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Brief Communication

Follow-up of patients with epilepsy harboring antiglycine receptor antibodies

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ABSTRACT

Objective: The long-term follow-up of patients with epilepsy harboring autoantibodies against the glycine receptor (also glycine receptor antibodies or GlyR-Ab) is not well-known. Our aim was to investigate the 5-year prognosis and treatment response of patients with epilepsy who were seropositive for GlyR-Ab.
Methods: Clinical features; electroencephalogram (EEG), neuroradiological, and neuropathological findings; and treatment responses of patients with epilepsy with GlyR-Ab seropositivity were investigated.
Results: Thirteen (5.46%) of 238 patients with epilepsy were GlyR-Ab positive: focal epilepsy of unknown cause (FEoUC) was diagnosed in four (7.27%) out of 55 patients, mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS) in five (4.5%) out of 111 patients, epileptic encephalopathy (EE) in two (4%) out of 50 patients, and status epilepticus (SE) in two (9.09%) out of 22 patients. None of the patients developed any other neurological symptoms or cancer during the 5-year follow-up. Seven of them had seizures that were resistant to antiepileptic drug (AED). Immunotherapy was used in two patients (with FEoUC and EE) improving seizure control. Three patients with MTLE-HS benefited from epilepsy surgery, and another patient with EE showed spontaneous remission.
Conclusion: Glycine receptor antibodies are detected in a wide spectrum of epileptic disorders with unclear pathogenic significance. Two GlyR-Ab seropositive patients with AED-resistant epilepsy treated with intravenous immunoglobulin (IVIg) showed clear benefit from immunotherapy. Future studies will be valuable in determining the role of screening patients with drug-resistant epilepsy for GlyR-Ab in order to identify patients who may benefit or respond to immunotherapy.

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1. Introduction

Autoantibodies against the glycine receptor (GlyR-Ab) were reported to be associated with stiff person syndrome and progressive encephalomyelitis with rigidity and myoclonus (PERM), followed by limbic encephalitis and epilepsy [1–7]. However, their pathogenic roles in epilepsy are not well-established, and there is no data about the long-term follow-up of patients with epilepsy harboring GlyR-Ab.

Our aim was to report the 5-year follow-up data of a series with GlyR-Ab to provide an insight on the clinical significance of GlyR-Ab in patients with various epilepsy syndromes.

2. Methods

2.1. Participants

We screened all files of our epilepsy outpatient clinic for patients diagnosed as having epilepsy and found GlyR-Ab seropositivity in previous studies investigating the presence of antineuronal antibodies. Seizure types, epileptic syndromes, and drug resistance were classified according to the published International League Against Epilepsy (ILAE) criteria [8]. Clinical findings such as gender, age at seizure onset, antiepileptic drug (AED) response, cognitive dysfunction, history and family history of epilepsy, status epilepticus (SE), comorbidity, psychiatric problems, prognosis at last visit, history of cancer, and immune treatments were investigated retrospectively. All magnetic resonance imaging (MRI), routine and long-term video-electroencephalogram (EEG), and positron emission tomography (PET) results were analyzed

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by an experienced epileptologist. For operated patients, postoperative prognosis and available neuropathological findings were examined.

2.2. Antibody testing

Sera of included patients were tested for GlyR-Ab using an assay with live human embryonal kidney 293 (HEK293) cells. Moreover, several other well-characterized neuronal autoantibodies such as contactin-associated protein 2 (CASPR-2), *N*-methyl-D-aspartate receptor (NMDA-R), voltage-gated potassium channel (VGKC)-complex, leucine-rich glioma inactivated 1 (LGI1), glutamic acid decarboxylase (GAD), and a-amino-3-hydroxy-5-methyl-4-isoxazoleproprionic acid receptor (AMPA-R) were investigated.

Glycine receptor antibodies were detected by binding the HEK293 cells transfected with plasmids encoding α1 subunit of the glycine receptor. Transfected cells were incubated with patients' sera and the appropriate Alexa Fluor secondary antibody, as described earlier [2]. All positive sera were retested using an immunoglobulin G (IgG)-specific secondary antibody (Alexa Fluor 488-anti-IgG, Invitrogen, CA, USA). The intensity of the staining was assessed visually by two independent observers and scored on a range from 0 (negative) to 4 (very strong), as previously described [2,3], and only scores greater than one were accepted as positive.

