Bilateral Perisylvian Syndrome With Autonomic Seizures and Autonomic Status Epilepticus: A Case Report With Long-Term Follow-up

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Summary. We report a long-term follow-up of a 38-year-old woman diagnosed with bilateral perisylvian syndrome. The patient showed mental retardation, pseudobulbar palsy, spastic hemiparesis and refractory focal epilepsy with prolonged autonomic seizures; diabetes mellitus type 1 was also diagnosed. Despite that the patient had repeated stereotyped episodes of nausea, retching, vomiting, pallor, mydriasis, hypersalivation and urine incontinence, epilepsy was diagnosed years after symptoms had started. Brain MRI revealed bilateral perisylvian polymicrogyria. Treatment of combined therapy of oxcarbazepine and lamotrigine gave complete seizure remission for 8 years. When seizures re-appeared, treatment option of lamotrigine and levetiracetam was followed by a significant clinical improvement. To our knowledge, this is the first publication depicting the association between bilateral perisylvian syndrome, diabetes, partial autonomic seizures, and autonomic status epilepticus.

Keywords: bilateral perisylvian syndrome, autonomic seizures, epilepsy, diabetes, status epilepticus, polymicrogyria.

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INTRODUCTION

Bilateral perisylvian syndrome (BPS) is a rare neurological disorder characterised by pseudobulbar palsy, cognitive deficit and epilepsy associated with bilateral perisylvian cortical dysplasia on neuroimaging studies. We report a long-term follow-up of a 38-year-old woman diagnosed with BPS according to the typical clinical and magnetic resonance imaging (MRI) features. The patient showed mental retardation, pseudobulbar palsy, spastic hemiparesis and refractory focal epilepsy with prolonged autonomic seizures. Diabetes mellitus type 1 was also diagnosed. Brain MRI revealed bilateral perisylvian polymicrogyria (PMG). Despite she had repeated episodes of autonomic seizures, epilepsy was diagnosed years after symptoms started. Treatment with oxcarbazepine (OXC) and lamotrigine (LTG) gave complete seizure remission for 8 years. When seizures re-appeared, treatment with LTG and levetiracetam (LEV) was followed by a significant clinical improvement. These findings emphasise the

