



## OPEN ACCESS

## EDITED BY

Yi-Chia Wei,  
Chang Gung Memorial Hospital, Taiwan

## REVIEWED BY

Ruzica Kravljanac,  
The Institute for Health Protection of Mother  
and Child Serbia, Serbia  
Martha Feucht,  
Medical University of Vienna, Austria

## \*CORRESPONDENCE

Feng Gao

✉ epilepsy@zju.edu.cn

Liu Liu

✉ osier0615xw@zju.edu.cn

<sup>†</sup>These authors have contributed equally to this work.

## SPECIALTY SECTION

This article was submitted to Pediatric Neurology, a section of the journal Frontiers in Pediatrics

RECEIVED 21 November 2022

ACCEPTED 15 February 2023

PUBLISHED 03 March 2023



## CITATION

Wang Y, Ren X, Shen Y, Hua Y, Xu L, Zhang W-r, Sheng G, Jiang P, Yuan Z, Liu L and Gao F (2023) Case report: Pediatric anti-gamma aminobutyric acid-B receptor encephalitis with benign prognosis.  
Front. Pediatr. 11:1104001.  
doi: 10.3389/fped.2023.1104001

## COPYRIGHT

© 2023 Wang, Ren, Shen, Hua, Xu, Zhang, Sheng, Jiang, Yuan, Liu and Gao. This is an open-access article distributed under the terms of the [Creative Commons Attribution License \(CC BY\)](https://creativecommons.org/licenses/by/4.0/). The use, distribution or reproduction in other forums is permitted, provided the original author(s) and the copyright owner(s) are credited and that the original publication in this journal is cited, in accordance with accepted academic practice. No use, distribution or reproduction is permitted which does not comply with these terms.

# Case report: Pediatric anti-gamma aminobutyric acid-B receptor encephalitis with benign prognosis

Yeping Wang<sup>1,2</sup>, Xiaoyan Ren<sup>1,3</sup>, Yu Shen<sup>1,3</sup>, Yi Hua<sup>1</sup>, Lu Xu<sup>1</sup>, Weiran Zhang<sup>1</sup>, Guoxia Sheng<sup>1</sup>, Peifang Jiang<sup>1</sup>, Zhefeng Yuan<sup>1</sup>, Liu Liu<sup>1\*†</sup>  and Feng Gao<sup>1\*†</sup> 

<sup>1</sup>Department of Neurology, Children's Hospital, Zhejiang University School of Medicine, National Clinical Research Center for Child Health, Hangzhou, China, <sup>2</sup>Department of Pediatric, Jinhua Maternity and Child Health Care Hospital, Jinhua, China, <sup>3</sup>Department of Neurology, Ningbo Women and Children's Hospital, Ningbo, China

**Objective:** To explore the clinical characteristics of pediatric anti-gamma-aminobutyric acid-B receptor (GABA<sub>B</sub>R) encephalitis to enhance the understanding and improve the diagnostic and therapeutic strategies for this disease.

**Methods:** We report a rare case of a female pediatric patient with anti-GABA<sub>B</sub>R encephalitis who was treated at the Children's Hospital of Zhejiang University School of Medicine. Literature search was performed to explore the clinical characteristics of pediatric anti-GABA<sub>B</sub>R encephalitis.

**Results:** The patient exhibited recurrent epileptic seizure, status epilepticus, and psychiatric symptoms at the age of 11 years and 10 months. Anti-GABA<sub>B</sub>R antibodies were positive in cerebrospinal fluid and serum. Brain magnetic resonance imaging (MRI) exhibited abnormal signals in the left hippocampus. Symptoms and abnormality of brain MRI were improved after administration of immunosuppressants, anti-seizure and antipsychotic drugs. Two of pediatric anti-GABA<sub>B</sub>R encephalitis with clinical data were identified through literature search. Analysis of these three cases suggested that the pediatric patients primarily experienced limbic encephalitis, with no tumor incidence. A favorable immunotherapy response was demonstrated with a superior prognosis in all the cases.

**Conclusions:** We reported a pediatric anti-GABA<sub>B</sub>R encephalitis case with early age of onset. Prompt autoimmune antibody testing and tumor screening, as well as immunomodulatory treatment immediately after a definitive diagnosis are warranted to improve prognosis.

## KEYWORDS

anti-GABA<sub>B</sub>R encephalitis, autoimmune encephalitis, pediatric, benign prognosis, immunotherapy

## Introduction

Autoimmune encephalitis (AE) broadly refers to a type of encephalitis that is mediated by autoimmune mechanisms, particularly by antineuronal antibodies such as those against neuronal cell surface receptors or synaptic proteins, and intracellular targets (1, 2). With the advancement of experimental antibody detection techniques and expansion of the neuronal antibody spectrum, an increasing number of antibody-related AE cases have been diagnosed in recent years.

