Autoimmune Glial Fibrillary Acidic Protein Astrocytopathy in Children: A Retrospective Study

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Research

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Abstract

Objective: To describe the clinical features of autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy in children.

Method: Data from 11 pediatric patients with autoimmune GFAP astrocytopathywas retrospectively analyzed.

Results: All of the patients showed encephalitis and meningoencephalitis or meningoencephalomyelitis with or without myelitis, include fever (45.4%), headaches (27.3%), dizziness (18.2%), drowsiness (18.2%) and mental disorders (18.2%). Cerebrospinal fluid (CSF) were detected in all patients. The white cell counts (WBC) (90.9%), lactic dehydrogenase levels (72.7%), protein level (36.4%), and adenosine deaminase activity (ADA) level (27.3%) were elevated, and the CSF glucose levels (72.7%) were slightly reduced. Nine patients (90%) were found to have brain abnormalities, of which five (50.0%) patients had abnormal symmetrical laminar patterns or line patterns hyperintensity lesions on T2-weighted and fluid-attenuated inversion recovery (FLAIR) images in the basal ganglia, hypothalamus, subcortical white matter and periventricular white matter. The linear radial enhancement pattern of the cerebral white matter was only seen in two patients, the most common being abnormal enhancement of leptomeninges (50%). Five patients had longitudinally extensive spinal cord lesions.

Conclusion: The findings of pediatric patients with autoimmune GFAP astrocytopathy is different from the previous reports.

Introduction

In 2016, autoimmune glial fibrillary acidic protein (GFAP) astrocytopathy was first reported as a kind of meningoencephalomyelitis associated with GFAP-IgG, a spectrum of autoimmune inflammatory central nervous system (CNS) disorders, and was subsequently confirmed internationally [1]. This disorder involved meningeal, brain parenchymal, the spinal cord, or optic nerve inflammation and injury, and is characterized by corticosteroid responsive. The main clinical manifestations include fever, headaches, abnormal vision, mental disorders, ataxia, dyskinesiaand autonomic dysfunction. It is often accompanied by a hallmark brain linear perivascular radial gadolinium enhancement on magnetic resonance imaging (MRI) [2–5]. Autoimmune GFAP astrocytopathy has been described almost exclusively in adult patients, with the few pediatric cases being reported predominantly as case reports. [6–10]. Limited previous studies described the clinical data and MRI characteristics in children as similar to those in adults [10], the clinical features of Autoimmune GFAP astrocytopathy in children still need to be defined. In this study, we have recruited 11 pediatric cases with autoimmune GFAP astrocytopathy, and focused on the clinical data and MRI features in order to identify characteristic features which can increase diagnostic success.

Patients And Methodology

This study protocol was approved by the medical ethics committee of the Hunan Children's hospital of the University of South China. This retrospective study was approved by the institutional review board. Informed consent was waived due to the retrospective analysis of anonymized data.

1. Patients

We enrolled 11 pediatric patients who were admitted to our hospital (Department of Neurology) between January 2018 andApril 2021 with encephalitis and meningoencephalitis or meningoencephalomyelitis who were only responds by corticosteroid treatment. All of the patients underwent serum and/or CSF testing, and all of them positive for GFPA antibody by cell-based assay (CBA). All of the samples were collected during the early active disease stage, and before corticosteroid treatment. The patients were subjected to detailed clinical examinations, routine cerebrospinal fluid (CSF) examinations, MRI and/or CT analysis. Patient data was retrospectively evaluated through medical record reviews.

2. Cell-based assay

At present, the detection methods of GFAP antibodies includes histological assay, cell-based assay (CBA) and immunohistochemical assay. This product uses the CBA method, as it has high specificity and sensitivity. Cell Based Assay (CBA) is an indirect immunofluorescence assay based on cell transfection. The principle of this assay is to transfect GFAP gene into mammalian cells to express GFAP antigen in mammalian cytoplasm. Green fluorescent protein (GFP) was also expressed in transfection as an internal reference for detection. Then the transfected cells were fixed on 96-well microplates to make antigen plates. The GFAP antibodies in human serum, plasma and cerebrospinal fluid samples were detected semi-quantitatively by indirect immunofluorescence.

The autoantibodies were detected by CBA method. Autoimmune encephalitis autoantibody test kit was used. The brief introduction is as follows: First, dilute the serum to be tested by 1:10, or use the original fluid of cerebrospinal fluid to incubate the cell patch, at room temperature for 60 minutes; Wash the cell patch with detergent for 3 times, 5 minutes each time. Dilute FITC-labeled goat anti-human IgG secondary antibody (1:50) and incubate the cell patch at room temperature for 30 min. The cell patch was cleaned again, sealed, and observed under a fluorescence microscope. The fluorescence signal was significantly higher than the background signal, and the serum located in the cell membrane could be identified as the positive serum of autoantibodies. When the titer of the positive serum is tested, the serum or cerebrospinal fluid is diluted in a gradient, and the operation is carried out according to the above method. The titer value of the positive serum is taken as the highest dilution multiple of the positive signal that can be detected.