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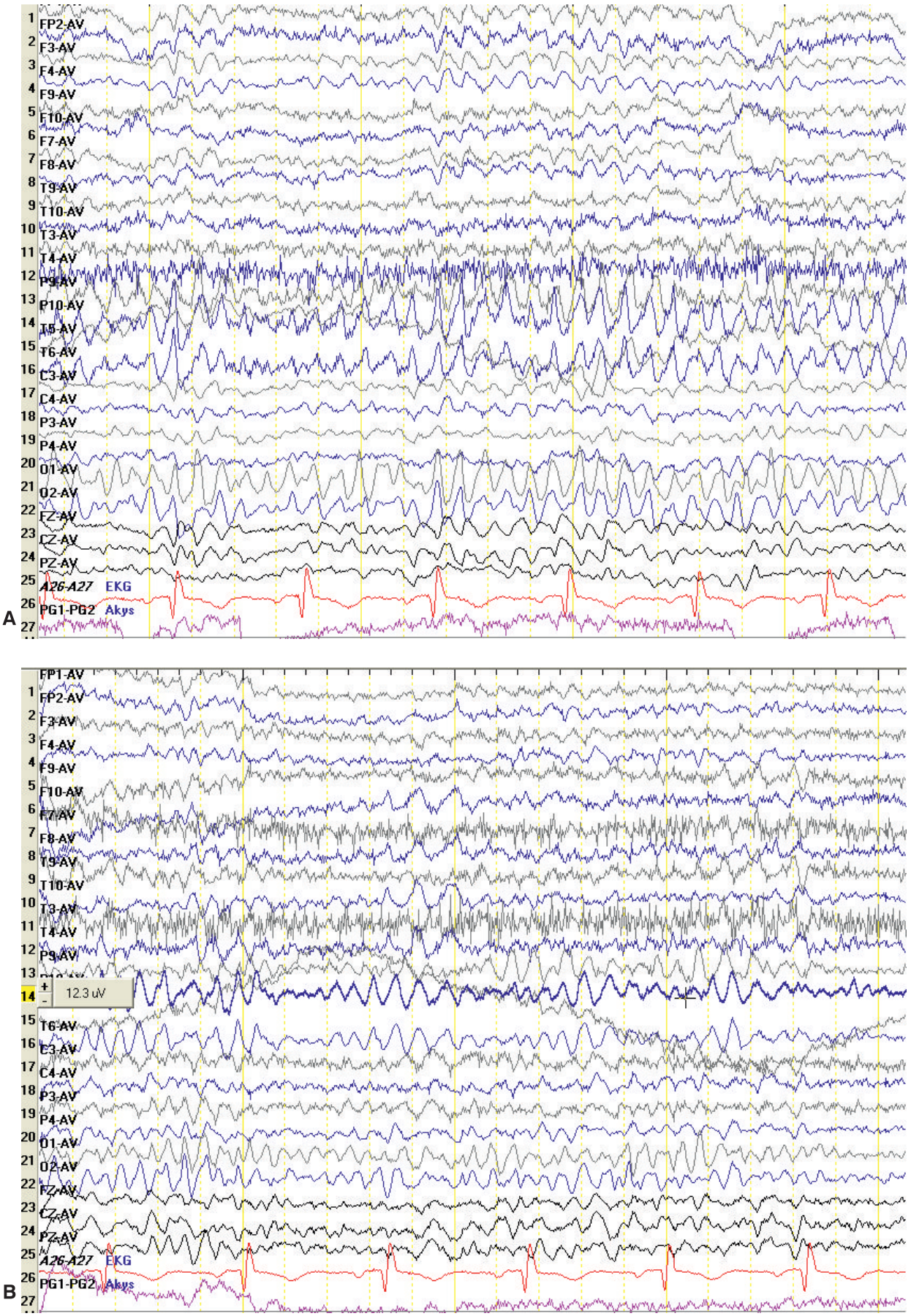

Fig. 1. **Ictal EEG: the run of sharp waves in the right parieto-temporal region (A). Interictal EEG: slow activity in the right fronto-temporal region (B).**

