Relapsing Autoimmune GFAP Astrocytopathy: Case Report

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Abstract

Introduction. *Glial fibrillary acidic protein (GFAP) is the main component of intermediate astrocyte filaments. In 2016, anti-GFAP antibodies (Ab) were identified as the specific biomarker for the first established CNS inflammatory disorder subsequently called autoimmune GFAP-astrocytopathy (A-GFAP-A). Since GFAP is localized intracellularly, GFAP Ab do not appear to be directly pathogenic though serve as a biomarker of immune inflammation. Although presence of GFAP-Ab in the serum (but not in the CSF) could be observed in various CNS immune-mediated diseases, detection of GFAP-Ab in CSF is only characteristic for A-GFAP-A. A-GFAP-A usually develops after the age of 40 and mostly manifests acutely or subacutely with symptoms of meningoencephalomyelitis or its focal forms. Linear perivascular radial cerebral white matter enhancement is a specific MRI finding of A-GFAP-A. Concomitant neoplasms or autoimmune disorders, as well as co-expression of other antineuronal antibodies are not uncommon in A-GFAP-A. Usually, disease responds well to immunotherapy, and prolonged remission could be achieved, however recurrent disease course and fulminant cases are also described in the literature. In these cases, long-term immunosuppression is required. Data on epidemiology, etiological factors, and precise pathogenesis of A-GFAP-A are still limited. Due to the lack of long-term follow-up data, diagnostic criteria, generally accepted treatment strategies or prognostic risk factors for relapse and outcome of the disease have not yet been established and precised. We present the first description of a case of relapsing A-GFAP-A in Russia and an analysis of the current data on the pathogenesis, clinical features, as well as the diagnostic challenges and treatment approaches for A-GFAP-A.*

Keywords: *GFAP; glial fibrillary acidic protein; autoimmune GFAP astrocytopathy; autoimmune encephalitis; meningoencephalitis; meningoencephalomyelitis*

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Клинический случай рецидивирующей аутоиммунной GFAP-астроцитопатии

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Аннотация

Введение. *Глиальный фибриллярный кислый белок (GFAP) является ключевым компонентом промежуточных филаментов астроцитов. В 2016 г. антитела к GFAP (GFAP-АТ) были идентифицированы в качестве специфичного биомаркера впервые установленного воспалительного заболевания ЦНС, которое назвали аутоиммунной астроцитопатией, ассоциированной с GFAP-АТ (A-GFAP-A). Поскольку GFAP локализован внутриклеточно, непосредственно GFAP-АТ, по-видимому, не патогенны, но служат биомаркером иммунного воспаления. Диагностическая ценность обнаружения GFAP-АТ в цереброспинальной жидкости выше, чем в сыворотке крови, поскольку изолированное выявление GFAP-АТ в крови (но не в цереброспинальной жидкости) может наблюдаться и при других иммуноопосредованных заболеваниях с поражением центральной нервной системы. A-GFAP-A обычно поражает лиц старше 40 лет и в большинстве случаев проявляется острым или подострым развитием симптомов менингоэнцефаломиелита или его ограниченных форм. Характерным для A-GFAP-A МРТ-признаком является линейное периваскулярное радиальное контрастное усиление в белом веществе полушарий головного мозга, локализующееся перпендикулярно по отношению к желудочкам. Сопутствующие новообразования или аутоиммунные расстройства, а также ко-экспрессия с антинейрональными антителами — не редкость при A-GFAP-A. Заболевание, как правило, хорошо поддается иммунной терапии, хотя рецидивирующее течение, требующее длительной иммуносупрессии, и единичные случаи летального исхода также имеют место.*

Сведения об эпидемиологии, этиологии и патогенезе A-GFAP-A ещё достаточно ограничены. В связи с отсутствием данных долгосрочного наблюдения диагностические критерии, общепринятые схемы лечения, прогностические факторы для оценки риска рецидива и исхода заболевания не установлены. В статье представлено первое в России описание клинического случая рецидивирующей A-GFAP-A, а также приведён анализ литературы с освещением накопленных к настоящему времени знаний о патогенезе, клинической картине, а также трудностях диагностики и лечения A-GFAP-A.