3.Testing of other antibodies

We also tested for some common antibodies, the presence of myelin oligodendrocyte glycoprotein (MOG), aquaporin-4 (AQP4)-M1, AQP4-M2, anti-N-methyl-D-aspartate receptor (NMDAR), Yo, was assessed in patients with GFPA antibodies.

Results

1.Antibody test results

Among the 11 patients who underwent serum and/or CSF testing, we found nine cases of autoantibodies against GFAP in CSF and serum samples, and two cases showed autoantibodies against GFAP only in the CSF samples.

Among these 11 participants, two patients with other common antibodies, one patient was positive for MOG antibodies, and the other was positive for NMDAR antibodies.

2. Demographic data and clinical manifestations

There are 5 female patients and 6 male patients (ratio=0.83). The median age at the onset of disease was 52 months (range: 11 months to 128 months). For all patients, we performed a whole-body MR, computed tomography (CT) or ultrasonic for tumor screening. Only three patients were found to have tumors (one ependymoma in the brain; one a yolk sac tumor in the testis; and one is uncertain in the retroperitoneal space). More than half of patients presented with flu-like symptoms.The main symptoms observed included fever (45.4%), headaches (27.3%), dizziness (18.2%), drowsiness (18.2%), mental disorders (18.2%), and so on.

3. Cerebrospinal fluid (CSF) findings

Routine CSF analysis included the total white cell counts (WBC), chlorine levels, glucose levels, protein levels, lactic dehydrogenase levels and the adenosine deaminase activity (ADA) levels. CSF abnormalities were found in 10 patients (90.9%), which we summarized in Table 1. On admission, 10 patients had elevated white blood cell counts (median: 24010^6, range: $26\text{-}55010^6$, normal ranges: $0\text{-}2010^6$), and eight patients had slightly elevated lactic dehydrogenase levels (median: 39 IU/L, range: 33-80 IU/L, normal ranges: 0-30 IU/L). Four patients had elevated protein levels (median: 0.75 g/L, range: 0.63-1.56 g/L. normal ranges: 0-0.5 g/L), and three patients had elevated ADA levels (median: 4.5 U/L, range: 4.4-5.2 U/L, normal ranges: 0-4 U/L). The CSF glucose level was reduced in eight patients (median: 2.46 mmol/L, range:1.83-2.74 mmol/L, normal ranges: 2.8-4.2 mmol/L).

4. MRI findings

10 out 11 patients had brain MRI scans at the initial attack, with nine of them (90.0%) were showing signs of abnormalities after MRI scans. One patient had a brain CT scan, which showed normal results. From the brain MRI, nine patients were showed to have abnormal hyperintensity lesions on T2-weighted and fluid-attenuated inversion recovery (FLAIR) images, which we summarized in Table 1. The range of abnormal hyperintensity MRI lesions in the thalamus (60.0%), basal ganglia (50.0%), periventricular white matter (50.0%), juxtacortical white matter (50.0%), cerebellum (40.0%), pons (30.0%), cortical gray (10.0%) by including. In our case, the brain MRI images of five patients shows abnormal T2-weighted imaging and FLAIR imaging of hyperintensity signals were seen in the bilateral thalamus, basal ganglia,

periventricular white matter and juxtacortical white matter, with symmetrical laminar or line patterns, growing along the vascular space (Virchow-robin space)(Figure 1, Figure 2). Lesions with T2-weighted large, patchy patterns were found, and some lesions also contained cortical, white matter and deep nerve-corpuscles. Cortical abnormalities were found in only one patient. All of the patients received gadolinium-enhancement on the brain, of which eight showed abnormal enhancement, abnormal leptomeninges enhancement was the most common (40.0%) (Figure 1). In this study, we only found two patients who revealed linear perivascular radial gadolinium enhancement in the white matter perpendicular to the ventricle (Figure 2). Other enhancements sometimes appeared to punctuate the basal ganglia and hypothalamus, while most of the lesions showed no enhancement.

Six patients had cervical, thoracic and lumbar spinal cord MRI scans, and while two of these exhibited abnormal imaging, all of them revealed longitudinally extensive spinal cord lesions (LESCLs) (Table 1, Figure 1). The lesions shown in the T2-weighted images patch and punctate patterns in the spinal cord's central canal with slight enhancement found in two patients.