2.3. Immunohistochemistry studies

Paraffin-embedded brain tissue was obtained from surgical specimens of a patient (Patient 7) diagnosed as having mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS). Control samples included two paraffin-embedded spleen samples (obtained from neurologically healthy individuals) and lung adenocarcinoma samples with abundant inflammatory infiltrates. Immunohistochemical analysis of inflammatory infiltrates was performed as previously reported [9].

3. Results

Sera of 13 (5.46%) out of 238 screened patients showed GlyR-Ab. None of these patients were positive for other investigated antineuronal antibodies. These patients comprised four (7.27%) out of 55 patients with focal epilepsy of unknown cause (FEoUC) [2], five (4.5%) out of 111 patients with MTLE-HS [3], two (4%) out of 50 patients with epileptic encephalopathy (EE) [10], and two (9.09%) out of 22 patients with SE [11].

One of these patients, who has already been diagnosed as having multiple sclerosis (67-year-old bed-ridden female, with cerebrospinal fluid (CSF) examinations compatible with multiple sclerosis only), had died in the early course because of complications of septic shock 4 months after de novo super-refractory SE occurring in the course of pneumonia [11]. Hence, no further data could be obtained from this patient.

The clinical, laboratory, and follow-up findings of the remaining 12 seropositive patients are summarized in Table 1, and PET images of a patient (Patient 10) are depicted in Fig. 1. None of these patients had a history of encephalitic onset or PERM or developed any other neurological symptoms or cancer during the 5-year follow-up. Psychiatric disorders were documented in half of the patients, and one had psychotic spells. Mild to severe cognitive problems were also present in most of our patients. Magnetic resonance imaging showed nonspecific white matter lesions (WMLs) in two patients and diffuse atrophy in one patient having EE, apart from diagnostic changes of HS (Table 1). Only one patient reported history of rapidly progressive cognitive decline related to EE (Patient 1), one patient had a viral prodrome (Patient 12), and six (50%) out of 12 patients had developed autonomic findings during disease course.

One of the patients with SE (Patient 12 in Table 1), who had an unclassified EE, experienced an unusual course after prodromal viral infection. The disease started at the age of 3 years with myoclonus and bilateral convulsive seizures triggered by fever. The boy also had ataxia, polyneuropathy, and sleep apnea. Electroencephalogram showed background slowing, generalized epileptic discharges, and photosensitivity. Cerebrospinal fluid findings were normal, and oligoclonal bands were absent. After a stable period lasting many years, his seizures worsened again, and at the age of 17 years, he had a single episode of convulsive SE, at which time GlyR-Ab were detected. Genetic investigations revealed variants in SCN1A gene. He showed another unexplained clinical improvement without any immune treatment or any substantial change in his AED regimen. He has remained seizure-free for the last four years and had a distinct cognitive improvement: his intelligent quotient (IQ) scores increased from 54 to 72 in four years (Alexander's IQ test).

Another GlyR-Ab positive patient (Patient 2) diagnosed as having EE started to have daily myoclonic seizures at 9 months of age, followed by myoclonic–astatic seizures partly responsive to two rounds of adrenocorticotropic hormone (ACTH) therapy. Afterwards, he experienced generalized tonic seizures and motor and mental decline. Electroencephalograms showed generalized multifocal spike/polyspike–slow waves with diffuse theta and delta slowing, with generalized paroxysmal fast activity and photosensitivity. He had moderate mental retardation, and his condition was classified as Lennox–Gastaut syndrome (LGS). He did not use any further immunotherapy since his seizures were milder under polytherapy with three AEDs.