Ключевые слова: *GFAP; глиальный фибриллярный кислый белок; аутоиммунная GFAP-астроцитопатия; аутоиммунный энцефалит; менингоэнцефалит; менингоэнцефаломиелит*

Этическое утверждение. Исследование проводилось при добровольном информированном согласии пациента, в том числе на публикацию клинического случая.

Источник финансирования. Авторы заявляют об отсутствии внешних источников финансирования при проведении исследования.

Конфликт интересов. Авторы декларируют отсутствие явных и потенциальных конфликтов интересов, связанных с публикацией настоящей статьи.

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Introduction

In 2016, the researchers led by V. Lennon (Mayo Clinic, Rochester, MN, USA) presented a novel autoantibody (Ab) to the cytosolic protein of intermediate astrocyte filaments. As its antigen he identified glial fibrillary acidic protein (GFAP), the main protein of intermediate astrocyte filaments, that is crucial for keeping them morphologically stable, forming the blood–brain barrier, and regulating the synapse function [1, 2]. Testing with tissue-based (TBA) and cell-based (CBA) assay of over 100,000 serum and/or cerebrospinal fluid (CSF) samples found anti-GFAP Ab in 103 patients of those with suspected autoimmune neurological disorder [1]. Retrospective analysis of the relevant medical records showed that most of the seropositive patients clinically had glucocorticosteroid-sensitive menyngoencephalitis with or without concomitant myelitis, which resembles nonvasculitic autoimmune inflammatory meningoencephalitis as described earlier [3, 4]. Thus, they introduced a new clinical entity called autoimmune GFAP-meningoencephalitis (or A-GFAP-A) that is distinct from other conditions typically considered in the differential diagnosis including infections, granulomatoses, canrcinomatosis, demyelinating diseases, and CNS vasculitis and lymphoma. Further studies proved specific CSF GFAP seropositivity to establish A-GFAP-A [5–7].

In this paper, we present first known A-GFAP-A clinical case in Russia.

Clinical case

Patient M., male, 66 y.o., who had mild COVID-19 in January 2021, was immunized with bicomponent Sputnik-V in April–May 2021. In mid-May, the patient traveled to Thailand where he experienced significant general fatigue, daytime drowsiness, and decreased appetite. Upon his return to Moscow on 5 July 2021, his wife found him spatially and temporally disoriented, hallucinating, and feverish with a body temperature elevated up to 38ºC (100.4ºF). Symptoms that developed over the next two weeks included ascending numbness of lower limbs (up to the costal arch), impaired coordination, and frequent urination, later acute urine retention. The patient was admitted to the hospital and underwent trocar cystostomy. His condition gradually deteriorated, with short-term memory loss, loss of independent mobility, and episodes of emotional agitation.

The MRI of the brain and the cervical spinal cord (July 2021) showed multiple T2-hyperintense lesions in the periventricular white matter of the hemispheres, the brainstem, and the cervical spinal cord with signs of activity: contrast enhancement of the periventricular lesions and the lesion at the level of C2 vertebra on the post-contrast T1-weighted images (T1+C). The MRI image was interpreted as a demyelinating process. Blood and CSF tests excluded neurosarcoidosis, neuromyelitis optica spectrum disorder (NMOSD) with anti-aquaporin-4 (AQP-4) Ab, herpes simplex encephalitis, and tuberculous encephalopathy. The diagnosis of multiple sclerosis relapse was established. The patient received pulse regimen of IV dexamethasone (total dose 144 mg) and symptomatic alimemazine and hydroxyzine with suboptimal improvements (relief of positive psychotic symptoms, improved alertness, standing with assistance).