Two of the patients had overlapping syndrome. One of these patients had NMDAR antibodies, and this patient's MRI showed abnormal hyperintension in the bilateral hypothalamus, basal ganglia, periventricular white matter and juxtacortical white matter on T2-weighted imaging and FLAIR imaging with abnormal leptomeninges enhancement. The second patient, who had MOG antibodies, MRI showed unilateral basal ganglia, hypothalamus and temporal lobe with multiple patches T2WIhypersignal with abnormal leptomeninges enhancement and longitudinally extensive spinal cord lesions (Figure 3). There was no abnormal enhancement in brain parenchyma lesions.

Treatment

All of the patients were initially treated with intravenous immunoglobulin (IVIG, 2g/day for five days), Eight patients received methylprednisolone (20mg/kg/d, for three to five days). During the follow-up, subsequent oral prednisone (10-60mg/day) was prescribed for 10 patients. After discharge, one patient was lost to the follow-up.

Discussion

GFAP is an intermediate astrocyte protein, located between the smaller microfilaments and larger microtubules, and is the primary component of intermediate filaments in astrocytes. It has important biological functions, including the maintenance of astrocytes' morphological stability, involvement in the blood-brain barrier formation, and the regulation of synapse function. Autoimmune GFAP astrocytopathy is a recently defined autoimmune disease. Since GFAP antibodies have specific biomarkers [4,11−12], autoimmune GFAP astrocytopathy diagnosis primarily depends on GFAP antibody detection in the serum or SCF. So far, very few pediatric cases have been reported. In this study, we recruited 11 pediatric patients with GFAP antibodies in GSF and/or serum samples (titer ≥ 1:32) and all of them were only responds by corticosteroid treatment. We retrospectively revealed the characteristic clinical features of those pediatric patients.

The peak age of onset among our patients was 52 months, and most of them were preschool children. The youngest patient was 11 months, which was younger than any previous study [10, 15]. As far as we know, 11 months is the youngest age case to have been reported. The female and male ratio is 0.83, which is unlike the ratio found in adult patients. Like the previous studies, most patients have an acute or subacute onset. Clinical manifestations were encephalitis and meningoencephalitis, including fever (45.4%), headaches (27.3%), dizziness (18.2%), drowsiness (18.2%), and mental disorders (18.2%) [3, 9, 10, 13, 14, 15, 16, 17]. In our case, all of the patients who suffered from myelitis were showed longitudinally extensive transverse myelitis, like the previous study. Some clinical manifestations in adults were rarely seen in pediatric patients, such as consciousness disturbance, area postrema syndrome, prolonged gastrointestinal symptoms and so on,[7, 18, 19] were not seen in this study. Flanagan reported that 66% of the tumors were detected within 2 years of onset of symptoms, including ovarian teratoma, adenocarcinoma and glioma, yet we found that only three patients had a tumor, which is much lower than the frequency found in other reports.[4]Therefore, patients should be monitored for underlying neoplasms within 2 years of GFAP disease onset.

CSF analysis from our patients with autoimmune GFAP astocytopathy showed that more than half had characterized inflammatory CSF. The high frequency of elevated CSF WBC count and slightly elevated protein levels and ADA levels is consistent with the literature [13]. This high frequency of elevated CSF WBC count and protein level is not the only marker of this condition, but also occurs in infectious and neoplastic causes of meningoencephalitis. ADA plays an important role in the growth and differentiation of lymphocytes and macrophages, and some research suggest that the high ADA levels might be associated with immunological pathology during the early stage of autoimmune GFAP astrocytopathy[3]. We found that some patients (72.7%) with a transiently mild decline of glucose level, while the lactic dehydrogenase (72.7%) were elevated, which were seldom reported in previous studies and uncommon in immune diseases. Hypoglycorrhachia is normally seen in the patients with tuberculous meningitis (TBM). It caused by release of glycolytic enzyme in the brain and glucose consumption by itself, but the reason for the hypoglycorrhachia in autoimmune GFAP astrocytopathy is unknown. As we know, this is the first time the changes of CSF lactic dehydrogenase in autoimmune GFAP astrocytopathy have been discussed. The lactic dehydrogenase is mainly related to the degree of cell necrosis and the damage of the cell membrane. Elevated lactic dehydrogenase was mainly found in local hypoxic necrosis, bacterial meningitis, cerebral infarction, lymphoma, brain trauma, hydrocephalus and so on. The reasons for the elevation of lactic dehydrogenase of this disease is uncertain, but we suggest that it maybe related to theimpaired brain cells and injured cell membranes found in autoimmune GFAP astrocytopathy.

