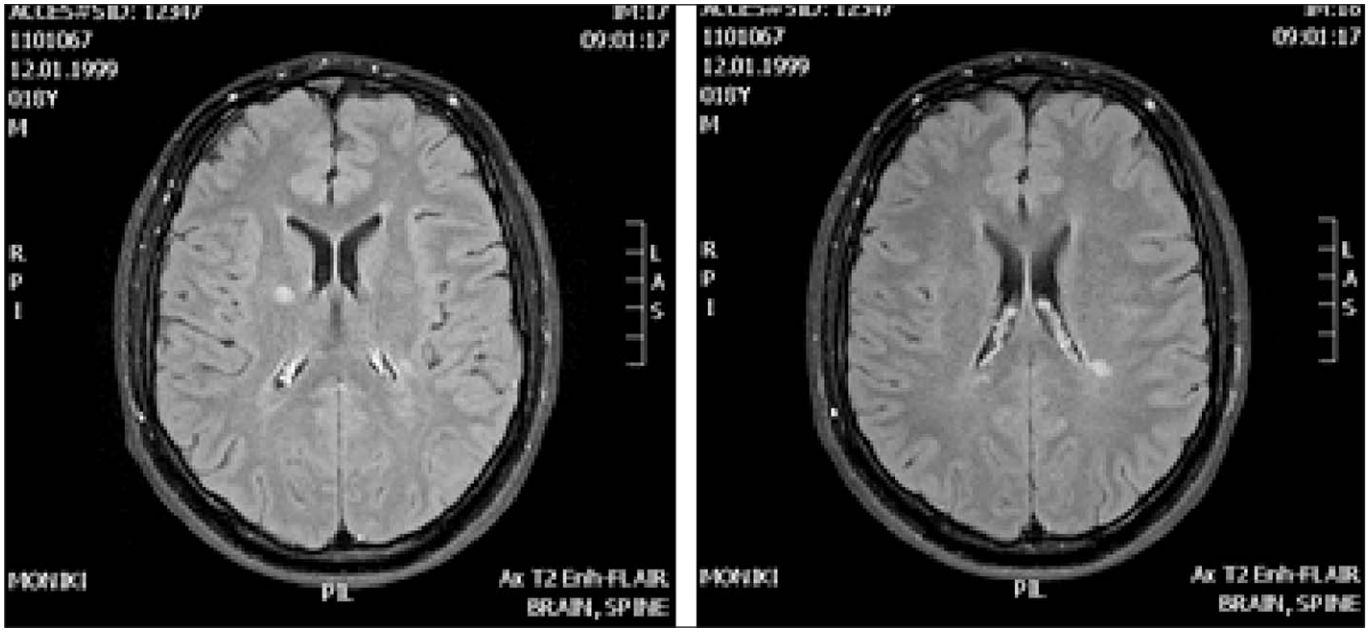

Fig. 3. *Patient X., 17 years old. MRI of the brain. The appearance of new foci in the white matter of the brain hemisphere. In the subcortical white matter of the right parietal lobe, as well as periventricular to the posterior horn of the left lateral ventricle and in the subcortical nuclei on the right, three lesions are found that are hyperintense on T2-FLAIR, up to 6.6 mm in size, elongated or rounded in shape: the axes of the lesions are oriented perpendicular to the corpus callosum.*

The patient continued treatment with IFN_β, but at the age of 18 new exacerbation occurred with a clinical picture of optic neuritis and myelitis. After methylprednisolone pulse therapy, the patient was tested for MOG antibodies; the test was positive (15.3 pg/ml; normal range 0–15 pg/ml).

In the second patient, the disease course was less typical, the symptoms of demyelinating process superimposed on other neurological and somatic symptoms, which led to a prolonged and unproductive evaluation before establishing the correct diagnosis.