One month later, the patient was readmitted to the hospital due to residual psychoneurological deficits. *Brain*

and spinal cord MRI (August 2021) found multifocal T2-hyperintense lesions in the brain (unchanged as compared to the previous imaging) and along the entire length of the spinal cord. T1+C images showed diffuse contrast enhancement (dirty-appearing white matter) along the centrum semiovale perivascular spaces, focal enhanced lesion in the brainstem, and multiple enhanced lesions along the entire length of the spinal cord. MRI abnormalities were interpreted as inflammatory process (suspected vasculitis). Instrumental and laboratory tests excluded CNS damage due to systemic vasculitis, primary CNS angiitis, antineuronal Ab-associated encephalitides, myelin oligodendrocyte glycoprotein (MOG) associated disease, and West Nile, dengue, chikungunya, and Japanese viral encephalitides. The patient's diagnosis was reviewed as vasculitis with affected cerebral and spinal small veins and secondary inflammatory changes in the white matter of the hemispheres, the brainstem, and the spinal cord. The patient received pulse regimen of IV methylprednisolone (total dose 5,000 mg) with pronounced improvements (steadier gait, independent mobility, totally regressed cognitive impairment, better urinary control, that allowed to remove cystostomy catheter). PO prednisolone (80 mg QD) with tapering was indicated.

Two months after the discharge (October 2021), the patient, who then received tapered prednisolone (20 mg QD), had a relapse manifested as increasing general fatigue, daytime drowsiness, cognitive impairment, and unsteady gait. *Brain and spinal cord MRI (October 2021)* showed negative changes including the increased number of T2-hyperintense lesions in the deep and periventricular white matter and more intense contrast enhancement in the hemispheric white matter, in the brainstem (primarily the pons and the middle cerebellar peduncles), and the intramedullary lesions (Fig. 1). The patient received pulse regimen of IV methylprednisolone (total dose 5,000 mg) with significant symptom regression. PO prednisolone (80 mg QD) with further tapering was indicated.

The patient's condition was stable during the next year. Control *brain and spinal cord MRI (December 2021)* demonstrated positive changes (Fig. 2). *Brain MRI (April 2021)* demonstrated no changes.

In October 2022, the patient who then received tapered methylprednisolone (8 mg QD) again had subfebrile fever, increasing daytime drowsiness, and unsteady gait. The patient was therefore admitted to the Research Center of Neurology.

Comorbidities: type 2 diabetes, stage 2 hypertension, cardiovascular risk 4, and prostatic hypertrophy.

Neurological status: The patient is fully oriented. Mild cognitive impairment (MoCa 24/30 points; with short-term memory mostly impaired). No meningeal signs. No cranial nerve abnormalities. No obvious pareses. Normal limb muscle tone. Brisk tendon reflexes (L>R). Bilateral positive Babinski sign, Rossolimo's hand sign, and palmomental reflex. Coordination tests with intention tremor or dysmetria (R=L). The patient is unstable in the Romberg test. Painless voluntary urination. Predisposition to constipation. Decreased vibration sensitivity on the knee joints and no vibration sensitivity on the ankle joints and the shinbones (L=R). Ataxic gait on wide base.

