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Landau — Kleffner syndrome — epileptic aphasia in children — possible role of Toxoplasma gondii infection

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The association of unusual types of aphasia and epilepsy (Landau–Kleffner syndrome) has been described in three children. The children were 5 to 11 years of age and all have EEG abnormalities. Speech disorders appeared after epileptic seizures. No organic causes of the disease have been found in axial computed tomography. In all described cases the increased titer of IgG antibodies against Toxoplasma gondii has been observed. The authors suggest that the Toxoplasma gondii infection should be taken into account as a possible cause of Landau–Kleffner syndrome.

Since Landau and Kleffner [7] described in 1957 six children with aphasia and EEG abnormalities, the association of unusual types of aphasia and epilepsy has been recognized as a specific syndrome. Till 1986 more than 130 cases of epileptic aphasia have been reported [2].

The Landau–Kleffner syndrome is characterized by rapid onset of speech disorders, sometimes without any epileptic seizures and leads in relative brief period of time to profound or total loss of acquired language. In reported cases, the syndrome of acquired epileptic aphasia appeared between 4 and 7 years of age [1, 10]. In three-quarters of the cases the onset appeared before the age of 7 years. Prior to onset, the psychomotor development and language were normal. Usually results of neuroradiological examinations (arteriography, pneumoencephalography, CT scan) have failed to demonstrate any morphological abnormalities.

In 60% cases of Landau–Kleffner syndrome different kinds of behavioural disturbances can be observed [5].

EEG abnormalities are present, by definition, in all children with Landau—Kleffner syndrome. They are commonly bilateral and often have a predominantly posterior location. In most cases the EEG abnormalities occur in association with certain types of epileptic seizures, though not necessarily at the very beginning of the disorder. The course of the Landau–Kleffner syndrome is progressive at the very early period of the disease, but over the years the stabilization or even improvement of speech disorders can be seen. In previously described cases the long term follow-up was available for only a few cases.

In our paper we would like to present three cases of Landau–Kleffner syndrome, we were able to observe in Department of Child Neurology of Child Health Centre in Warsaw.

Case 1

A 5-year-old boy was hospitalized in Department of Child Neurology because of epileptic seizures and aphasia.

R. M. was born in 1982 after a normal pregnancy and labour, and weighed 2520 g at birth. He received an exchange transfusion in the first week of life. He sat up at six months, walked at 15 months. At the age of nearly 4 years appeared the first partial epileptic seizures and disturbances of speech expression. His speech began to deteriorate shortly afterwards, and paraphasia and verbal stereotypia were seen. The level of IgG immunoglobulin against Toxoplasma gondii in serum was elevated 1 : 1024. During the following 6 months this level increased to 1 : 8000. He received antiepileptic treatment, however, seizures took place 1—2 times a week.

At the age of 5 years he was admitted to Child Health Centre in Warsaw. The clinical neurologic examination was normal apart from aphasia. The mild mental retardation was observed. His speech remained deteriorated. He spoke with short sentences. With his back turned to the examiner he did not perceive spoken instructions, but he reacted on gestures indicated the task wanted. Examination of the CSF, blood, urine, fundus of the eyes all gave normal results.

EEG was severely abnormal with generalized paroxysms which shifted from side to side over both of the hemispheres. Spikes, sharp waves, and spike-wave complexes were registered. Primary hearing loss was excluded by tone-audiometry. There was slight abruptness in behaviour. CT scan did not show any evidence of structural brain pathology apart from slight cortical atrophy in parieto-temporal regions.

During the hospitalization antiepileptic treatment was changed and epileptic seizures ceased. Because of high titer of IgG against Toxoplasma gondii (1 : 32000 in Immunofluorescence Test), the treatment with Bactrim and Fansidar started. In a few weeks the obvious improvement of verbal expression was observed. Treatment and education continued mainly through the visual channel. He still had little comprehension of spoken language, but could understand 100 to 200 words and build these into short sentences of simple construction.

The boy was discharged from the hospital being under the control of Neurology Polyclinic Unit.

Case 2

A 11-year-old boy was admitted to Department of Child Neurology because of epileptic seizures and aphasia. No family history of epilepsy.

G.D. was born in 1976. Pregnancy, birth and early development was uncomplicated. He weighed 4500 g at

birth. Articulation, hearing and comprehension were normal. At the age of 10 appeared the first epileptic tonic-clonic seizure with the loss of consciousness, after which his speech became increasingly incomprehensible, and he began to show difficulty in verbal communication. Initially, he was hospitalized in local hospital, and later in Neurology Department of Child Health Centre. On admission, the neurological examination was negative, apart from disturbances of verbal expression and outbursts of rage with aggressiveness. There was no evidence of hearing loss and there was a normal response to pure tone audiometry. When given an animal sound he was able to point correctly to the picture of the appropriate animal. In executive speech he produced only isolated words.

EEG examination showed fast activity caused by antiepileptic treatment with several theta waves. Examination of CSF, blood, urine did not reveal any abnormalities. Axial computed tomography showed slight enlargement of anterior horns of lateral brain ventricules. Ophthalmic examination was normal.

During the hospitalization the titer of IgG antibodies against Toxoplasma gondii was found to be very high in serum (Immunohaemagglutination Test $> 1 : 4096$, Immunofluorescence Test $1 : 10240$, ELISA > 300 i.u.) and the child had been treated with Bactrim and Fansidar.

He was re-examined 2 months later. Epileptic seizures ceased. He showed a clearly subnormal auditory-verbal memory span, slight difficulties of articulation, and oral dyspraxia. He is still under the control of our Neurology Polyclinic Unit.