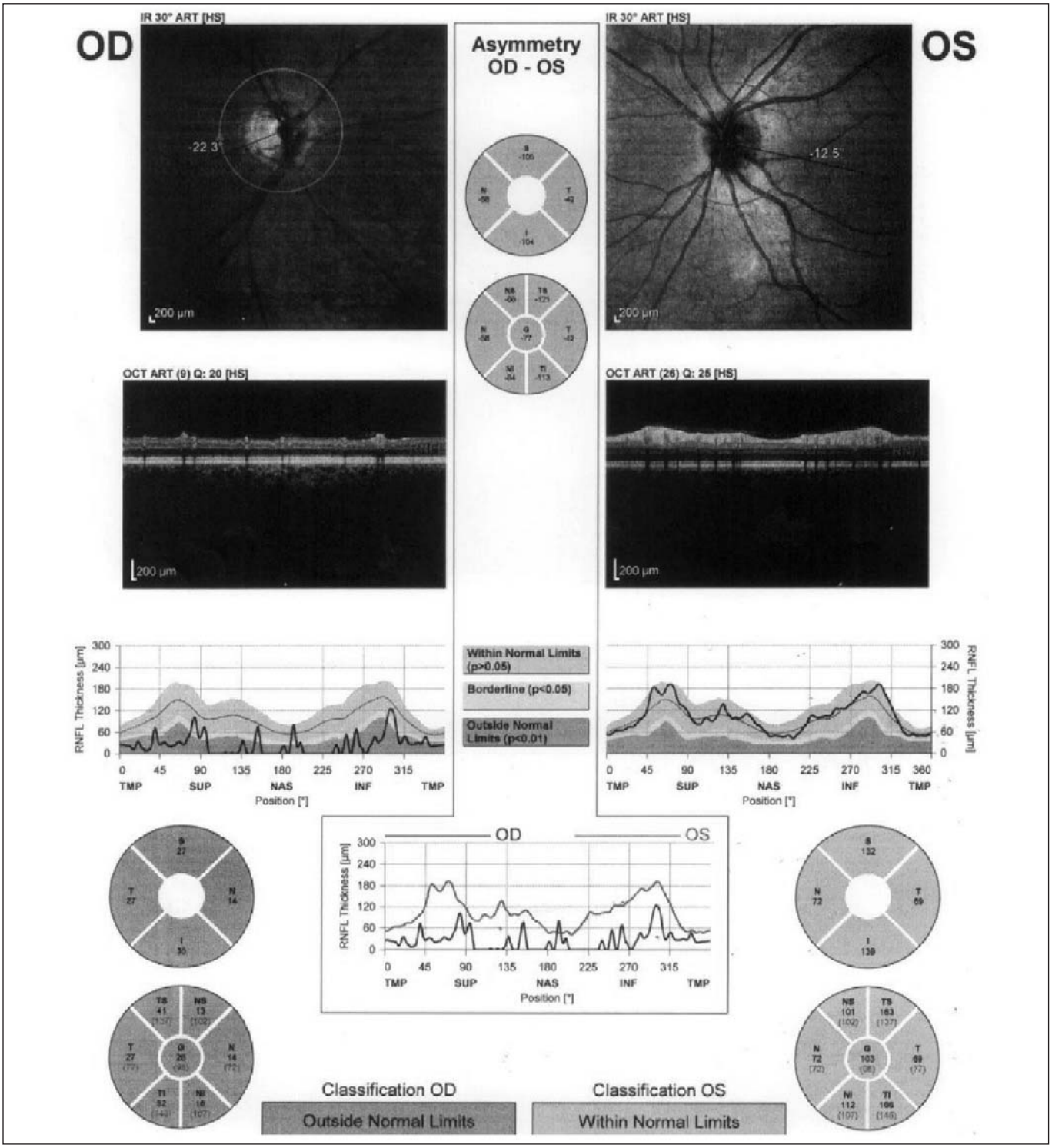

Fig. 4. *Patient V., 25 years old. OCT. Atrophy of the right optic nerve, reduction of the peripapillary nerve fiber thickness in all quadrants on the right, the thickness of the peripapillary nerve fibers on the left is not changed.*

***Female patient V.**, born in 1991, from childhood was diagnosed with stomatitis 1–3 times a year, at the age of 15 years "blindness in the right eye", in Helmholtz Moscow Research Institute of Eye Diseases she was diagnosed with retrobulbar neuritis in the right eye, and a standard treatment was carried out, which, however, did not lead to the reversal of the symptoms. Atrophy of the right optic nerve developed, which was further confirmed by optical coherence tomography (OCT, Fig. 4).*

From the age of 15 to 23 years old, there were no significant changes in the patient's neurological status, although she was observed at V.A. Nasonova Institute of Rheumatology for bilateral uveitis and recurrent joint pain (a rheumatic disease