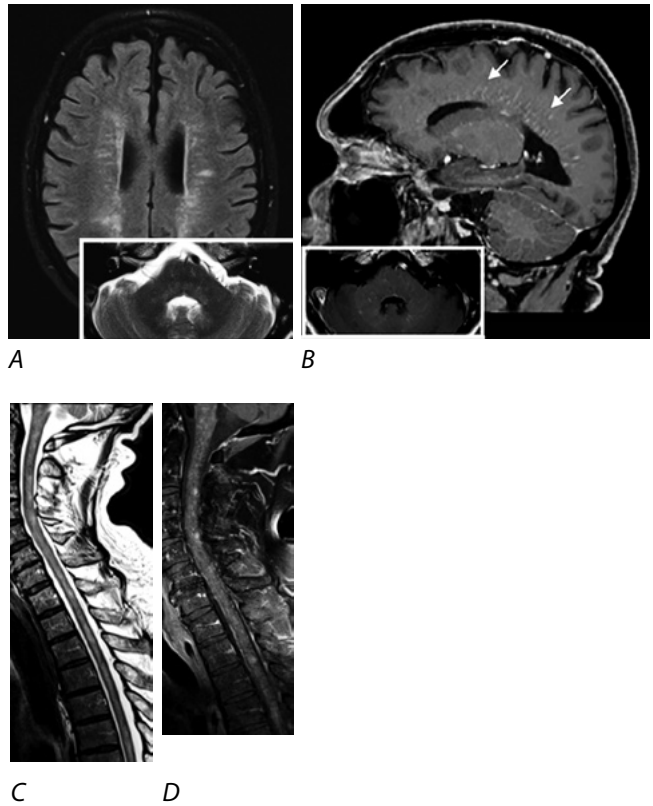

Fig. 1. Patient M.'s brain and spinal MRI (October 2021).
A — T2/T2-FLAIR: multiple hyperintense white matter lesions in the cerebral hemispheres (elongated and perivascular), the pons, the medulla oblongata, and the middle cerebellar peduncles; *B* — T1+C: linear radial perivascular contrast enhancement in the white matter of the cerebral hemispheres, the brainstem, the cerebral peduncles, and the cerebellum; *C* — T2/T2-STIR: multiple ill-defined hyperintense lesions along the entire length of the spinal cord; *D* — T1+C: focal heterogeneous contrast enhancement in the spinal cord.

Test results:
- CSF analysis (July 2021): cytosis 80/3; lymphocytes (reference: 0–10), protein 0.84 g/L (reference: 0.15–0.45), glucose 1.7 mmol/L (reference: 2.2–3.3);
- CSF analysis (August 2021): cytosis 155/3; lymphocytes, protein 0.599 g/L, normal glucose level;
- oligoclonal IgG bands in serum and CSF (July 2021): type 3;
- oligoclonal IgG bands in serum and CSF (August 2021): type 2;

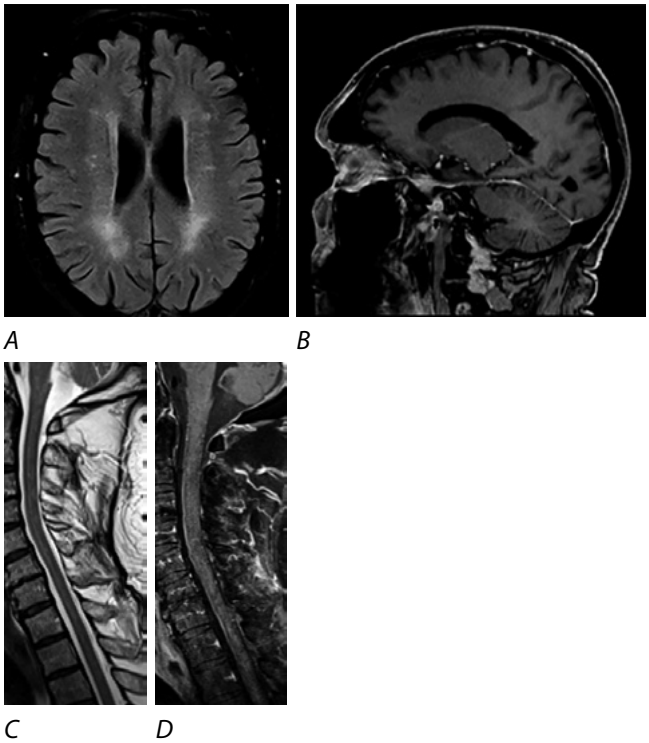

Fig. 2. Patient M.'s brain and spinal cord MRI (December 2021).
A, C — T2-FLAIR/T2-STIR: partially resolved focal changes in the brain and spinal cord. *B, D* — T1+C: no abnormal enhancement in the brain matter; decreased volume and intensity of abnormal enhancement in the spinal cord.