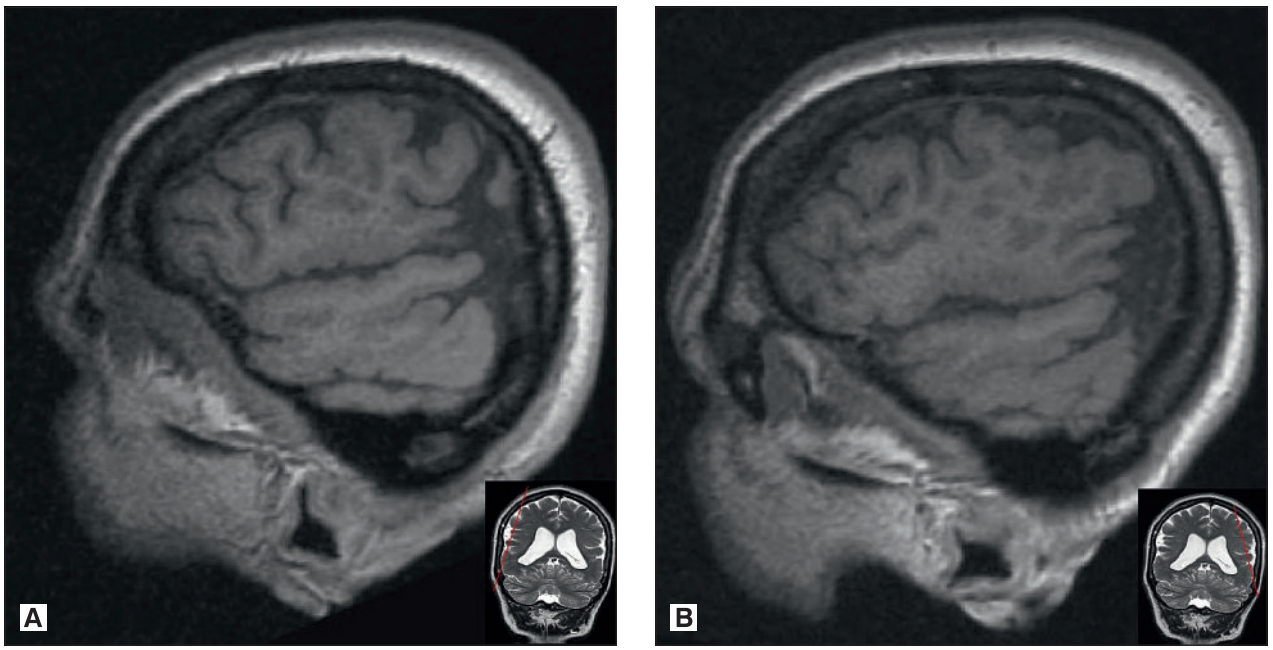

Fig. 2. **Brain MRI, T1-weighted, right (A) and left (B) sagittal. Primary and secondary sulci of cortex are abnormal. Dorsal parts of lateral sulci turn into significantly enlarged subarachnoidal space in parietal lobes, perisylvian polymicrogyria is present.**

importance of long-term follow-up, suggesting that the prognosis for epilepsy may not be predicted based on early response to treatment or presence of structural encephalic abnormalities, as reported in the literature. To our knowledge, this is the first publication depicting the association between BPS, diabetes, partial autonomic seizures and autonomic status epilepticus (SE).

CASE REPORT

A 38-year-old Lithuanian woman was admitted to our department because of extended episodes of nausea, retching, vomiting, pallor, mydriasis, hypersalivation and urine incontinence. Episodes lasted up to 3 hours, seizure frequency was from several to 7 per day. During the majority of them the patient was fully responsive and during some of them she became unresponsive and flaccid but no generalized tonic-clonic (GTC), motor or sensory phenomena had been observed. The patient's birth was complicated, obstetrical forceps were used. Right hemiparesis developed in 2-month-old, oromotor incoordination, mental retardation were observed later, therefore cerebral palsy with right spastic hemiparesis, pseudobulbar palsy and mental retardation were diagnosed suggesting cerebral palsy was due to peri-natal trauma. Genetic counseling revealed normal karyotype (46, XX), no chromosomal or metabolic disorders. The patient has a younger healthy sister.

Autonomic seizures started when the patient was 13 years old. Diabetes mellitus type 1 was diagnozed, insulin therapy administered, but prolonged autonomic features were not associated with blood glucose levels and did not disappear. Computerised tomography (CT) scan showed brain atrophy. Focal epilepsy was diagnosed at the age of 27 (14 years later) and antiepileptic drug (AED) monotherapy started with Carbamazepine (CBZ), then Valproic acid (VPA), then OXC had no effect. OXC 600 mg/day with LTG 400 mg/day provided complete remission from 2003 till 2011. Nevertheless, seizures restarted in June, 2011.

Physical examination revealed slurred speech, the patient was disorientated and could walk with support, pseudobulbar palsy, spastic paraparesis of both legs were observed. Tendon reflexes were high in the right extremities, coordination tests were performed with ataxia, right Babinski's reflex was prominent. Meningeal signs were absent.

Laboratory tests revealed increased glucose level in urinalysis (1.7 mmol/l). Glycolized haemoglobin, complete blood count, biochemical blood tests, ECG were normal. Electroencephalogram (EEG) showed an epileptiform activity in the right hemisphere (Fig. 1). Brain MRI revealed decreased volume of cerebrum, especially in parietal and temporal lobes, abnormal primary and secondary sulci of cortex and bilateral perisylvian PMG (Figs. 2, 3).

BPS and symptomatic epilepsy with simple partial autonomic seizures and autonomic SE, diabetes mellitus type 1 were diagnosed. Combination of LTG 400 mg/day with LEV 2000 mg/day decreased seizure frequency from several per day to one per month.

