

Case Report

Ohtahara syndrome progressing to West syndrome

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Received: 18 September 2020

Accepted: 13 April 2021

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ABSTRACT

West syndrome is a severe epilepsy syndrome composed of the triad of infantile spasms, hypsarrhythmia on electroencephalography (EEG) and mental retardation. It is sometimes due to the progression of a rare and fatal condition called early infantile epileptic encephalopathy (Ohtahara syndrome). Here we describe the case of a 3 year old male, who is a known case of West syndrome, presenting with recurrent breakthrough convulsions.

Keywords: Ohtahara syndrome, West syndrome, Breakthrough seizures, Rare disease

INTRODUCTION

Ohtahara syndrome, also known as early infantile epileptic encephalopathy (EIEE), is a rare epilepsy syndrome characterised by onset of seizures before three months of age. Its incidence is estimated to be 1/100,000 births in Japan and 1/50,000 births in the UK.¹ However, its incidence in India remains unknown. Prognosis is poor with death usually occurring in infancy (50% before age of 2).¹ In the series of Yamatogi and Ohtahara, 75% of patients developed West syndrome between 2 and 6 months of age and 12% subsequently developed Lennox-Gastaut syndrome.² The patients who live past the infancy suffer from significant mental retardation. Here, we describe an extremely rare case of a 3 year old male child who had Ohtahara syndrome in infancy that progressed to West syndrome and had multiple events of breakthrough seizures during the course of this disease.

CASE REPORT

A 3 year old male child presented with complaint of generalised tonic clonic seizures (GTCS) since 3 days. There were total 3 episodes, each lasting for about 15 minutes involving tonic and clonic movement in all four limbs and up-rolling of eyeballs. These episodes were

followed by post-ictal drowsiness. These episodes were not associated with tongue bite, micturition or defecation.

He was a known case of Ohtahara syndrome that had progressed to West Syndrome. He was born by an uncomplicated vaginal delivery at 39 weeks of gestation with birth weight of 3.4 kilograms. He had his first GTCS on his 14th day after birth. Sleep EEG on his 30th day after birth revealed bilateral, asymmetric and independent IED (interictal epileptiform discharges) with generalised discharges suggestive of EIEE. MRI (magnetic resonance imaging) on his 40th day after birth revealed CSF (cerebrospinal fluid) hygroma in bilateral fronto-parieto-temporal regions. Multiple medications like topiramate, clonazepam, levetiracetam and valproate have been tried with limited benefits. Since then, he has also had symmetrical tonic spasms that occurred in clusters and lasted a few seconds. His EEG at 11 months of age had typical hypsarrhythmic pattern and hence diagnosis of West syndrome was made. He had four episodes breakthrough seizures in the past with unknown triggers, each leading to hospital admission at the age of 4 months, 11 months, 16 months and 2 years. His family history was insignificant.

At the time of his most recent presentation, his vitals and the results of routine laboratory investigations were in the

normal range. However, he had severe acute malnourishment (SAM) and significant retardation in neurological development. His current episode of seizure was terminated by intravenous midazolam. He was then admitted in the nutritional rehabilitation centre where he received nutritional support and oral antiepileptic medications. He was discharged after 14 days with the prescription of medications including adrenocorticotrophic hormone (ACTH), valproate, levetiracetam, clonazepam, topiramate and trihexphenidyl. We explained the danger signs, nature of the disease and prognosis to the parents of the patient. His follow-up after one month was uneventful.

DISCUSSION

EIEE is one of the earliest presenting epileptic encephalopathy. Ohtahara et al described an epilepsy syndrome affecting very young infants with characteristic electro-encephalographic changes and termed it early infantile epileptic encephalopathy with suppression-burst. The syndrome is clinically characterized by early onset seizures presenting in 30% of cases within the first 10 days of life, by tonic spasms as seizure types (either generalized and symmetrical or lateralized) and with less frequency by focal and myoclonic seizures. The intercritical EEG findings show high voltage bursts of slow waves mixed with multifocal spikes, with phases of flat suppression.³⁻⁵ Mutations in several genes have been implicated, including ARX, STXBP1, KCNQ2, SLC25A22, and CDKL5.⁶⁻⁹ Structural cerebral anomalies are often detected by brain MRI, including cerebral asymmetry, hemimegalencephaly, lissencephaly and focal-cortical dysplasia.^{5,9} Hypotonia, severe developmental delay and respiratory problems are associated with these seizure types.