GABA is a vital inhibitory neurotransmitter in the central nervous system that plays a critical role in controlling neuronal excitability by binding to specific receptors. GABA<sub>A</sub>, GABA<sub>B</sub>, and GABA<sub>C</sub> receptors are the three classes of GABA receptors. Among these receptors, GABA<sub>A</sub>R and GABA<sub>C</sub>R are ligand-gated chloride channels, whereas GABA<sub>B</sub>R is a G-protein coupled receptor. However, GABA<sub>B</sub>R plays an essential role in neurotransmission and maintenance of synaptic stability (3). It is widely distributed in the brain and spinal cord, with the highest concentrations in the hippocampus, thalamus, and cerebellum. Therefore, it is closely associated with learning, memory, and cognitive functions (4).

Anti-gamma-aminobutyric acid-B receptor (GABA<sub>B</sub>R) encephalitis is a relatively rare type of AE. Additionally, most anti-GABA<sub>B</sub>R encephalitis cases have been reported in adults, and the disease has been rarely observed in children. Here we elaborate on the clinical manifestations of a case of pediatric anti-GABA<sub>B</sub>R encephalitis and analyze the clinical characteristics of the disease through literature review.

## Case presentation

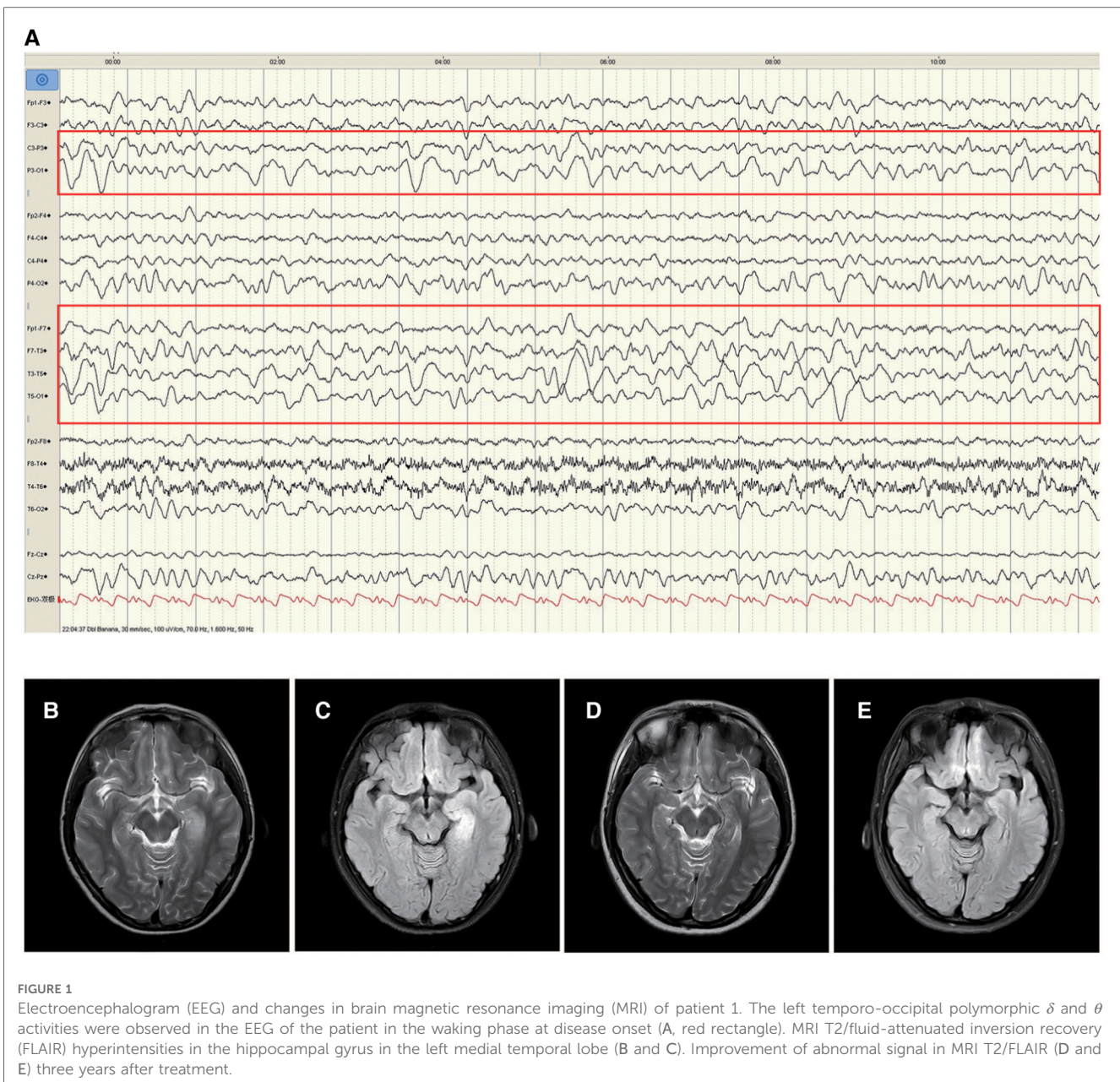
Patient 1 was a 16-year-old girl, who experienced 2–3 episodes of seizure per day in sleep, with the onset age of 11 years and 10 months. The seizure was manifested as secondarily generalised tonic–clonic seizures that lasted 2–3 min before self-resolution. The patient experienced one episode of status epilepticus (SE) lasting 2 h. No abnormalities were observed in the medical, personal, or family history