From the brain MRI results, 90.0% of patients have abnormalities on T2-weighted and FLAIR sequences. Lesions can involve all of the nervous system, including the cortex, subcortical white matter, nerve nuclei of the deep brain (basal ganglia, hypothalamus, cerebellar dentate nuclei), brainstem, cerebellum, meninges, ventricle and callosum. In our case, the most common abnormalities were laminar patterns or line patterns hyperintense in bilateral thalamus, basal ganglia, periventricular white matter and juxtacortical white matter on T2-weighted imaging and FLAIR imaging. Those lesions, especially in the periventricular white matter and juxtacortical white matter, were just like the distribution along the Virchow-Robin space, which were different from the adult abnormalities [2–5, 10, 12]. The Virchow-Robin space is surrounding the walls of vessels as they course from the subarachnoid space through the brain parenchyma, and it does not communicate directly with the subarachnoid space. The Vichow-Robin space can provide the changes for the extraneous antigen into the brain, and the interstitial fluids partly participate in the immunomodulatory effect. Also, it can be one way in which the disease spreads [29]. The autoimmune GFAP astrocytopathy revealed marked inflammatory responses around the perivascular region and small blood vessels [2, 5, 13, 20, 21], emanating from GFAP-enriched peri-lateral ventricular regions, frequently seen in the basal ganglia, hypothalamus, and the white matter (subcortical or/and around the ventricle). We speculated that in our case, the five patients showed bilateral hyperintense in the thalamus, basal ganglia, periventricular white matter and juxtacortical white matter, were related to the accumulation of inflammatory cells, antigens and antibodies in the perivascular space and the Vichow-Robin space. It should be noted that previous studies have proposed that bilateral thalamus abnormal hyperintense signal was the characteristic manifestation of autoimmune GFAP astrocytopathy, [3]and some studies can see similar signal changes in the bilateral basal ganglia, thalamus and white matter [2–5, 10, 12].The characteristic pattern of brain linear perivascular radial gadolinium enhancement in the white matter, perpendicular to the ventricle, were only seen in two patients in our study, which is also consistent in the pattern of inflammation around the small vessels [22]. However, in our cases, it is markedly lower than in adults' patients. Although previous studies have pointed out that brain linear perivascular radial gadolinium enhancement is a characteristic manifestation of the disease, Jonathan Wickel also pointed out that radial perivascular emphasis is not necessarily associated with GFAP antibodies [30].

Four patients showed abnormal enhancement of leptomeninges, which rarely occurs in autoimmune encephalitis. GFAP, an intermediate astrocyte protein between the smaller microfilaments and larger microtubules, is the primary component of intermediate filaments in astrocytes. It has important biological functions, including the maintenance of astrocytes' morphological stability, involvement in blood-brain barrier formation, and the regulation of synapse function. Perhaps that enhancement was caused by gadolinium leaking from the damaged blood-brain barrier, but the reason is unknown. The previously study indicated that the radial enhanced patterns were relative to the gadolinium leakage from compromised vascular walls [2, 23]. This raises some questions: Why are the radial enhancing patterns rare in pediatric patients? Is it that pediatric patients of this disease are seldom injured in the small vascular walls? Previous studies have shown that all of them were normal on DWI, but our findings were different. The reason for this is also uncertain. Myelitis is relative rare compared adult patients [10,24–28]. In our cases, all of two myelitis pediatric patients showed longitudinally extensive myelitic abnormalities, and a slight enhancement.

Conclusion

In conclusion, clinical manifestations were encephalitis and meningoencephalitis and brain MRI imaging reveal hyperintensity lesions in bilateral thalamus, basal ganglia, periventricular white matter and juxtacortical white matter, with symmetrical laminar or line patterns, especially with the abnormal enhancement of leptomeninges, and had inflammatory CSF characterized, the possibility of autoimmune GFAP encephalitis was suggested. Our data suggests that this disease was corticosteroid-responsive only. Therefore, early diagnosis and treatment is very important. CSF and serum GFAP-IgG should be examined in pediatric patients with the above as early as possible.

This study provides some interesting findings and issues that are important for clinical diagnosis. However, we only had 11 pediatric patients with autoimmune GFAP astrocytopathy, which represents a very small sample size, so future studies should be undertaken in a larger population.

Abbreviations

ADA adenosine deaminase activity

CBA cell-based assay

CNS central nervous system

CSF cerebrospinal fluid

CT computed tomography

DWI diffusion-weighted sequences imaging

FLAIR fluid-attenuated inversion recovery

GFAP glial fibrillary acidic protein

LESCLs longitudinally extensive spinal cord lesions

MRI magnetic resonance imaging

TBM Tuberculous meningitis

WBC white cell counts

Declarations

Ethics approval and consent to participate

All experiments were approved the medical ethics committee of the Hunan Children's hospital of Nahua university. This retrospective study was approved by the institutional review board. Informed consent was waived due to the retrospective analysis of anonymized data.

Consent for Publication

Not applicable.

Availability of data and material

All data generated or analysed during this study are included in this published article and its supplementary information files.

Competing interests

The authors declare that they have no competing interests.