Among our patients, immune treatments were used in 2 cases with success. One of them (Patient 4) with FEoUC had a worsening course under conventional AEDs. He did not show any benefit from vagus nerve stimulation and from intravenous methylprednisolone (IVMP). However, seizure frequency (5–15 times per day) improved after intravenous immunoglobulin (IVIg) (2 g/kg in consecutive 5 days), and he had 2–4 seizures per month. As the seizure frequency increased (>5 seizures per week) in a few months after IVIg, this therapy was readministered as monthly IVIg regimen (0.4 g/kg, for 3 months) and on 5 consecutive days (at a total dose of 2 g/kg) providing an improvement (<5 seizures per week) maintained for more than one year. Electroencephalograms showed generalized slowing and bilateral independent centroparietal epileptogenic foci, more prominent on the left side.

The second patient (Patient 1) with immune treatment was a 22-year-old woman with normal developmental milestones. She had experienced bilateral convulsive seizures at the age of 13 years. Thereafter, she started to show mildly progressive cognitive decline with normal metabolic, genetic screening, and normal CSF findings. She also had tonic seizures and atypical absences and was diagnosed as having unclassified EE. Electroencephalogram showed generalized discharges and focal spikes over the right frontotemporal region with paroxysmal slow waves. Her initial brain MRI result was normal but showed progressive atrophy in five years. She received IVIg treatment (same regimen), and soon after this therapy, her seizure frequency decreased from 3 bilateral convulsive seizures per day to one milder and shorter seizure per month. This improvement lasted for two months, and the patient continued to experience daily seizures after three months of discontinuation of immunotherapy.

Furthermore, two GlyR-Ab seropositive patients with MTLE-HS showed an unusual benign course, and the remaining three underwent epilepsy surgery with beneficial results (two before and one after the detection of the antibodies). There was a single patient (Patient 7) with available postsurgery brain tissue for the examination. Although this brain sample did not exhibit infiltrates of T (CD3, CD8) and B lymphocytes (CD20), plasma cells (CD79a), and IgG and complement deposits, CD68 + macrophages were observed mostly in perivascular regions (Fig. 2).

4. Discussion

Our study indicates that epilepsy associated with GlyR-Ab presents with heterogeneous clinical forms and with variable outcomes. Many

Table 1
The clinical and laboratory findings and prognosis of the patients with GlyR-Ab.

No/Sex	Score[a]	Age/age at onset	Epilepsy syndrome	History	Family history	Psychiatric disorder	Neurological exam/cognitive dysfunction	MRI/PET findings	AED-resistance/immune treatment	Status during last visit[b]
1/F	3	22/13 y	EE	Unremarkable	Epilepsy	None	N/moderate	Diffuse atrophy/N.A.	Yes/responsive to IVIg	Frequent BCS
2/M	3	26/9 mo	EE	Scoliosis	Deafness	None	Spasticity/severe	N/left F hypom.	Yes/partly responsive to prior ACTH therapy	Frequent myo only, rare BCS, 3 AED
3/M	4	42/17 y	FEoUC (T)	Unremarkable	Unremarkable	Depression	N/not present	N/N.A.	No/no	Good
4/M	4	24/3 y	FEoUC (F)	FS	Consanguinity, FS in brother	Psychotic spells, borderline	N/mild	N/left superior P hypom.	Yes/no response to VNS/responsive to IVIg	Frequent focal seizures, 3 AED
5/F	3	38/16 y	FEoUC (T)	HT, migraine, hyperthyroidism	Consanguinity/epilepsy	Depression	N/mild attention and secondary memory disorder	N/N.A.	No/no	Good/seizure after drug withdrawal
6/F	3	33/14 y	FEoUC (T)	HT, hyperthyroidism	Consanguinity, epilepsy and CD	Unremarkable	N/not present	N/N.A.	No/no	Good
7/F	3	38/14 y	MTLE	Asthma	Unremarkable	Depression	N/verbal memory defect, frontal dysfunction	Left HS/left T hypom.	Yes/no	1–2 seizures per year after surgery
8/M	3	60/17 y	MTLE	Diabetes and renal failure	Normal except twin birth	Depression (suicide)	N/FL and verbal memory disorder	HS (bilateral R > L) and WML/N.A.	No/no	Good/seizure-free for 8 y
9/M	2	56/9 y	MTLE	FS	Unremarkable	Unremarkable	N/No formal testing	Left HS/N.A.	No/no	Good/rare seizures
10/F	3	32/15 y	MTLE	FS	Unremarkable	Unremarkable	N/FL and visual memory disorder	Right HS/bilateral mesial T (R > L), L parietal hypom.	Yes/no	Seizure-free after epilepsy surgery
11/M	2	52/9 y	MTLE	FS, HT	Unremarkable	Dysthymia-obsessive personality	N/FL and verbal memory disorder	Right HS/N.A.	Yes/no	Seizure-free after epilepsy surgery
12/M	4	22/3 y	EE with status epilepticus	FS, sleep apnea	Unremarkable	Unremarkable	Ataxia/moderate	Nonspecific WML/N.A.	Yes/rejected immune treatment	Rare myo, stable