and upon physical examination. CSF test exhibited a white blood cell count of  $30 \times 10^6/L$ , comprising mainly monocytes (90%). No abnormalities were observed in CSF biochemistry, smear, and culture. Enteroviruses (hepatitis E virus, enterovirus type 71, coxsackievirus A16), Epstein–Barr virus, herpes simplex virus, and oligoclonal bands were negative in blood and CSF. Blood biochemistry, genetic metabolic profile, tumor markers, antinuclear antibodies, and erythrocyte sedimentation rate were normal. Video-electroencephalography (VEEG) indicated slowing of the basic rhythm in background activity during waking periods. Persistent polymorphic  $\delta$  and  $\theta$  rhythms were observed in the left temporo-occipital region during wakefulness and sleep (Figure 1A). The B-scan ultrasonography of the thyroid, liver, gallbladder, kidneys, retroperitoneum, and uterus; chest computed tomography (CT); electrocardiogram; and head magnetic resonance imaging (MRI) were normal. The patient experienced recurrent seizure incidence despite being symptomatically treated with acyclovir, mannitol, and levetiracetam (12.5 mg/kg-d). On day 23 after disease onset, brain MRI exhibited hyperintensities on T2 weighted image (T2WI) and fluid-attenuated inversion recovery (FLAIR) in the left medial temporal hippocampus (Figures 1B,C). Anti-GABA<sub>B</sub>R antibodies were positive in both CSF (1:3.2) and serum (1:32). However, antibodies against NMDAR, AMPAR, GABA<sub>A</sub>R, LGI1, and CASPR2 and paraneoplastic antibodies were not observed in the CSF or serum. The patient was then administered levetiracetam (25 mg/kg-d) combined with carbamazepine (10 mg/kg-d) to control