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Authors Contributions

Conceptualization: Xiamei Zhuang.

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Formal analysis: Xiaoming Li.

Investigation: Ke Jin.

Resources: Xiamei Zhuang, Junwei Li.

Supervision: Ke Jin, Xiaoming Li.

Validation: Ke Jin.

Writing-original draft: Xiamei Zhuang.

Writing-review & editing: Ke Jin, Xiaoming Li, Junwei Li.

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References

1. Fang B, McKeon A, Hinson SR, et al. Autoimmune glial fibrillary acidic protein astrocymune glial fibrillary acidic protein astrocytopathy: a novel meningoencephalomyelitis. JAMA Neurol.2016:73(11):1297–1307.
2. Long Y, Liang J, Xu H, et al. Autoimmune glial fibrillary acidic protein astrocytopathy in Chinese patients: a retrospective study. Eur J Neurol. 2018;25:477–83.
3. Kimura A, Takekoshi A, Yoshikura N, et al. Clinical characteristics of autoimmune GFAP astrocytopathy. J Neuroimmunol. 2019;15:332:91–98.
4. Flanagan EP, Hinson SR, Lennon VA, et al. Glial fibrillary acidic protein immunoglobulin G as biomarker of autoimmune astrocytopathy: Analysis of 102 patients. Ann Neurol. 2017;81:298–309.
5. Shu Y, Long Y, Chang Y, et al. Brain Immunohistopathology in a Patient with Autoimmune glial fibrillary acidic protein astrocytopathy. Neuroimmunomodulation. 2018;25:1–6.
6. Li X, Peng B, Hou C, et al. A child of autoimmune glial fibrillary acidic protein astrocytopathy who had onset with meningitis. Chin J Pdeiatr. 2019;57:882–4.
7. Oger V, Bost C, Salah L, et al. Mild encephalitis/encephalopathy with reversible splenial lesion syndrome: An unusual presentation of anti-GFAP astrocytopath. Eur J Paediatr Neurol. 2020;26:89–91.
8. Handoko M, Hong W, Espineli E, et al. Autoimmune glial fibrillary acidic protein astrocytopathy following herpes simplex virus encephalitis in a pediatric patient. Pediatr Neurol. 2019;98:85–6.
9. Sauas M, Tzartos J, Kuculali, Ci. Et al. Glial fibrillary acidic protein (GFAP)-antibody in children with focal seizures of undetermined cause. Acta Neurol Belg.2020.4;24: DOI:10.1007/s13760-020-01361-y.
10. Dubey D, Hinson SR, Jolliffe EA, et al. Autoimmune GFAP astrocytopathy: Prospective evaluation of 90 patients in 1 year. J Neuroimmunol. 2018;321:157–63.
11. Zekeridou A, McKeon A, Flanagan EP, et al. A path to understanding autoimmune GFAP astrocytopathy. Ear J Neurol. 2018;25:421–2.
12. Kunchok A, Zekeridou A, McKeon A, et al. Autoimmune glial fibrillary acidic protein astrocytopathy. Curr Opin Neurol. 2019;32:452–8.
13. Shan F, Long Y, Qin W. Autoimmune glial fibrillary acidic protein astrocytopathy: a review of the literature. Front Immunol. 2018;9:2802.
14. Kudo T, Kimura A, Higashida K, et al. Autoimmune glial fibrillary acedic protein astrocytopathy presenting with slowly progressive myelitis and longitudinally extensive spinal cord lesions. Intern Med. 2020;01(21):2777–81. 59(.
15. Huang H, Bai K, Fu Y, et al. Glial fibrillary acidic protein astrocytopathy in pediatric patients: a retrospective study. Front Pediatr. 2020;8;626564.
16. Zhang Y, Bhekharee AK, Zhang X, et al. NMOSD or GFAP astrocytopathy? A case report. Mult Scler Relat Disord. 2020 Aug;43:102202.