DISCUSSION

BPS is a migration disorder of brain associated with distinctive clinical and imaging features. The clinical spectrum vary from mild speech difficulties to severe disability, intractable seizures, cognitive and behavioral prob-

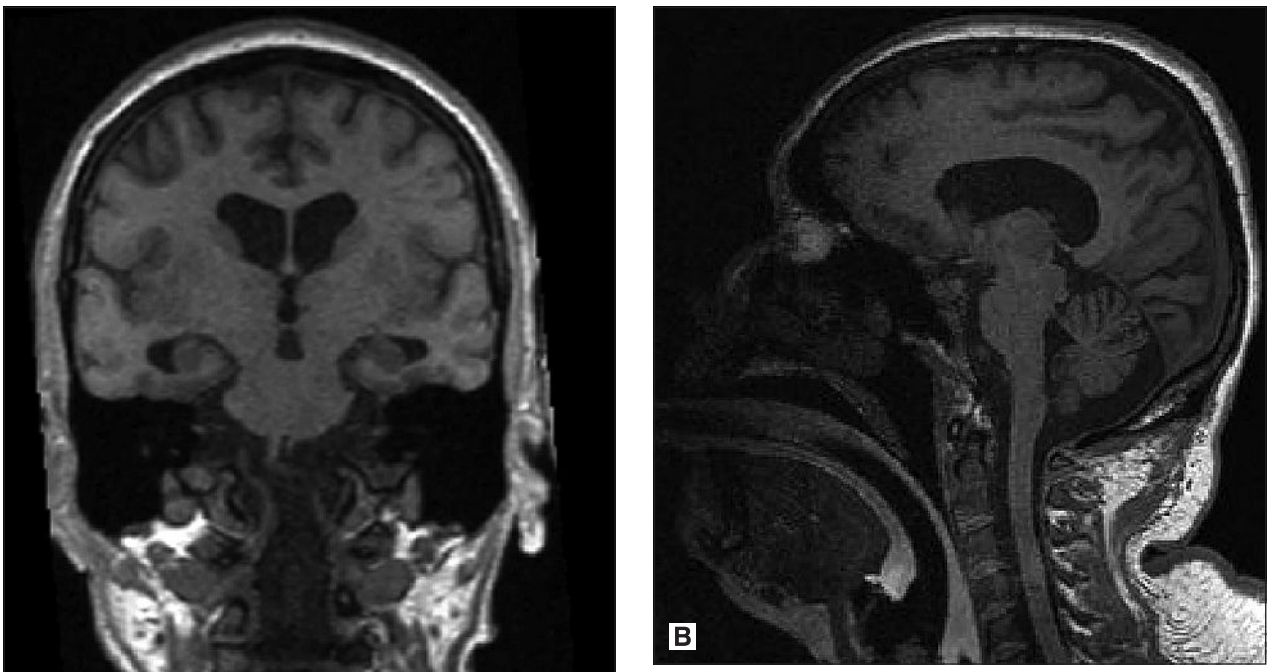

Fig. 3. **Brain MRI. T1-weighted, coronal: perisylvian polymicrogyria is seen bilaterally (A). T1-weighted, sagittal: volume of parietal and temporal lobes are bilaterally more significantly decreased than in other lobes (B).**

lems. The exact cause is not known, although bilateral cerebral hypoperfusion, possible injury during neuronal migration, post-migrational vascular accident and gene mutation are postulated [1, 5].

Bilateral PMG is divided into several types: frontal (presents with cognitive and motor delay, spastic quadriparesis, epilepsy, mostly all cases are sporadic), frontoparietal (manifests with severe cognitive and motor delay, seizures, dysconjugate gaze, cerebellar dysfunction, inheritance type is autosomal recessive, gene locus found on 16q12.2-21), parasagittal parieto-occipital (presents with partial seizures, mental retardation, all reported cases were sporadic), generalized (manifests with cognitive, motor delay and seizures, most cases autosomal recessive), perisylvian (pseudobulbar palsy, cognitive impairment and epilepsy are essential signs). This PMG type is heterogeneous, only several reported families were linked to gene locus on Xq28) [1]. Normal karyotype (46, XX) with no chromosomal or metabolic disorders was found in our patient. The patient has younger healthy sister, therefore, no further genetic tests were performed.