- no PCR DNA of the Mycobacterium tuberculosis, type 1 and/or 2 herpes simplex virus, the cytomegalovirus, and/or the Epstein—Barr virus in CSF (July 2021);
- no antibodies to West Nile, dengue, chikungunya, and/or Japanese encephalitis viruses (IgM) in serum and CSF (October 2021);
- no antibodies to neuronal antigen (IgG) inserum and CSF;
- no anti-neutrophil cytoplasmic antibodies (IgM) and/or antibodies to extractable nuclear antigens (IgG);
- no AQP-4 Ab;
- no MOG Ab;
- normal ACE activity;
- blood electrolytes (July 2021): sodium 121 mmol/L (reference 130–157), normal potassium level;
- blood electrolytes (August 2021, October 2021): normal sodium and potassium levels;
- chest CT: post-inflammatory changes in the left upper lobe and the right middle lobe. No other abnormalities.
- brain MRI (November 2022) compared to April 2021 MRI showed negative changes including enlargement of diffuse T2 hyperintense lesions in the deep white matter of both cerebral hemispheres, the brainstem, and both cerebellar hemispheres, which are elongated and perivascular with intense contrast enhancement (Fig. 3);

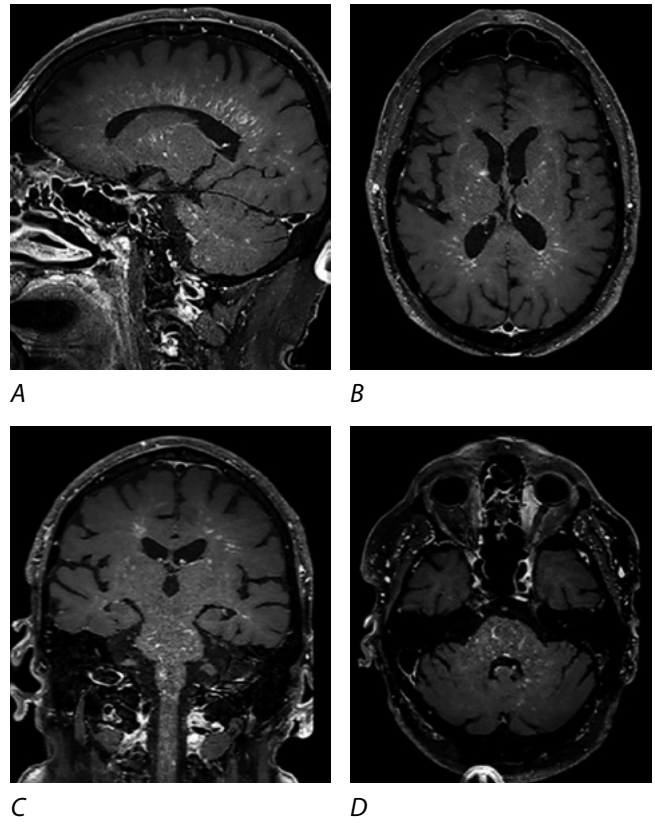

Fig. 3. Patient M.'s brain MRI (November 2022).
T1+C: contrast enhancement in the periventricular and deep white matter of the cerebral hemispheres (*A–C*), the brainstem (*C, D*), the cerebral peduncles (*D*), and both cerebellar hemispheres (*A, D*).

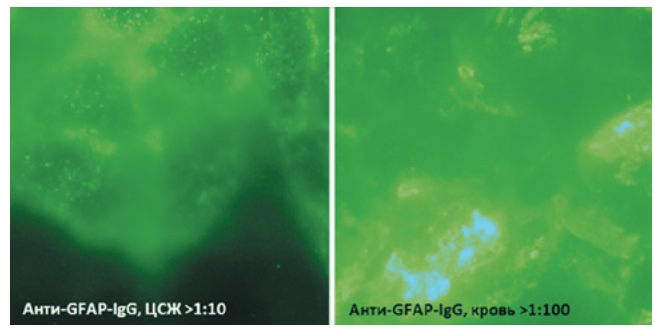

Fig. 4. GFAP Ab (IgG; indirect immunofluorescence) both in patient M.'s CSF (*A*) and serum (*B*) (November 2022).

- CSF analysis: cytosis 129/3; protein 0.75 g/L, normal glucose level;
- GFAP Ab (IgG; indirect immunofluorescence) both in CSF (Fig. 4, A) and serum (Fig. 4, B).

Based on the clinical presentation of relapsing encephalomyelitis, neuroimaging findings, and GFAP Ab in the patient's CSF and serum, we established A-GFAP-A diagnosis.