17. Ding J, Ren K, Wu J, et al. Overlapping syndrome of MOG-IgG-associated disease and autoimmune GFAP astrocytopathy. J Neurol.2020 Sep;267(9):2589–2593.
18. Wang Q, Ma C. The onset of autoimmune glial fibrillary acidic protein astrocytopathy with prolonged gastrointestinal symptoms: a case report. Acta Neurol Belg.2020,Feb 28; DOI:10.1007/s13760-020-01314-5.
19. Ciron J, Sourdrille F, Biotti D, et al. Area postrema syndrome: another feature of anti-GFAP encephalomyelitis. Mult Scler,2020,26(2):253–255.
20. Li J, Xu Y, Ren H. et la. Autoimmune GFAP astrocytopathy after viral encephalitis: a case report. Mult Scler Relat Disord. 2018;21:84–7.
21. Yuan Z, Li H, Huang L, et al. CS8 + T cell predominance in autoimmune glial fibrillary acidic protein astrocytopathy. Ear J Neurol.2021,DOI:10.1111/ene.14778.
22. Kong Y, McKeon A, Koh OS, et al. Teaching neuroImages: linear radial periventricular enhancement in glial fibrillary acidic protein astrocytopathy. Neurology. 2021 Jan 06; DOI:10.1212/WNL.0000000000011496.
23. Saraste M, Bezukladova S, Matilainen M, et al. Increased serum glial fibrillary acidic protein associates with microstructural white matter damage in multiple sclerosis: GFAP and DTI. Mult Scler Relat Disord. 2021,Feb 01;50:102810.
24. Zarkali A, Cousins O, Athauda D, et al. Glial fibrillary acidic protein antibody-positive meningoencephalomyelitis. Pract Neurol. 2018;18:315–9.
25. Wang H, Chin JH, Fang BY, et al. Autoimmune glial fibrillary acidic protein astrocytopathy manifesting as subacute meningoencephalitis with descending myelitis: a case report. BMC Neurol. 2020 Dec 10; 20(1):443.
26. Kudo T, Kimura A, Higashida K, et al. Autoimmune glial fibrillary acidic protein astrocytopathy presenting with slowly progressive myelitis and longitudinally extensive spinal cord lesions. Intern Med.2020 Nov 01; 59(21):2777–2781.
27. Li XL, Han J, Zhao HT, et al. Autoimmune glial fibrillary acidic protein astrocytopathy with lesions distributed predominantly in the entire spinal cord. Ther Adv Neurol Disord. 2020;13:1756286420909973.
28. Oger V, Boast C, Salah L, et al. Mild encephalitis/encephalopathy with reversible splenial lesion syndrome: an unusual presentaltion of anti-GFAP astrocytopathy. Ear J Paediatr Neurol.2020 May; 26:89–91.
29. Kwee RM, Kwee TC. Virchow-Robin spaces at MR imaging. Radiographics. 2007;27(4):1071–86.
30. Wichel J, Chung HY, Kirchhof K, et al. Encephalitis with radial perivascular emphasis: Not necessarily associated with GFAP antibodies. Neurol.

Tables

Table 1. Data of 11 pediatric patients with autoimmune GFAP astrocytopathy

No.	Gender	Age (month)	Symptoms	Another antibody	CSF abnormality	Main MRI features
1	f	42	fever	Negative	WBC: 34110^{6}/L glucose: 2.7 mmol/L ADA: 4.48 U/L	Brain: Bilateral juxtacortical WM, cerebellum Meningeal abnormality Sc: normality
2	m	84	dizzy emesis	NMDAR	WBC:5010^{6}/L glucose: 2.54 mmol/L lactic dehydrogenase: 33.00IU/L ADA: 4.40 U/L	Brain: Bilateral basal ganglia, thalamus, periventricular WM and callosal Meningeal abnormality Sc: NA
3	f	11	mental disorder	Negative	WBC: 12010^{6}/L	Brain: normality Sc: NA
4	m	67	headache fever	Negative	WBC: 3010^{6}/L lactic dehydrogenase: 71.00IU/L ADA:4.5U/L	Brain: NA Sc: NA
5	f	89	drowsiness dizzy	Negative	WBC: 24010^{6}/L glucose: 2.41 mmol/L lactic dehydrogenase: 80.00IU/L protein: 1.56 g/L	Brain: Bilateral basal ganglia, thalamus, juxtacortical WM and cerebellum Meningeal abnormality Sc: T1-L1
6	f	52	fever cough	Negative	WBC: 5510^{6}/L glucose: 2.46 mmol/L lactic dehydrogenase: 39.00IU/L protein: 0.88 g/L	Brain: Bilateral basal ganglia, thalamus, periventricular WM and pons Sc: normality
7	m	128	headache emesis	Negative	WBC: 55010^{6}/L glucose: 2.54 mmol/L lactic dehydrogenase: 35.00IU/L ADA: 5.20 U/L	Brain: pons Sc: NA
8	m	14	mental disorder	Negative	normality	Brain: Bilateral periventricular WM Sc: NA
9	f	68	drowsiness headache	MOG	WBC: 2610^{6}/L glucose: 2.42 mmol/L	Brain: Unilateral thalamus, cortical gray, juxtacortical WM, deep gray matter and cerebellum Meningeal abnormality Sc: C2-C7, T8-T12
10	m	45	fever	Negative	WBC: 40010^{6}/L glucose: 2.74 mmol/L lactic dehydrogenase: 36.00IU/L protein: 0.63 g/L	Brain: Bilateral thalamus, basal ganglia, juxtacortical WM, periventricular WM, cerebellum T1-weighted “radial enhancing” Meningeal abnormality Sc: normality
11	m	24	fever	Negative	WBC: 5510^{6}/L glucose: 1.83 mmol/L lactic dehydrogenase: 73.00IU/L	Brain: Bilateral basal ganglia, thalamus, juxtacortical WM, periventricular WM, callosal and pons T1-weighted “radial enhancing” Meningeal abnormality Sc: normality

ADA: adenosine deaminase activity, CSF: cerebrospinal fluid, F: female; GFAP: glial fibrillary acidic protein, M: male, MOG: myelin oligodendrocyte glycoprotein; MRI: magnetic resonance imaging ; NA: no application; NMDAR: N-methyl-D-aspartate receptor; Sc: spinal cord, WM: white matter; WBC: white blood cell.