The most encountered clinical findings in patients with bilateral perisylvian PMG in Mavili E et all. study was mental–motor retardation in 89%, speech problems in 84% and cerebral palsy in 57% of patients, epilepsy and microcephaly were present in 53% of patients [2]. Epilepsy was found in almost 90% of BPS cases reported by Kuzniecky et al. [3]. Mean age at seizure onset in BPS was estimated to be 7.9 years [4]. Our patient had all three signs of perisylvian PMG: mental retardation, speech problems (pseudobulbar palsy) and cerebral palsy (right spastic hemiparesis); epilepsy for our patient started later (first seizures – when patient was 13 years old).

CT scan may not always identify PMG. MRI is essential in PMG diagnosis: the surface of the cerebral cortex is irregular, the border between gray and white matter pleated, cortical thickness variable [2]. Newer imaging techniques like positron emission tomography (PET) scan, magnetoencephalographic (MEG) scan, subtraction ictal SPECT co-registered with MRI (SISCOM) are useful in identifying mild PMG forms, epileptogenic focus, evaluating functional extension of the cortical anomaly or assessing feasibility of surgery. However, only histopathological examination makes PMG diagnosis definite. Our patient's MRI revealed PMG, decreased volume of cerebrum, abnormalities in cortical sulci.

Epileptic spectrum in BPS is broad with seizures presenting themselves as infantile spasms, GTC, typical and atypical absences, drop attacks progressing to Lennox-Gastaut syndrome [3, 4]. This case is unique as seizures of our patient were all autonomic, without sensory, motor or GTC types. Semiology of autonomic seizure suggests abnormalities in insular regions.

Autonomic seizures in childhood should be differentiated from Panayiotopoulos/Gastaut syndrome. In this syndrome, seizures are autonomic, 50% last at least 30 minutes and may persist for hours, EEG reveals normal background with predominant occipital spikes [6]. But Panayiotopoulos/Gastaut syndrome belongs to benign occipital epilepsy group: neurologic examination and imaging studies remain normal, spontaneous remission occurs within 2 years. In Gastaut type seizures are often followed

by throbbing headache with or without vomiting, onset is typically with visual symptoms, consciousness usually spared [6]. Neurological examination of our patient was abnormal, EEG showed no occipital spikes, finally, MRI revealed bilateral perisylvic PMG – these findings do not coincide with Panayiotopoulos/Gastaut syndrome.

Diabetes mellitus type 1 was also diagnosed to our patient. Recent studies report interface between diabetes mellitus type 1 and epilepsy. A significantly higher frequency of epileptic seizures in children and adolescents with diabetes was found in German and Austrian study [7]. Probably mechanism lies in anti-glutamic acid decarboxylase (GAD) antibodies production: GAD catalyzes conversion of glutamic acid, excitatory amino acid, to the inhibitory gamma-aminobutyric acid (GABA). GABA-secreting neurons and pancreatic beta cells (which may also secrete GABA as paracrine molecule) mostly express GAD [8]. Metabolic conditions such as hypoglycemia and hyperglycemia, ketoacidosis and hyperosmolarity may be also implicated, even if their mechanisms are minimaly understood. Moreover, epilepsy can be a feature of other autoimmune or inflammatory disorders (systemic lupus erythematosus, Hashimoto's tiroiditis, multiple sclerosis, etc.) [9].

Malformations of cortical development are the second most common cause of refractory partial epilepsy in adults after hippocampal sclerosis [10], poorly controlled in about 60% of patients [4]. Prognosis for epilepsy cannot be predicted based on early response to treatment [11], chromosomal abnormalities and malformations may also be associated with poor prognosis. Our patient was treated with CBZ, VPA, OXC without effect, only OXC 600 mg with LTG 400 mg provided complete remission for 8 years. We do not have any explanation to this, neither we can find any reason for relapse. When seizures restarted, treatment with LTG 400 mg and LEV 2000 mg/day decreased seizure frequency from several per day to 1 seizure per month.

In conclusion, BPS is more common than previously thought, it should be suspected clinically in any infant or child presenting with oromotor dysfunction, pseudobulbar signs, developmental delay and seizures. Patient can have only one type of seizures or only partial SE.

STATEMENT OF CONFLICTS OF INTEREST

The authors state no conflicts of interest.