The patient received pulse regimen of IV methylprednisolone (total dose 5,000 mg). Considering the relapsing disease, we initiated anti-B-cell therapy (rituximab 1,000 mg ×2 with a 2-wk interval) with positive changes including relieved drowsiness and reversed vestibulo-atactic syndrome. We prescribed PO methylprednisolone (16 mg QD) for 1 month with tapering and eventual discontinuation. We recommended neurologic and endocrinologic follow-up, continued rituximab 1,000 mg twice a year, and PET/CT with FDG tracer to rule out paraneoplastic disease.

Discussion

GFAP is the fourth glial autoantigen with proven clinical significance after AQP-4, MOG, and SOX-1 [8]. Since GFAP is an intracellular (cytoplasmic) antigen, GFAP-specific cytotoxic T-cells must be crucial for the immune response while GFAP Ab must be a GFAP-autoimmunity diagnostic biomarker rather than a pathogen [6, 9].

A-GFAP-A may be triggered by neoplasms, conditions associated with T-cell function dysregulation (including HIV infection and use of immune checkpoint inhibitors), and history of infections [5–7, 9, 10]. Association between infections and A-GFAP-A is not fully understood. However, many patients (30–40%) have symptoms of systemic inflammation (subfebrile fever, rhinorrhea, sore throat, cough) within 1 month before the onset of CNS signs and symptoms [5–7, 11, 12]. Additionally, we aware of cases of A-GFAP-A deve loped post herpetic infections (Herpes simplex virus, Varicella zoster virus) [5, 11, 13]. Patient M. also had influenza-like prodromal syndrome. Besides, epidemiology data on symptom onset during Thailand travel and the recent history of COVID-19 do not allow us to exclude an infection as a possible trigger of disease development despite the negative results of CSF test for a wide range of infections.

Over a quarter of patients with A-GFAP-A have a past or present history of neoplasms, with ovarian teratoma accounting for almost half of these neoplasms. In addition, adenocarcinomas and carcinomas of almost all organs have been reported [5–7, 11, 14, 15]. In the case presented, routine cancer screening revealed no malignancy. Relapsing disease and the fact that over half of the neoplasms in patients with A-GFAP-A can be prospectively predicted two years after the onset of neurological symptoms [5, 6] emphasize the need for cancer suspicion in our patient.

Immune-mediated A-GFAP-A origin may be also proved by high prevalence of concomitant autoimmune conditions including type 2 diabetes (as in patient M.), psoriasis, thyroiditis, rheumatoid arthritis, myasthenia gravis, ulcerative colitis, and focal alopecia as well as reports on co-expression of antineural/glial Ab (such as NMDAR, $GABA_AR$, and AQP-4 Ab) in patients with A-GFAP-A [6, 7, 16, 17].

Although A-GFAP-A has been reported in patients ranging in age from 2 to 103 years, it is typically found in middle-aged patients (44–50 years). A-GFAP-A is equally prevalent in males and females, although paraneoplastic teratoma cases predominate in females [5–7, 15, 18]. The disease usually has an acute or subacute onset (<2 months). The most common A-GFAP-A clinical phenotypes include meningoencephalitis and encephalitis (44–61%) followed by (meningo)encephalomyelitis (11–32%), with much rarer isolated myelitis (2–11%) and meningitis (1–9%) [5–7]. The most common manifestations include altered and impaired consciousness, cognitive impairment (primarily worsened executive functions and short-term memory), mental, meningeal, vestibulo-atactic, myelopathic, and brainstem symptoms, autonomic dysfunction, and heterogeneous visual disturbances [5–7, 11, 14, 19]. Slightly less common manifestations include epilepsy, urinary dysfunction, parkinsonism, movement disorders (such as tremor, myoclonus, dystonia, chorea, and hyperekplexia), *area postrema* syndrome, and peripheral nervous system involvement [12, 20–24]. This case combined typical A-GFAP-A manifestations and gross urinary dysfunction probably caused by extensive spinal (including caudal) involvement and excessive daytime drowsiness probably caused by diencephalic involvement.