epileptic seizures, followed by administration of methylprednisolone (10 mg/kg  $\times$  3d). Although the epileptic events reduced, symptoms such as disorganised speech, easily frightening, agitation, and auditory hallucinations appeared. Further treatment with methylprednisolone (18.75 mg/kg  $\times$  3d) combined with intravenous immunoglobulin (IVIG; 20 g  $\times$  3d) and sertraline (50 mg qn) was administered. The patient scored 3 on the mRS when the symptoms were most severe. Following treatment, the epileptic seizures ceased one month after onset, psychiatric symptoms disappeared, and the mRS score was 0. Re-examination of brain MRI indicated a slight improvement in abnormal hippocampal signals, which were significantly improved three years after disease onset (Figures 1D,E).

## Literature review

A literature search was conducted with the keywords ‘GABA<sub>B</sub>R’ and ‘encephalitis’ in databases such as PubMed and CNKI until December 2022. Only the articles written in English or Chinese were included. Anti-GABA<sub>B</sub>R encephalitis cases of pediatric patients (aged less than 18 years) with complete or partial clinical data were identified, and the clinical characteristics of all these pediatric patients were summarized. And the patients with only anti-GABA<sub>B</sub>R-positive and not secondary to any infections were included in analysis.

The database search yielded seven pediatric anti-GABA<sub>B</sub>R encephalitis cases (5–10). In 2014, Kruer et al. (8) reported a case of anti-GABA<sub>B</sub>R encephalitis in a 3-year-old male patient. The patient exhibited severe clinical phenotypes and rapid progression manifesting as confusion, lethargy, opsoclonus, dystonic tongue movements, ataxia, and chorea at onset, followed by complex partial seizures and SE during later phases. Laboratory tests indicated positive anti-GABA<sub>B</sub>R antibodies in serum and CSF (1:32 and 1:3.2, respectively). A white blood cell count of  $154/\mu l$  and a protein level of 59 mg/dl were observed in the initial CSF analysis. EEG exhibited generalised slow waves and epileptiform discharge. Brain MRI exhibited multifocal T2/FLAIR hyperintensities in the brainstem and cerebellum with involvement of the basal ganglia and hippocampus. Seizures were difficult to control even after treatment with various antiseizure medications (ASMs), intravenous immunoglobulin (IVIG), and methylprednisolone. The patient died of sepsis four weeks later. The case of the same patient was reported by Petit-Pedrol et al. (11) in 2014; the patient tested positive for anti-GABA<sub>A</sub>R antibodies in CSF (1:320) and serum (+, titer was not reported) in addition to anti-GABA<sub>B</sub>R antibodies. However, the clinical features of this patient were highly consistent with anti-GABA<sub>A</sub>R encephalitis. Additionally, Liu et al. (9) reported a case of an 11-year-old male patient who experienced AE 24 days after having Japanese encephalitis, and the main clinical manifestations were fever, headache, irritability, and aggressive behaviour. Anti-GABA<sub>B</sub>R antibodies were positive in CSF and negative in serum. EEG and brain MRI findings were unknown. The patient displayed some mood problems even after immunotherapy. Neither of these two patients were recruited for analysis and



discussion in consideration since they did not meet the inclusion criteria. Another cohort study described a case of pediatric anti-GABA<sub>B</sub>R encephalitis in a 16-year-old patient, although no clinical data of the patient were reported (7). Kang et al. reported 103 antibody-positive AE patients, which including two patients with anti-GABA<sub>B</sub>R antibodies (10). These two patients were presented with epilepsy and behavioral symptoms. Abnormalities in EEG and brain MRI were also found. Regrettably, one of these two patients was positive for both anti-CASPR2 and anti-GABA<sub>B</sub>R antibodies, while the detailed clinical information of these two cases was difficult to distinguish from the paper. Therefore, these cases were also excluded from the analysis.

Jeffery et al. (6) and Höftberger et al. (5) each reported a case of a patient aged  $\leq 18$  years having anti-GABA<sub>B</sub>R encephalitis in their cohort studies, with partial descriptions of clinical data. These two

patients were labelled Patient 2 and Patient 3, respectively. Both patients were aged 16 years at disease onset. Patient 2 presented with seizures, delirium, and psychosis, with a serum anti-GABA<sub>B</sub>R antibody titer of 1:1920; the symptoms were completely resolved after treatment with steroids and plasma exchange (PLEX). Patient 3 presented with typical limbic encephalitis (LE) (details unknown), with a positive anti-GABA<sub>B</sub>R antibody in serum; the symptoms were completely resolved after treatment with steroids, IVIG, and PLEX. Tumor was not observed in these two patients. The clinical characteristics of the three analyzed pediatric cases with anti-GABA<sub>B</sub>R encephalitis are summarized in **Table 1**. The mean age of disease onset was 14.6 years (11 years 10 months–16 years). All the three patients exhibited typical clinical symptoms of LE, tested negative in tumor screening, and displayed a good prognosis after immunotherapy.

TABLE 1 Clinical characteristics of three idiopathic pediatric patients with anti-GABA<sub>B</sub>R encephalitis.

	Sex	Onset Age	Clinical manifestation	CSF examination	Brain MRI	EEG	Anti-GABA <sub>B</sub> R	Treatment	Tumor	Outcome	Follow-up	Reference
1	F	11y10m	Seizure, SE, psychiatric symptoms	WBC 30 × 10 <sup>6</sup> /L	T2/FLAIR: abnormal signals in the left hippocampus	Slowing of the basic rhythm in background activity during waking periods; persistent polymorphic δ and θ rhythms were observed in the left temporo-occipital region during wakefulness and sleep	Serum (1:32) CSF (1:3.2)	Steroids + IVIG + LEV, CBZ + Sertraline	N	Complete resolution	51 m	Present report
2	F	16y	Seizure, delirium, psychiatric symptoms	NA	NA	NA	Serum (1:1920) CSF (NA)	Steroids + PLEX	N	Complete resolution	14 m	Jeffery et al, 2013
3	F	16y	LE (no detail)	NA	NA	NA	Serum (+, NA) CSF (NA)	Steroids + IVIG + PLEX	N	Complete resolution	18 m	Höftberger et al, 2013

CBZ, carbamazepine; CSF, cerebrospinal fluid; EEG, electroencephalogram; F, female; FLAIR, fluid-attenuated inversion recovery; IVIG, intravenous immunoglobulin; LE, limbic encephalitis; LEV, levetiracetam; MRI, magnetic resonance imaging; N, No; NA, not available; PLEX, plasma exchange; SE, status epilepticus.