Figures

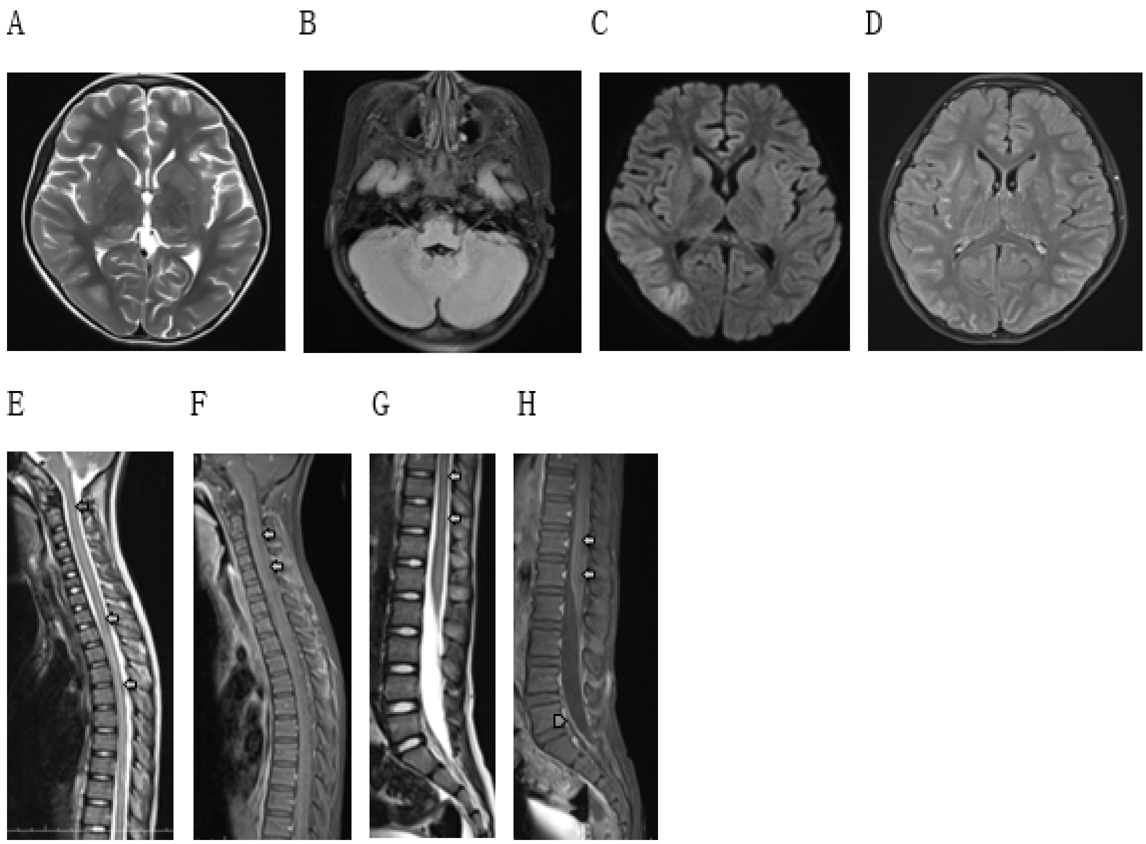

Figure 1

Imaging findings in pediatric patients with autoimmune GFAP astrocytopathy. Magnetic resonance imaging (MRI) showing abnormal hyperintensity lesions on T2-weighted and fluid-attenuated inversion recovery (FLAIR) images in basal ganglia, hypothalamus (A) and cerebellum (B). Diffusion-weighted sequences imaging (DWI) showed abnormal hyperintensity lesions in the callosum and cortical (C). Gadolinium-enhanced brain MRI (T2-FLAIR) showed enhancement leptomeninges (D). Spinal cord MRI showed longitudinally extensive spinal cord lesions (LESCLs)(arrows) (E, G) and slight enhancement(arrows), pia enhancement (arrowhead) (F,H).