AED, antiepileptic drug; BCS, bilateral convulsive seizure; CD, cognitive dysfunction; EE, epileptic encephalopathy; FL, frontal lobe; FEoUC, focal epilepsy of unknown cause; FS, febrile seizure; F, female; HS, hippocampal sclerosis; hypom., hypometabolism; HT, head trauma (reported but no evidence in MRI and relevant reports); L, left; M, male; mo, month; N, normal; MTLE, mesial temporal lobe epilepsy; LGS, Lennox–Gastaut syndrome; myo, myoclonia; N.A., not available; P, parietal; R, right; T, temporal lobe; VNS, vagal nerve stimulation; WML, white matter lesion; y, year.

[a] Numbers indicate the antibody binding intensity scored visually on a range from 0 (negative) to 4 (very strong) in 2012 and 2017.

[b] Good prognosis implied that the patient has less than one convulsive seizure of any kind monthly (auras excluded).

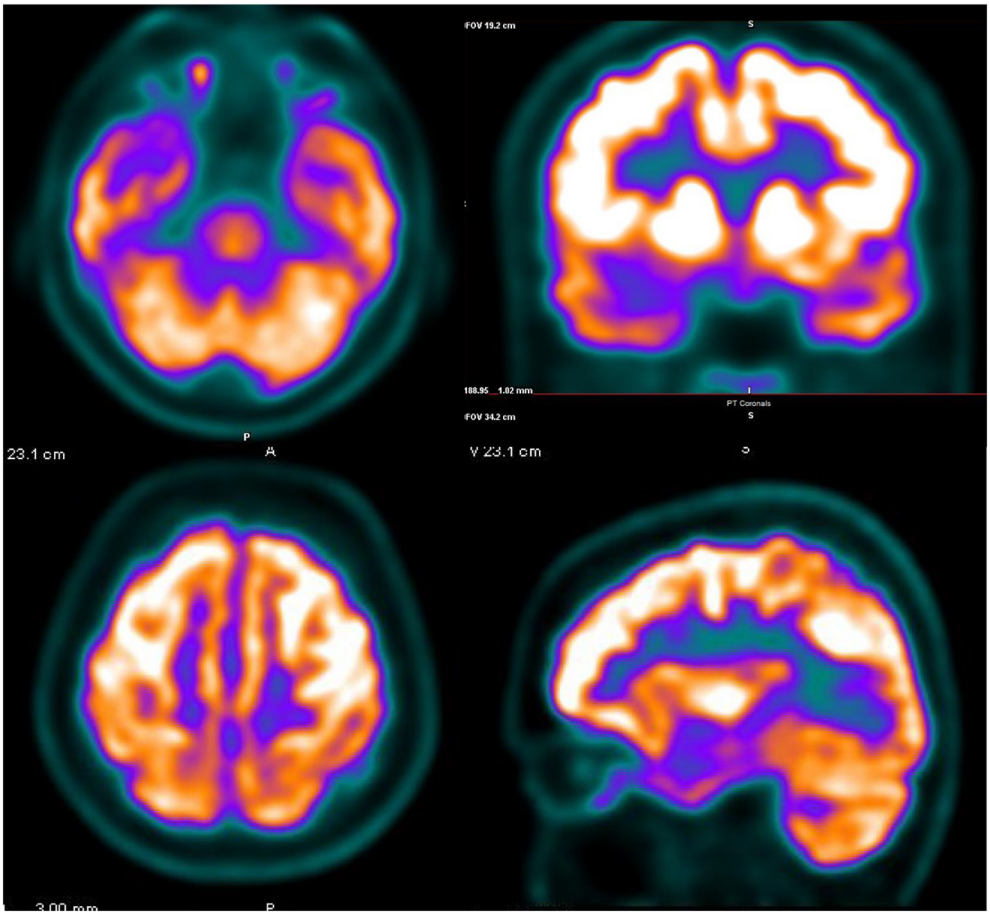

Fig. 1. PET images displaying left parietal and bilateral temporal hypometabolic activity more prominent on the right of Patient 10 remaining seizure-free after epilepsy surgery.

of our seropositive patients (41.67% of all seropositives), especially those with FEoUC (75%), showed an AED-responsive course. Secondly, these patients showed some atypical features, such as late-onset EE with remissions and exacerbations and an unusual benign course for MTLE-HS. Most notably, two patients with drug-resistant epilepsy showed benefit from immunosuppressive treatments.

In a previously reported cohort of 52 patients with GlyR-Ab, including mostly patients with PERM, five were diagnosed as having limbic encephalitis or EE. Most of them responded well to immunotherapy. Interestingly, brain MRI results showed signal alterations in the temporal lobes and also nonspecific WMLs in a minority, whereas 26 patients had normal MRI results [1]. Four of our patients could be investigated with PET, revealing hypometabolism in two patients with normal brain MRI result (Table 1). Our data suggested that PET imaging may be more sensitive at least in some of these patients with negative MRI findings. Positron emission tomography is cited as a useful tool to detect neuroinflammation, and hypermetabolic activities are frequently seen in the early stages of autoimmune encephalitis [12,13]. We think that our PET findings showing hypometabolism are compatible with the presence of an autoimmune neuroinflammatory process at the chronic