## Discussion

This case study reports a pediatric anti-GABA<sub>B</sub>R encephalitis case with the earliest onset age to date. The patient exhibited severe epileptic seizure, SE, psychiatric problems, behavioral abnormalities, elevated CSF cell counts, left hippocampal hyperintensities (as indicated on the T2WI and FLAIR MRI), and positive anti-GABA<sub>B</sub>R in serum and CSF. Immunotherapy was found to be an effective strategy. In addition, only seven pediatric anti-GABA<sub>B</sub>R encephalitis cases were identified through literature search, of which two cases with only anti-GABA<sub>B</sub>R-positive and not secondary to any infections, and their clinical characteristics were analyzed.

Fifteen cases of adult anti-GABA<sub>B</sub>R encephalitis were first reported by Lancaster et al. in 2010 (12). This disease is a GABA<sub>B</sub>R antibody-mediated AE that often involves the limbic system and exhibits the median onset age of 50–65 years on adults (Table 2, Supplementary data S1). The disease exhibits a male predisposition (60%–82%) in adults (13), with seizures as the first symptom followed by incidences of confusion and memory deficits, abnormal behavior, hallucinations, language disorder, sleep disorder, and cerebellar ataxia in a few cases (14–16). Epileptic seizures in patients with anti-GABA<sub>B</sub>R encephalitis are predominantly present as generalized tonic-clonic seizure (17–19). SE is common and displays a high propensity of progressing into refractory epilepsy when multiple ASMs are ineffective. The three pediatric cases summarized in

this study presented with LE with epileptic seizures. SE occurred only in Patient 1, although its incidence in other two patients reported in literature is unknown due to lack of information. These clinical characteristics are similar to those reported in studies on adult anti-GABA<sub>B</sub>R encephalitis (Table 2).

Slow-wave activity was observed in the EEG of Patient 1 in this study with no information on the other two included cases. EEG abnormalities comprising predominantly slow waves, followed by epileptiform discharge (18–21) were detected in more than 80% of adult anti-GABA<sub>B</sub>R encephalitis cases (22, 23). Si et al. indicated that the distribution range of the slow-wave activity reflects the severity of anti-GABA<sub>B</sub>R encephalitis (24). In addition, changes in brain imaging can also facilitate the diagnosis and treatment of anti-GABA<sub>B</sub>R encephalitis. Signal anomalies in the unilateral or bilateral medial temporal lobe were observed in T2/FLAIR-weighted images of approximately 45% of patients with anti-GABA<sub>B</sub>R encephalitis (2), and some patients developed hippocampal sclerosis with disease progression (25). Furthermore, limbic system involvement was associated with a poor prognosis (26). In Patient 1 in this study, abnormalities were seen in T2/FLAIR-weighted images in the left hippocampus in early phase of the disease and were significantly reduced after treatment. Although the specificity of imaging manifestations is limited in the acute phase of anti-GABA<sub>B</sub>R encephalitis, long-term brain MRI follow-up can help clinicians in understanding the underlying pathological and physiological processes, thereby providing a theoretical basis for diagnosis and treatment.

TABLE 2 Differences between adults and pediatric patients with anti-GABA<sub>B</sub>R encephalitis.

	Sex	Median onset Age (y)	No. of cases	Manifestation	Cognitive /psychiatric symptoms	Refractory epilepsy	SE	EEG abnormalities	Brain MRI abnormalities	Tumor	Prognosis
Adults	M	50–65	501	LE	Y	Y	Y	Y	Y	50%–60%	Mostly good
Children	F	Juvenile	3	LE	Y	N	NA	NA	Y	Low	Good

EEG, electroencephalogram; F, female; LE, limbic encephalitis; M, male; MRI, magnetic resonance imaging; N, No; NA, not available; SE, status epilepticus.