Blood tests showed hyponatremia at onset (and further normal sodium levels). This is consistent with literature data on the prevalence of hyponatremia in more than half of patients with A-GFAP-A [17]. Hyponatremia origin remains unclear. Almost all patients with A-GFAP-A demonstrate inflammatory CSF analysis pattern. The analysis typically indicates lymphocytic pleocytosis (average: 60–225/μL), with an increase in lymphocytes (mostly), monocytes, and neutrophils, and an elevated protein level (average: 0.75–2.00 g/L) [5–7, 14]. Intrathecally synthesized oligoclonal IgG is found in 42–77% of patients [6, 7, 14]. Interestingly, ca. 15% of the A-GFAP-A population demonstrate decreased CSF glucose levels at normal serum glucose levels. Underlying mechanism and clinical significance of the phenomenon are unclear. Hypoglycorrhachia combined with meningeal symptoms and MRI findings of meningeal contrast enhancement in patients with A-GFAP-A may lead to an erroneous diagnosis of infectious (primarily tuberculosis) meningitis [25, 26]. Lymphocytic pleocytosis, hyperproteinarchy, and oligoclonal IgG intrathecal synthesis were documented in all CSF analyses of patient M. during 1.5 years of follow-up. The CSF glucose level was decreased in the initial clinical episode (CSF PCR did not find Mycobacterium tuberculosis DNA), while repeat testing in one month showed a normal glucose level.

Both CSF Ab and serum GFAP Ab are important for A-GFAP-A diagnosis. However, GFAP-seropositive CSF, as more sensitive and specific, is crucial for A-GFAP-A diagnosis [1, 5–7]. Serum GFAP Ab (without CSF GFAP Ab) may be co-expressed in other immune-mediated CNS diseases (autoimmune encephalitides, NMOSD, multiple sclerosis, acute disseminated encephalomyelitis), although significance of this phenomenon is to be determined [15, 17, 27]. Because GFAP is the cytosolic protein of intermediate astrocyte filaments, its Ab detection methods are limited. The method of cellular antigen presentation followed by immunofluorescence visualization of GFAP Ab (indirect immunofluorescence) is the main method used to detect GFAP Ab [5–7]. In this clinical case, GFAP Ab were positive in both serum and CSF, which, combined with clinical and neuroimaging findings, allowed us to diagnose A-GFAP-A.

MRI shows changes in the brain and the spinal cord in most patients with A-GFAP-A. Multiple lesions are most commonly localized in the periventricular white matter, slightly less commonly in the brainstem (including the *area postrema*), in the basal ganglia, in the deep and subcortical white matter, and the spinal cord. Additionally, the cerebellum and the meninges may be involved [6, 7, 16]. T2/T2-FLAIR-hyperintense changes of the brain matter may be multifocal and confluent and mimic the MRI pattern of leukodystrophy or demyelination (especially in the presence of intramedullary and contrast-enhanced lesions) [6, 28, 29]. Thus, at the disease onset, the MRI findings of patient M. were interpreted as active demyelination, which, together with type 3 oligoclonal IgG synthesis and exclusion of neurosarcoidosis and viral encephalitis, led to the erroneous diagnosis of multiple sclerosis.

A-GFAP-A intramedullary lesions may be localized in any part of the spinal cord including the conus medullaris. In over 80% of cases, it is represented by longitudinally extensive transverse myelitis (≥ 3 adjacent spinal segments) involving gray matter and mostly centrally localized [6, 7, 30]. The presented clinical case was characterized by similar involvement of the matter along the spinal cord.

Approximately two thirds of A-GFAP-A cases demonstrate abnormal contrast enhancement in T1+C images, even sometimes with normal T2/T2-FLAIR. There may be focal, heterogeneous, leptomeningeal, and ependymal abnormal contrast enhancement and enhancement of cranial nerves and GFAP-enriched areas that are adjacent to the central canal of the spinal cord in patients with A-GFAP-A [6, 7, 30, 31]. However, linear perivascular radial contrast enhancement in the white matter of the cerebral hemispheres is the most typical and the most common (30–55%) pattern in A-GFAP-A patients [6, 7, 14, 16]. This pattern is not pathognomonic for A-GFAP-A and may be found in patients with lymphomatoid granulomatosis, intravascular lymphoma, neurosarcoidosis, and CNS vasculitis including patients without cerebral infarctions and with established angiographically negative primary vasculitis of CNS small vessels [32–35]. Some of the described cases of 'small-vessel vasculitis' are supposedly A-GFAP-A cases [6].