stage, associated with established epilepsy. Interestingly, one patient having MTLE with right HS on MRI also had an extended hypometabolic activity on the parietal lobe in addition to bilateral temporal hypometabolism (Table 1 and Fig. 1). It is worth to emphasize that hypometabolic activity, in both temporal and extratemporal regions, was previously reported in seropositive patients [3], a finding which may suggest screening the neuronal autoantibodies including GlyR-Ab.

Furthermore, five of our 12 patients had HS, a finding suggesting that these patients might have undergone a silent limbic encephalitis. Glycine is known as an inhibitory neurotransmitter [14]. Therefore, it is tempting to speculate that GlyR-Ab may play a role in seizure induction. Glycine receptors antibodies are known to be capable of accumulating on neurons and activating the complement system. Immunohistochemical investigation of the brain sample of a GlyR-Ab positive patient did not support the presence of active and massive inflammation but showed only moderate macrophage infiltration [1]. Thus, the absence of IgG and complement deposits on the analyzed brain specimen argues against a pathogenic role for GlyR-Ab and suggests that these antibodies emerge as by-products of seizure-initiated tissue damage.

Regardless of their roles in seizure pathogenesis, GlyR-Ab might be a marker of responsiveness to immunosuppressive treatments especially in patients with AED-resistant epilepsy with atypical clinical courses. There are only a few previous case reports with GlyR-Ab responding to immune treatments. A four-year-old boy with drug-resistant FEoUC responded well to steroids, in contrast to our patients [5]. Another boy had acute encephalopathic presentation with positivity for GlyR-Ab, and IVMP and IVIg achieved seizure control besides the improvement of ataxia [7]. Furthermore, there is a report of two adult patients with GlyR-Ab who had subacute onset of drug-resistant temporal lobe seizures (with hippocampal signal changes on MRI) associated with behavioral and memory problems. Remarkably, one of them presented with generalized convulsive SE. These patients responded to IVMP and IVIg [4]. We had also observed a patient with psychiatric disorder in addition to established FEoUC who benefited from IVIg, suggesting that autoimmunity linked to GlyR-Ab should be screened in such patients.