Research suggests that other neuronal antibodies, including those against VGCC, AMPAR, and GABA<sub>A</sub>R and classic paraneoplastic antibodies (Hu, Ri, amphiphysin, SOX-1), could be detected in approximately 7%–40% of patients with GABA<sub>B</sub>R encephalitis (5, 19, 25), leading to variation and overlap of clinical syndromes. Although the Patient 1 was tested to rule out antibodies against NMDAR, AMPAR, GABA<sub>A</sub>R, LGI1, and CASPR2, a comprehensive screening against the entire set of known AE antigens was not performed, which is one of the limitations of this study. In the other aspect, tumor incidence was identified in the anti-GABA<sub>B</sub>R encephalitis population, as most of the patients were middle-aged or elderly people. Studies have revealed that 50%–60% of patients with anti-GABA<sub>B</sub>R encephalitis develop tumor. Small cell lung carcinoma has been the mostly commonly observed tumor, followed by thymic carcinoma, bladder cancer, and breast cancer (5, 27, 28). Furthermore, tumor progression is the most common cause of death in anti-GABA<sub>B</sub>R encephalitis (21). However, this type of AE is highly responsive to immunotherapy. No tumor was found in the three cases of pediatric anti-GABA<sub>B</sub>R encephalitis summarized in this study. Nevertheless, considering the correlation between the disease and tumor, susceptibility to tumor in pediatric patients with anti-GABA<sub>B</sub>R encephalitis cannot be ruled out. Tumor was identified after encephalitis in the majority of previous cohort studies. Therefore, long-term follow-up is needed for pediatric patients with anti-GABA<sub>B</sub>R encephalitis, despite negative results observed in the initial tumor screening. Graus et al. updated the diagnostic criteria for PNS, which recommend repeated tumor screening every 4–6 months for 2 years for patients with high-risk phenotypes (e.g., encephalomyelitis, LE, opsoclonus-myoclonus) and high-risk antibodies (e.g., Hu, CV2, SOX1, Yo), if no tumor is found in the initial examination (29).

Treatment for AEs mainly includes immunomodulation therapy, treatment of primary tumor, and symptomatic treatment. Encephalitis associated with antibodies against cell-surface proteins are mediated primarily by humoral immunity which is respond good to immunosuppression. Furthermore, if a tumor is identified, early tumor treatment is particularly crucial for a good outcome. Studies have suggested that most patients with anti-GABA<sub>B</sub>R encephalitis demonstrate complete or partial recovery of neurological functions after receiving immunotherapy (5, 15, 16, 30, 31). Moreover, immunotherapy delay is an independent predictor for epilepsy (32). Therefore, immunotherapy should be administered promptly after definitive diagnosis. Currently, the recommended first-line immunotherapies include treatment with steroid, IVIG, and PLEX, whereas second-line immunosuppressants such as rituximab and cyclophosphamide are generally used to treat refractory cases. All the three pediatric patients reported in this study received immunotherapy, did not develop tumor, and had a good outcome.

Given the low incidence of anti-GABA<sub>B</sub>R encephalitis and the rarer incidence of the disease in pediatric patients, there were three pediatric cases with only anti-GABA<sub>B</sub>R encephalitis could be analysed until now. Among of these cases, we reported a case with an early onset age of 11 years and 10 months. The phenotype of pediatric anti-GABA<sub>B</sub>R encephalitis is similar to that in adults, in whom the disease presents primarily as LE;

however, tumors are rare in pediatric cases. With timely immunotherapy administration, the prognosis of pediatric patients may become superior to that of adult patients.

## Data availability statement

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding author/s.

## Ethics statement

The studies involving human participants were reviewed and approved by Ethics Committee of the Children's Hospital of Zhejiang University School of Medicine. Written informed consent to participate in this study was provided by the participants' legal guardian/next of kin. Written informed consent was obtained from the individual(s), and minor(s)' legal guardian/next of kin for the publication of any potentially identifiable images or data included in this article.

## Author contributions

YW: designed and conceptualized the study, interpreted and analyzed the data, and drafted and revised the manuscript for intellectual content. XR, YS, and YH: played a major role in the acquisition of data and revised the manuscript for intellectual content. LY, WZ, and GS: revised the manuscript for intellectual content. LL and FG: designed and conceptualized the study, interpreted, and analyzed the data, and revised the manuscript for intellectual content. All authors contributed to the article and approved the submitted version.

## Funding

Key Research and Development Programme of Zhejiang Province (Grant No. 2020C03038), National Natural Science Foundation of China (Grant No. 82001232), Zhejiang Provincial Natural Science Foundation of China (Grant No. LQ19H090002); Key social development projects of Jinhua science and technology plan project, Grant NO. 2022-3-128; Research and cultivation fund project of Jinhua Maternity and Child Health Care Hospital, Grant NO. HFB2021-2-03.

## Acknowledgment

The authors are deeply grateful to the family who participated in this research. This work was supported by the Key Research and Development Programme of Zhejiang Province (Grant No. 2020C03038), National Natural Science Foundation of China (Grant No. 82001232), and Zhejiang Provincial Natural Science Foundation of China (Grant No. LQ19H090002).

## Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Publisher's note

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated

organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article, or claim that may be made by its manufacturer, is not guaranteed or endorsed by the publisher.

## Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fped.2023.1104001/full#supplementary-material>.