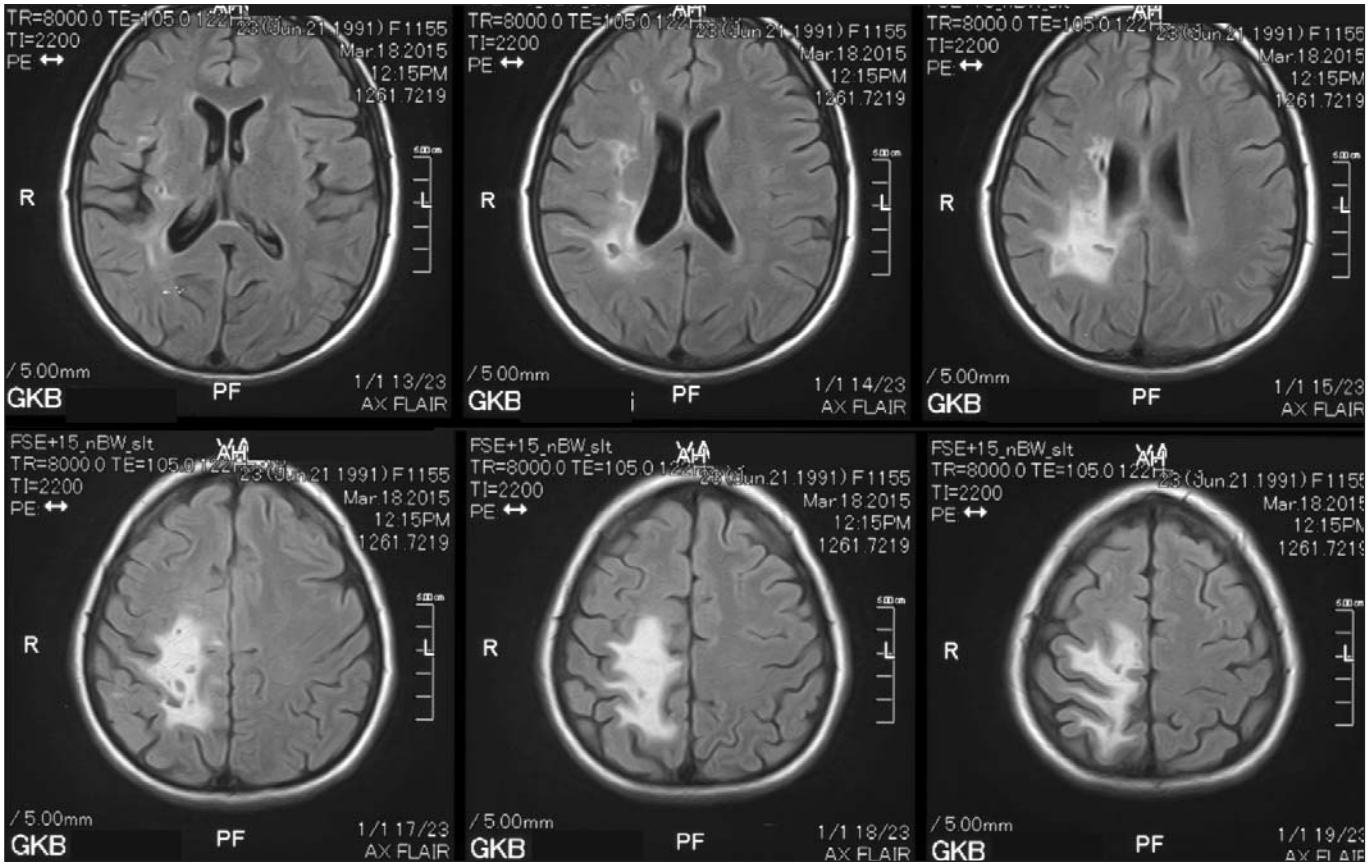

Fig. 5. *Patient V., 23 years old. MRI of the brain. Demyelination of the right hemisphere. Multiple foci in the right hemisphere, hyperintensive on T2-WI, hypointensive on T1-WI, with a maximum size of up to 1.1x0.6 cm; in addition, in the supraventricular portions of the white substance of the right frontoparietal region, a zone of a pathological MR-signal, hyperintensive on T2-WI and FLAIR, with distinct irregular contours, 5.3x3.6x5.3 cm, is visualized.*

was suspected); she was also observed by a dermatologist for psoriasis. Based on these data, as well as the negative dynamics of neurological changes, the rheumatologist suggested that the patient had Behcet's disease with the CNS damage, which was not confirmed by subsequent findings, including the negative pathergy test.

At the age of 23, persistent numbness appeared in the left half of the body, and, after a few months, an epileptic seizure occurred with a focal beginning in the left extremities and a subsequent secondary generalization. The brain MRI revealed a demyelinating disease with gliosis in the right hemisphere (Fig. 5).

Later, from the age of 23 to 27 years, an increase in left-sided spastic hemiparesis was observed, as well as rare (1–2 times a year) epileptic seizures with a focal onset in the left extremities and secondary generalization (Fig. 6). Such disease course in anti-MOG syndrome is extremely rare [6]; the debut of epileptic seizures in children with ADEM is more typical [7].

During the observation and treatment in our clinic (from the age of 23 to 27), numerous laboratory studies (tests for antineuronal antibodies, antinuclear factor, M and G class antibodies to cardiolipin, type of oligoclonal antibody synthesis, antibodies to aquaporin-4, anti-erythrocyte antibodies, rheumatoid factor, lupus anticoagulant, HLA phenotypes, antibodies to the NMDA receptor, as well as clinical and biochemical analyzes of blood and cerebrospinal fluid, urinalysis, coagulogram, etc.) did not reveal a definite pathology.