However, in one of our patients with a fluctuating course of an atypical EE, the seizures as well as his cognitive decline improved without any immune or conventional AED treatment, suggesting that GlyR-Ab might also be a nonspecific marker of a waxing and waning form of autoimmunity. Furthermore, our patients with MTLE-HS harboring GlyR-

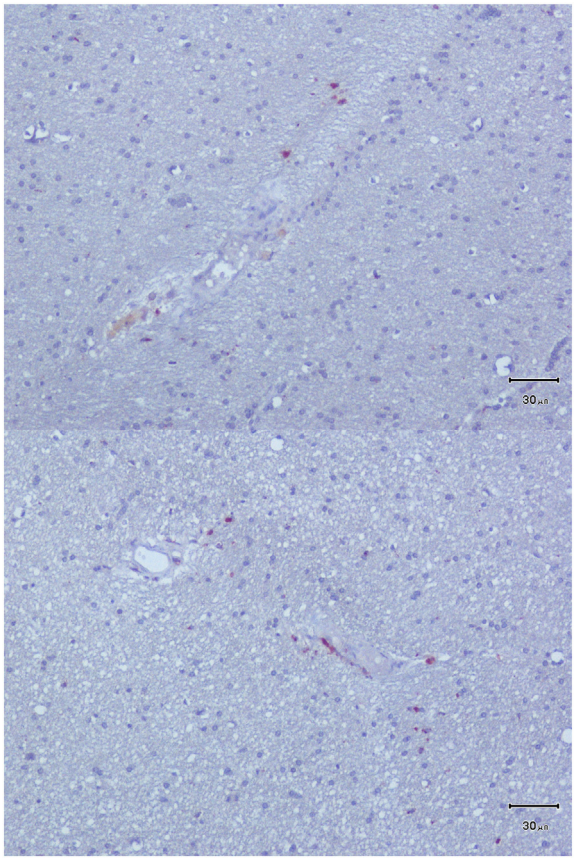

Fig. 2. Neuropathological findings of postsurgery brain tissue of a patient with MTLE-HS. Immunohistochemical staining of brain sections of a GlyR-Ab positive patient with epilepsy demonstrates scattered CD68 positive macrophages (brown mononuclear cells) in the perivascular region. Hematoxylin was used for counterstaining (blue).

Ab benefited well from conventional AEDs or epilepsy surgery, which was also a remarkable finding given that MTLE-HS is known as a AED-resistant constellation showing some inflammatory findings. Therefore, we may suggest that the significance of GlyR-Ab seropositivity may differ according to the epilepsy subtype. There may be causal association between GlyR-Ab and epilepsy and between immunotherapy and clinical improvement in a selected subgroup of patients harboring GlyR-Ab. At the moment, we could not define a distinct subgroup of patients with epilepsy in which GlyR-Ab seems to have a direct role in the pathophysiology; showing the need for future multicenter studies.

We found that the presence of GlyR-Ab showed close relationship with some of the recently described predictive factors for autoimmune etiology in some patients. Autonomic dysfunction was present in half of our patients and may be a remarkable finding to suggest an autoimmune etiology in chronic epilepsy [15]. Moreover, neuropsychological problems and depression were evident in our patients similar to previously reported GlyR-Ab positive cases [16]. However, the follow-up periods of all these reported cases were shorter than those of our series.

In conclusion, we suggest that screening for GlyR-Ab in patients with drug-resistant seizures or atypical courses should not be neglected. Our data supplied evidence that some patients harboring GlyR-Ab may benefit from immunotherapy possibly because of underlying autoimmune etiology. Future experimental studies in this field and larger multicenter collection of data are needed to better elucidate the clinical features of GlyR-Ab seropositive epilepsies and also to understand the contribution of GlyR-Ab to the pathophysiology of epilepsy.

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Conflicts of interest

None of the authors has any conflict of interest to disclose.