## References

- Lancaster E, Dalmau J. Neuronal autoantigens–pathogenesis, associated disorders and antibody testing. *Nat Rev Neurol*. (2012) 8(7):380–90. doi: 10.1038/nrneuro.2012.99
- Dalmau J, Graus F. Antibody-Mediated encephalitis. *N Engl J Med*. (2018) 378(9):840–51. doi: 10.1056/NEJMra1708712
- Ulrich D, Bettler B. GABA(B) receptors: synaptic functions and mechanisms of diversity. *Curr Opin Neurobiol*. (2007) 17(3):298–303. doi: 10.1016/j.conb.2007.04.001
- Benarroch EE. GABAB Receptors: structure, functions, and clinical implications. *Neurology*. (2012) 78(8):578–84. doi: 10.1212/WNL.0b013e318247cd03
- Hoftberger R, Titulaer MJ, Sabater L, Dome B, Rozsas A, Hegedus B, et al. Encephalitis and GABAB receptor antibodies: novel findings in a new case series of 20 patients. *Neurology*. (2013) 81(17):1500–6. doi: 10.1212/WNL.0b013e3182a9585f
- Jeffery OJ, Lennon VA, Pittock SJ, Gregory JK, Britton JW, McKeon A. GABAB Receptor autoantibody frequency in service serologic evaluation. *Neurology*. (2013) 81(10):882–7. doi: 10.1212/WNL.0b013e3182a35271
- Hayden Z, Borocz K, Csizmadia Z, Balogh P, Kellermayer Z, Bodo K, et al. Single-center study of autoimmune encephalitis-related autoantibody testing in Hungary. *Brain Behav*. (2019) 9(12):e01454. doi: 10.1002/brb3.1454
- Kruer MC, Hoftberger R, Lim KY, Coryell JC, Svoboda MD, Woltjer RL, et al. Aggressive course in encephalitis with opsoclonus, ataxia, chorea, and seizures: the first pediatric case of gamma-aminobutyric acid type B receptor autoimmunity. *JAMA Neurol*. (2014) 71(5):620–3. doi: 10.1001/jamaneuro.2013.4786
- Liu B, Liu J, Sun H, Xie M, Yang C, Pan Y, et al. Autoimmune encephalitis after Japanese encephalitis in children: a prospective study. *J Neurol Sci*. (2021) 424:117394. doi: 10.1016/j.jns.2021.117394
- Kang Q, Liao H, Yang L, Fang H, Hu W, Wu L. Clinical characteristics and short-term prognosis of children with antibody-mediated autoimmune encephalitis: a single-center cohort study. *Front Pediatr*. (2022) 10:880693. doi: 10.3389/fped.2022.880693
- Petit-Pedrol M, Armangue T, Peng X, Bataller L, Cellucci T, Davis R, et al. Encephalitis with refractory seizures, status epilepticus, and antibodies to the GABAA receptor: a case series, characterisation of the antigen, and analysis of the effects of antibodies. *Lancet Neurol*. (2014) 13(3):276–86. doi: 10.1016/S1474-4422(13)70299-0
- Lancaster E, Lai M, Peng X, Hughes E, Constantinescu R, Raizer J, et al. Antibodies to the GABA(B) receptor in limbic encephalitis with seizures: case series and characterisation of the antigen. *Lancet Neurol*. (2010) 9(1):67–76. doi: 10.1016/S1474-4422(09)70324-2
- Marinas JE, Matveychuk D, Dursun SM, Baker GB. Neuroimmunological antibody-mediated encephalitis and implications for diagnosis and therapy in neuropsychiatry. *Acta Neuropsychiatr*. (2020) 32(4):177–85. doi: 10.1017/neu.2019.50
- McKay JH, Dimberg EL, Lopez Chiriboga AS. A systematic review of gamma-aminobutyric acid receptor type B autoimmunity. *Neurol Neurochir Pol*. (2019) 53(1):1–7. doi: 10.5603/PJNNS.a2018.0005
- Wang Y, Yu Y, Hu Y, Li Y, Song F, Wang Y. Clinical and electroencephalographic features of the seizures in neuronal surface antibody-associated autoimmune encephalitis. *Front Neurol*. (2020) 11:280. doi: 10.3389/fneur.2020.00280
- Cui J, Bu H, He J, Zhao Z, Han W, Gao R, et al. The gamma-aminobutyric acid-B receptor (GABAB) encephalitis: clinical manifestations and response to immunotherapy. *Int J Neurosci*. (2018) 128(7):627–33. doi: 10.1080/00207454.2017.1408618