A rheumatic disease was also rejected, taking into account the normal picture of the peripheral blood and the absence of pathological changes in the joints according to numerous radiographic studies and MRI scans.

The patient was consulted in absentia by one of the world's leading experts on demyelinating diseases, Professor F. Fazekas from Austria. It was recommended that antibodies to MOG be tested, and the test turned out to be positive (20 pg/ml; normal range 0–15 pg/ml).

Discussion. Detection of anti-MOG syndrome is very important because a number of drugs used in treatment of multiple sclerosis may be ineffective, or even exacerbate the severity of clinical symptoms in patients with optic neuritis and / or myelitis, among which there may be patients with anti-MOG [8, 9].

Anti-MOG syndrome should be suspected in patients with a clinical picture of optic neuritis and/or myelitis and a negative test for the presence of antibodies to aquaporin-4 [10, 11].

The first line treatment for the syndrome is pulse therapy with intravenous methylprednisolone, but over time, the effectiveness of such therapy may decrease. Intravenous human immunoglobulin or plasmapheresis can be an adjunct or alterna-

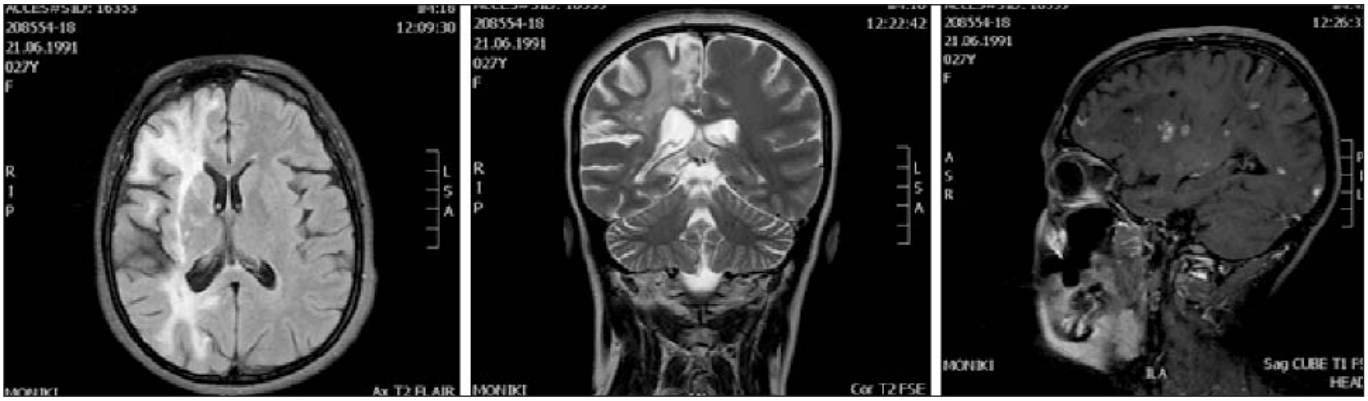

Fig. 6. *Patient V., 27 years old. MRI of the brain. Pronounced negative dynamics of changes in the right hemisphere. Compared with the studies performed in 2015 and 2016, there is an increase in the size of confluent pathological zones in the subcortical and deep sections of the white matter of the right hemisphere spreading to the posterior corpus callosum, represented by gliotic changes and perifocal swelling, 138x15x40 mm in size. In addition, the appearance of a new pathological area is observed in the subcortical and deep sections of the white substance of the right frontal lobe with edema, gliosis and single cystic foci, the size of which is approximately 57x40x40 mm. Right frontoparietal gyri are unequally thinned. The retraction of the anterior, posterior horns and the body of the right lateral ventricle towards these pathological changes is visualized. We can also see the foci of a pathological MR signal, hyperintense on T2-WI, FLAIR, isointense on T1-WI on the right in the area of subcortical structures, thalamus, and quadrature, up to 12x16x15 mm. After intravenous enhancement, an intense inhomogeneous accumulation of the contrast agent is determined in the form of foci prone to fusion in the area of pathological zones in the right hemisphere of the brain and in the area of the corpus callosum, in the thalamus and midbrain, most pronounced in the parietal region*

tive. If the disease is relapsing, or recovery of patients is too slow, the second-line therapy should be considered, including mycophenolate mofetil or azathioprine, and the third line – rituximab [12]. However, it should be emphasized that not only the therapy scheme, but also the diagnostic algorithm and even the taxonomic position of this syndrome in the classification of demyelinating diseases [13] are not fully developed. Obviously, further research is needed to solve these problems.

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