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References

[1] Carvajal-Gonzalez A, Leite MI, Waters P, Woodhall M, Coutinho E, Balint B, et al. Glycine receptor antibodies in PERM and related syndromes: characteristics, clinical features and outcomes. Brain 2014;137:2178–92.
[2] Ekizoglu E, Tuzun E, Woodhall M, Lang B, Jacobson L, Icoz S, et al. Investigation of neuronal autoantibodies in two different focal epilepsy syndromes. Epilepsia 2014; 55:414–22.
[3] Vanli-Yavuz EN, Erdag E, Tuzun E, Ekizoglu E, Baysal-Kirac L, Ulusoy C, et al. Neuronal autoantibodies in mesial temporal lobe epilepsy with hippocampal sclerosis. J Neurol Neurosurg Psychiatry 2016;87:684–92.
[4] Baysal-Kirac L, Tuzun E, Erdag E, Ulusoy C, Vanli-Yavuz EN, Ekizoglu E, et al. Neuronal autoantibodies in epilepsy patients with peri-ictal autonomic findings. J Neurol 2016;263:455–66.
[5] Wuerfel E, Bien CG, Vincent A, Woodhall M, Brockmann K. Glycine receptor antibodies in a boy with focal epilepsy and episodic behavioral disorder. J Neurol Sci 2014; 343:180–2.
[6] Chan DW, Thomas T, Lim M, Ling S, Woodhall M, Vincent A. Focal status epilepticus and progressive dyskinesia: a novel phenotype for glycine receptor antibody-mediated neurological disease in children. Eur J Paediatr Neurol 2016;21:414–7.
[7] Ude C, Ambegaonkar G. Glycine receptor antibody-associated epilepsy in a boy aged 4 years. BMJ Case Rep 2016;2016. https://doi.org/10.1136/bcr-2016-216468 [pii: bcr2016216468].
[8] Kwan P, Arzimanoglou A, Berg AT, Brodie MJ, Allen Hauser W, Mathern G, et al. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. Epilepsia 2010;51:1069–77.
[9] Tuzun E, Zhou L, Baehring JM, Bannykh S, Rosenfeld MR, Dalmau J. Evidence for antibody-mediated pathogenesis in anti-NMDAR encephalitis associated with ovarian teratoma. Acta Neuropathol 2009;118:737–43.
[10] Tekturk P, Baykan B, Erdag E, Peach S, Sezgin M, Yapici Z, et al. Investigation of neuronal auto-antibodies in children diagnosed with epileptic encephalopathy of unknown cause. Brain and Development 2018. https://doi.org/10.1016/j.braindev.2018.06.002 [Epub ahead of print].
[11] Atmaca MM, Tuzun E, Erdag E, Bebek N, Baykan B, Gurses C. Investigation of antineuronal antibodies in status epilepticus of unknown etiology: a prospective study. Acta Neurol Belg 2017;117:841–8.
[12] Steriade C, Moosa ANV, Hantus S, Prayson RA, Alexopoulos A, Rae-Grant A. Electroclinical features of seizures associated with autoimmune encephalitis. Seizure 2018;60:198–204.
[13] Cózar Santiago Mdel P, Sanchez Jurado R, Sanz Llorens R, Aguilar Barrios JE, Ferrer Rebolleda J. Limbic encephalitis diagnosed with 18F-FDG PET/CT. Clin Nucl Med 2016;41:e11-3.
[14] Zafra F, Ibáñez I, Bartolomé-Martín D, Piniella D, Arribas-Blázquez M, Giménez C. Glycine transporters and its coupling with NMDA receptors. Adv Neurobiol 2017; 16:55–83.
[15] Dubey D, Singh J, Britton JW, Pittock SJ, Flanagan EP, Lennon VA, et al. Predictive models in the diagnosis and treatment of autoimmune epilepsy. Epilepsia 2017; 58:1181–9.
[16] Zuliani L, Ferlazzo E, Andrigo C, Casano A, Cianci V, Zoccarato M, et al. Glycine receptor antibodies in 2 cases of new, adult-onset epilepsy. Neurol Neuroimmunol Neuroinflamm 2014;3(1(2)):e16. https://doi.org/10.1212/NXI.0000000000000016.