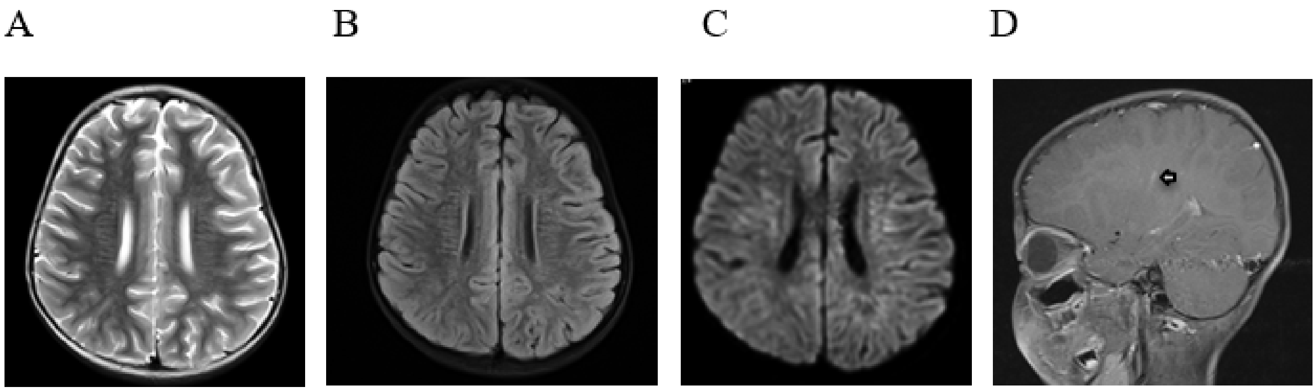

Figure 2

Brain MRI of pediatric patients with autoimmune GFAP astrocytopathy. The abnormal hyperintensity lesions on T2-weighted and FLAIR images were observed in subcortical/around the ventricle white matter (A, B), DWI showed hyperintensity lesions (D). Gadolinium-enhanced brain MRI (T2-FLAIR) showed a linear perivascular radial enhancement pattern (arrow) (D).

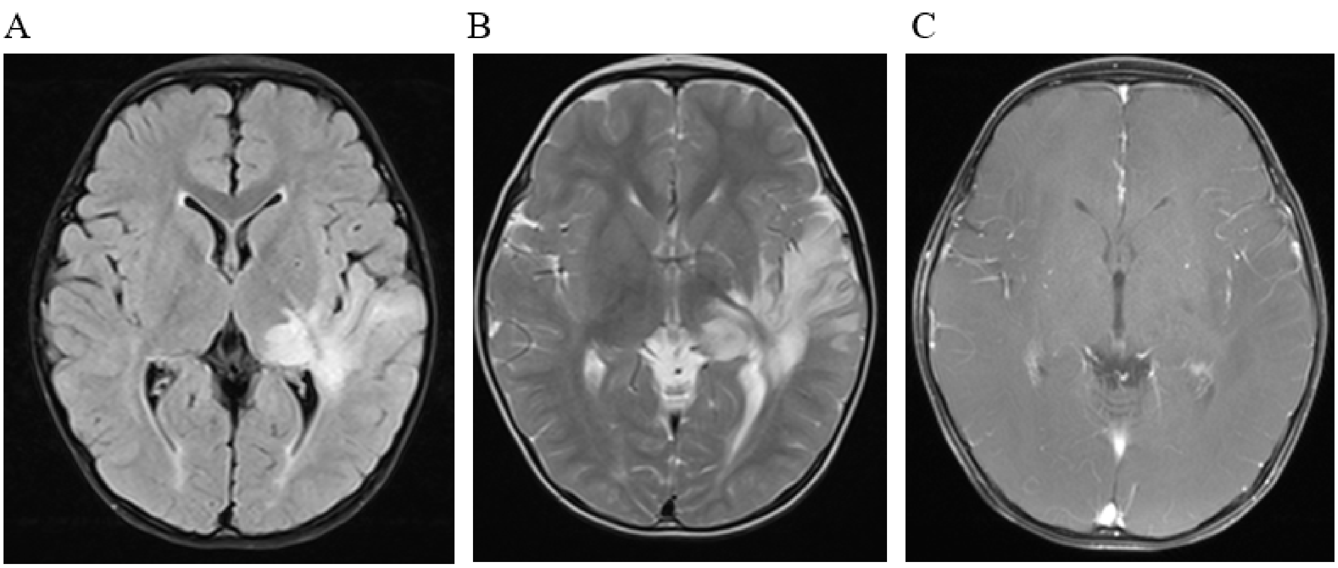

Figure 3

Imaging findings of pediatric patients with autoimmune GFAP astrocytopathy and with positive MOG antibodies. The abnormal hyperintensity lesions on T2-weighted (A) and FLAIR images (B) were observed in unilateral basal ganglia, hypothalamus and temporal lobe and without abnormal enhancement