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References

1. Jansen A, Andermann E. Genetics of the polymicrogyria syndromes. J Med Genet 2005; 42: 369–78.
2. Mavili E, Coskun A, Per H, Donmez H, Kumandas S, Yikilmaz A. Polymicrogyria: correlation of magnetic resonance imaging and clinical findings. Childs Nerv Syst 2012; 28: 905–9.
3. Kuzniecky R, Andermann F, Guerrini R. The epileptic spectrum in the congenital bilateral perisylvian syndrome. CBPS Multicenter Collaborative Study. Neurology 1994; 44: 379–85.
4. Takano T, Matsuwake K, Yoshioka S, Takeuchi Y. Congenital polymicrogyria including the perisylvian region in early childhood. Congenital Anomalies 2010; 50: 64–7.
5. Baykan-Kurt B, Sarp A, Gokyigit A, Tuncay R, Caliskan A. A clinically recognizable neuronal migration disorder: congenital bilateral perisylvian syndrome. Case report with long-term clinical and EEG follow-up. Seizure 1997; 6: 487–93.
6. Berquist K. Idiopathic pediatric epilepsy syndromes. Continuum Lifelong Learning Neurol 2007; 13(4): 106–20.
7. Schober E, Holl R. Epilepsy in children and adolescents with type 1 diabetes. Diabetes Voice 2011; 56(2): 43–4.
8. Vincent A, Crino PB. Systemic and neurologic autoimmune disorders associated with seizures or epilepsy. Epilepsia 2011; 52(3): 12–7.
9. Bien CG, Scheffer IE. Autoantibodies and epilepsy. Epilepsia 2011; 52: 18–22.
10. Papayannis CE, Consalvo D, Kauffman MA, Seifer G, Oddo S, D'Alessio L, et al. Malformations of cortical development and epilepsy in adult patients. Seizure 2012; 21: 377–84.
11. Margari L, Presicci A, Ventura P, Buttiglione M, Andreula C, Perniola T. Congenital bilateral perisylvian syndrome with partial epilepsy. Case report with long-term follow-up. Brain Dev 2005; 27: 53–7.

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ABIPUSIS PERISILVINIS SINDROMAS SU AUTONOMINIAIS PRIEPUOLIAIS IR AUTONOMINIAIS *STATUS EPILEPTICUS*: KLINIKINIO ATVEJO APRAŠYMAS

Santrauka

Šiame straipsnyje pristatome 38 metų amžiaus moterį, kuriai diagnozavome abipusį perisilvinį sindromą. Pacientei nuo vaikystės pasireiškė sutrikusi intelekto raida, pseudobulbarinis paralyžius, spastinė hemiparezė, vėliau – gydyti atspari židininė epilepsija su užsitęsusiais autonominiais priepuoliais. Ligonei taip pat diagnozuotas ir gydytas I tipo cukrinis diabetas. Pacientei kasdien pasireiškė tipiški autonominiai *status epilepticus*, trukę 3 valandas ir ilgiau: pykinimas, žiaugčiojimas, vėmimas, seilėtekis, išblyškimas, midriazė, šlapimo nelaikymas. Ilgus metus šie simptomai sieti su cukrinio diabeto komplikacijomis, tačiau priepuolių metu hipoglikemijų nebuvo registruota. Atlikę galvos smegenų magnetinio rezonanso tomografijos tyrimą, stebėjome abipusę polimikrogiriją Silvijaus vagose. Tarppriepuolinėje elektroencefalogramoje išryškėjo lėtos bangos dešinėje frontotemporalinėje srityje, priepuolių metu – smailios bangos dešinėje parietotemporalinėje srityje. Paskyrus gydymą okskarbazepinu ir lamotriginu, pacientei 8 metus priepuolių nebuvo. Vėliau, pasikartojus priepuoliams, gydymas koreguotas, paskirtas lamotriginas ir levetiracetamas, priepuoliai reikšmingai suretėjo.

Raktažodžiai: abipusis perisilvinis sindromas, autonominiai priepuoliai, epilepsija, diabetas, *status epilepticus*, polimikrogirija.