- Wu H, Wang Y, Wei K, Qiao S, Liu L, Zhang R, et al. Clinical characteristics and elevated ProGRP and positive oligoclonal bands of 13 Chinese cases with anti-GABABR encephalitis. *Int J Dev Neurosci*. (2021). doi: 10.1002/jdn.10121
- Chen X, Liu F, Li JM, Xie XQ, Wang Q, Zhou D, et al. Encephalitis with antibodies against the GABAB receptor: seizures as the most common presentation at admission. *Neurol Res*. (2017) 39(11):973–80. doi: 10.1080/01616412.2017.1351062
- van Coevorden-Hameete MH, de Bruijn M, de Graaff E, Bastiaansen D, Schreurs MWJ, Demmers JAA, et al. The expanded clinical spectrum of anti-GABABR encephalitis and added value of KCTD16 autoantibodies. *Brain*. (2019) 142(6):1631–43. doi: 10.1093/brain/awz094
- Qiao S, Zhang YX, Zhang BJ, Lu RY, Lai QL, Chen LH, et al. Clinical, imaging, and follow-up observations of patients with anti-GABAB receptor encephalitis. *Int J Neurosci*. (2017) 127(5):379–85. doi: 10.1080/00207454.2016.1176922
- Lin J, Li C, Li A, Liu X, Wang R, Chen C, et al. Encephalitis with antibodies against the GABAB receptor: high mortality and risk factors. *Front Neurol*. (2019) 10:1030. doi: 10.3389/fneur.2019.01030
- Yeshokumar AK, Coughlin A, Fastman J, Psaila K, Harmon M, Randell T, et al. Seizures in autoimmune encephalitis-A systematic review and quantitative synthesis. *Epilepsia*. (2021) 62(2):397–407. doi: 10.1111/epi.16807
- Ghimire P, Khanal UP, Gajurel BP, Karn R, Rajbhandari R, Paudel S, et al. Anti-LG11, anti-GABABR, and anti-CASPR2 encephalitis in Asia: a systematic review. *Brain Behav*. (2020) 10(10):e01793. doi: 10.1002/brb3.1793
- Si Z, Wang A, Liu J, Zhang Z, Hu K. Typical clinical and imaging manifestations of encephalitis with anti-gamma-aminobutyric acid B receptor antibodies: clinical experience and a literature review. *Neurol Sci*. (2019) 40(4):769–77. doi: 10.1007/s10072-018-3679-5
- Dogan Onugoren M, Deuretzbacher D, Haensch CA, Hagedorn HJ, Halve S, Isenmann S, et al. Limbic encephalitis due to GABAB and AMPA receptor antibodies: a case series. *J Neurol Neurosurg Psychiatry*. (2015) 86(9):965–72. doi: 10.1136/jnnp-2014-308814
- Zhang X, Lang Y, Sun L, Zhang W, Lin W, Cui L. Clinical characteristics and prognostic analysis of anti-gamma-aminobutyric acid-B (GABA-B) receptor encephalitis in northeast China. *BMC Neurol*. (2020) 20(1):1. doi: 10.1186/s12883-019-1585-y
- Gaspard N. Guilty by association: KCTD16 and GABABR antibodies in paraneoplastic limbic encephalitis. *Epilepsy Curr*. (2019) 19(6):372–5. doi: 10.1177/1535759719877891
- Dalmau J, Geis C, Graus F. Autoantibodies to synaptic receptors and neuronal cell surface proteins in autoimmune diseases of the central nervous system. *Physiol Rev*. (2017) 97(2):839–87. doi: 10.1152/physrev.00010.2016
- Graus F, Vogrig A, Muniz-Castrillo S, Antoine JG, Desestret V, Dubey D, et al. Updated diagnostic criteria for paraneoplastic neurologic syndromes. *Neurol Neuroimmunol Neuroinflamm*. (2021) 8(4). doi: 10.1212/NXI.0000000000001014
- de Bruijn M, van Sonderen A, van Coevorden-Hameete MH, Bastiaansen AEM, Schreurs MWJ, Rouhl RPW, et al. Evaluation of seizure treatment in anti-LG11, anti-NMDAR, and anti-GABABR encephalitis. *Neurology*. (2019) 92(19):e2185–e96. doi: 10.1212/WNL.00000000000007475
- Kim TJ, Lee ST, Shin JW, Moon J, Lim JA, Byun JI, et al. Clinical manifestations and outcomes of the treatment of patients with GABAB encephalitis. *J Neuroimmunol*. (2014) 270(1–2):45–50. doi: 10.1016/j.jneuroim.2014.02.011
- Shen CH, Fang GL, Yang F, Cai MT, Zheng Y, Fang W, et al. Seizures and risk of epilepsy in anti-NMDAR, anti-LG11, and anti-GABAB R encephalitis. *Ann Clin Transl Neurol*. (2020) 7(8):1392–9. doi: 10.1002/acn3.51137