Case 3

R.N. born in 1976 was admitted to hospital at the age of 6 years.

He was born spontaneously after an uneventful pregnancy and weighed 4150 at birth. At the age of 7 months appeared epileptic seizures treated at local hospital. His speech development was normal. Short after 3 years of age he had a major tonic-clonic seizure. He received anticonvulsant treatment and no recurrence of such attacks has been observed. After the age of 4 his speech became increasingly incomprehensible, he stammered and in some months he was without language except for rare monotonous paraphasia.

At the time of admission he showed total loss of speech abilities. He seemed to understand gestures and pictures but not spoken commands. He showed considerable frustration if not understood and had occasional bouts of temper.

On examination he appeared to be physically normal but had both receptive and expressive aphasia. Hearing and visual comprehension were normal. CSF examination did not show any abnormalities. His EEG was diffusely abnormal and showed much seizure activity with spike-wave complexes 3-5Hz.

CT scan and angioscintigraphic examination were normal. Psychological

testing was performed and he was found to be mildly mental retarded. The titer of IgG antibodies against Toxoplasma gondii was at range higher than 1 : 2056 in Immunohaemagglutination Test and Bactrim and Fansidar were prescribed.

He was discharged from hospital but anticonvulsant medication and logopaedic exercises were continued.

The child has been just for 3 years under the control of our Polyclinic Unit. Since the hospitalization no epileptic seizures have been seen. The titer of IgG antibodies against Toxoplasma gondii decreased. His comprehension has further improved and he is able to say short complete sentences both in speech and writing. Now he is attending a school for aphasic children.

There is a preponderance of males over females among patients with Landau–Kleffner syndrome [2]. Most patients had been normal prior to onset of the syndrome. The peak of appearance seems to be around 3 to 5 years of age.

Etiology of Landau–Kleffner syndrome remains unknown. CT scan is almost always normal. In our cases we have not found organic causes in computed tomography either. Because structural damage is probably absent in most cases, some functional but persistent disturbance may explain the syndrome. According to Aicardi [1], epileptic activity in both temporal lobes, even if not manifested clinically, produces functional exclusion of the cortical areas that are the seats of repeated discharges, with resulting agnosia and secondary loss of speech. Accepting this hypothesis, the antiepileptic treatment would be useful in all cases, even if epileptic seizures did not appear. However, the relatively frequent occurrence of prolonged diffuse paroxysmal activity without any language disturbances does not argue in its favour. In some cases inflammatory nature of the disease was suspected. Worster-Drought [11] suspected that the disorder might be a form of low grade selective encephalitis, possibly of the autoimmune variety. Lou et al [8] reported inflammatory infiltrates in a biopsy specimen of temporal lobe in a patient with Landau–Kleffner syndrome. We have found increased titer of IgG antibodies against Toxoplasma gondii in all our cases. According to our observations the Toxoplasma gondii infection should be taken into account as a possible cause of Landau–Kleffner syndrome, even if the mechanisms of aphasia are still unknown. The structural damage of the cortical areas, which cannot be showed by computer tomography, may result in agnosia and secondary speech disturbances. During the treatment with Fansidar and Bactrim we have observed improvement of language. The hypothesis is unproved and needs more investigation.

In about half of the cases, seizures are the first manifestation of the Landau–Kleffner syndrome, but in 17—25% of patients epileptic history is negative [3, 4]. The frequency of epileptic seizures is variable. Sometimes they appear only once or twice in life, or several times a day. Usually

they well respond to antiepileptic treatment and no episode of status epilepticus is observed. Also in our patients fits disappeared during drug treatment. In Landau–Kleffner syndrome they seem to remit before adulthood, but because very few cases followed over many years, the ultimate prognosis is guarded [1, 9].

Abnormalities in the EEG are present in all cases of Landau–Kleffner syndrome. Spikes or sharp waves, or spike-wave complexes are generally bilateral with a predominance over the temporal and parietal regions. The typical feature is the variability of of the EEG abnormalities in time and intensity. Sleep, especially slow sleep, activates the record with diffusion of the paroxysmal discharges. EEG abnormalities tend to subside with increasing age. In 17 of 18 patients described by Dulac et al [6], in 1983 these changes disappeared by the age of 17 years.

Aphasia commonly starts with the first epileptic seizure, but sometimes speech disorders may be the first symptom of Landau-Kleffner syndrome. All our patients developed speech disorders after epileptic seizures. Because of an auditory verbal agnosia, patients are incapable of attributing a semantic value to acoustic signals and their consequent indifference makes them often appear as hypoacoustic or autistic children. In short time a profound or total aphasia may be seen. Initially, the course is progressive, but fluctuations, stabilization, or even improvement of speech over the years may occur. Among nine patients followed to adulthood by Mantovani and Landau [9], three had normal language, two had mild verbal difficulties, and three had significant persistent defects. One patient was not tested. Because long follow-up was available only for few cases, the prognosis is quite unpredictable. It tends to be more favourable in patients with relatively late onset, whereas onset before the age of 5 years is associated with a severe outlook [5]. In our patients, in case 2, the onset appeared at the age of 10 and the course was shorter.

The treatment of Landau–Kleffner syndrome consists of antiepileptic medication and logopaedic exercises. This treatment has been used in our cases and good results have been received. Some authors have given also ACTH and steroids.

Landau–Kleffner syndrome is heterogeneous entity, with different types of language disorder and quite different patterns of epilepsy and course. The purpose of this communication is to describe three new cases of Landau—Kleffner syndrome and call attention to Toxoplasma gondii infection as its possible cause.

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