Linear perivascular radial contrast enhancement in T1+C images, normal 3D-TOF MR angiography findings, the inflammatory CSF analysis profile, and good response to pulse regimen of IV methylprednisolone led to the diagnosis of vasculitis involving small vessels of the brain and the spinal cord in patient M. Noteworthily, in A-GFAP-A patients with initially normal MRI findings, characteristic abnormalities may be found on subsequent scans, sometimes even after immune therapy [25]. However, in most cases, abnormal contrast enhancement in T1+C images and, less commonly, hyperintense changes in T2/T2-FLAIR partially or fully resolve following immune therapy as in patient M.

Available data on A-GFAP-A management and outcomes are based on observational and retrospective studies [5–7, 11, 14]. No prospective controlled studies were conducted, and thus no routine therapy protocols have been developed. Acute A-GFAP-A management includes standard options for immune-mediated neurological conditions such as IV high-dose methylprednisolone (IVHDMP), IV human immunoglobulin (IVIG), and high-volume plasma exchange (HVPE).

In most cases immune therapy used to manage acute disease results in evident clinical benefits. J. Xiao et al. meta-analysis that included 324 A-GFAP-A, patients showed that the patients who received only IVHDMP, IVHDMP+IVIG, and only HVPE demonstrated approximately similar response to treatment ($p = 0.769$) [14], which allows clinicians to choose any therapeutic regimen based on clinical severity, comorbidities, and financial issues of the patient.

Immune therapy may be sufficient as acute management of monophasic A-GFAP-A course. However, relapsing disease requires long-term immunosuppression in 20–50% patients [5–7, 11, 36]. Relapses often develop in decreasing doses of PO steroids usually prescribed for short terms following acute immune therapy. Two relapses in patient M. can be also explained by too early decrease of prednisolone dose. Mycophenolate mofetil, azathioprine, rituximab, or cyclophosphamide are recommended in relapsing or refractory A-GFAP-A although meta-analysis showed that azathioprine is less effective for relapse prevention than other options [14].

In this clinical case we selected rituximab due to rapid onset of its action as long-term immune therapy, which allowed us to use rituximab for management of acute A-GFAP-A when the patient was admitted to our Center with his third symptomatic relapse and to refuse from the long-term PO prednisolone use that would have been necessary following cyclophosphamide, mycophenolate mofetil, or azathioprine therapies, which is especially important in patients with concomitant diabetes. Another cause of relapsing disease may be paraneoplastic disease origin, and we recommended to patient M. PET/CT with FDG tracer to rule it out.

If timely and adequately managed, the prognosis for most patients with A-GFAP-A is good. As documented after the long-term follow-up (median 20 months) of 38 patients, the mean score on the modified Rankin scale was 1 [6] although poor response to immune therapy and significant remnant neurological deficit are also possible [5, 36]. A series of 22 clinical cases included 2 fatal outcomes in the patients who refused immunotherapy [7].

Conclusion

The presented A-GFAP-A clinical case and diagnostic search clearly illustrate the potential challenges physicians may face when examining such patients. A-GFAP-A is difficult to differentiate from other immune-mediated disorders and infectious diseases. Clinical findings and results of laboratory tests that mimic those found in patients with infectious (primarily tuberculosis) meningitis or CNS demyelinating diseases (NMOSD, multiple sclerosis, acute disseminated encephalomyelitis) often delay correct diagnosis and initiation of specific therapy, thus contributing to a worse prognosis. Further studies are needed to better understand A-GFAP-A, to develop its diagnostic criteria and therapeutic algorithms, as well as to increase awareness of medical professionals and GFAP Ab testing capacities in Russia.

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