There is no cure for EIEE and patients require constant supervision and care. Antiepileptic drugs such as benzodiazepines, valproate, levetiracetam, zonisamide and phenobarbital have shown limited success in controlling seizures as has pyridoxine. A ketogenic diet has been reported to show some success in seizure control. In those with associated metabolic disorders, once these conditions have been treated there can be an improvement in the course of EIEE. Similarly, EIEE patients with certain structural abnormalities have benefited from surgical intervention, if unilateral.¹ Our patient was managed by valproate and levetiracetam. The prognosis is poor with severe intellectual delay and resistance to drug treatment and to ketogenic diet. Transition to West syndrome can be seen similar to that in our patient.

West syndrome or infantile spasm syndrome (ISS) is a rare form of epilepsy usually affecting children in early infancy. The peak age of onset is between 3 and 7 months; onset after 18 months is rare, though onset up to 4 years of age has been reported.¹⁰ Incidence of West syndrome in children ranges from 2 to 3.5 per 1000

thousand live births.¹¹ West syndrome comprises of characteristic triad of infantile spasms, developmental delay and hypsarrhythmia on EEG. In the typical manifestation, the seizures appear within the first year of life, usually between 4 and 6 months, with episodes of axial spasms of short duration occurring in clusters and at awakening. Psychomotor delay might precede, follow or coincide with the spasms. In rare occasions, the spasms might not manifest clearly and might express with less obvious signs, which are referred to as subtle spasms.

The intercritical EEG presents with a high voltage arrhythmia and asynchronous, slow and sharp waves in a chaotic distribution with multifocal spikes and polyspikes. Critical EEG might show a pattern of synchronous and symmetric spike-wave discharges.¹² Prognosis in most of the cases is severe, both for the control of seizures and for intellectual delay. The underlying causes of ISS are numerous. Symptomatic causes are the most common, being identified in about 60-70% of cases. Among these, the most frequent are the outcomes of hypoxic-ischemic encephalopathy and perinatal strokes, neurocutaneous syndromes including Sturge-Weber syndrome and tuberous sclerosis complex, structural brain disorders, malformative syndromes, inborn errors of metabolism and as recently shown immunologic factors. Gene mutations have been recognized as a causative event of West syndrome.¹²

There are multiple treatment options for ISS which can be used together or individually under different situations. Hormonal, pharmacologic, ketogenic diet and surgery are the eventual options for treatment. ACTH is widely used with a wide range of dosage, but the most carried out is 2-3 IU/kg/day. ACTH treatment is usually conducted for 3-4 weeks. Pharmacologic treatment is linked to the use of vigabatrin (50-125 mg/kg/day) alone or in association with other drugs. A ketogenic diet is recommended by several authors, firstly by Kossoff who reported good results in more than 45% of the children treated with this diet.¹³ Surgery is rarely used and restricted to cases of documented focal epileptogenesis and when pharmacologic treatment did not help.¹⁴ A similar management was done in our patient.

CONCLUSION

In West syndrome, breakthrough seizures can occur due to poor nutritional status, infections, stress. Thus, managing these factors help in adequate seizure control. As this disease has potentially no cure, prognosis and the nature of the disease has to be explained thoroughly to the parents/guardians of the patient. Trigger factors and danger signs should also be explained to the parents/guardians of the patient so that breakthrough seizures can be either prevented or promptly treated. Management of such a patient can be difficult in developing countries, especially in resource poor areas.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: Not required

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Cite this article as: Patel T, Patel S. Ohtahara syndrome progressing to West syndrome. *Int J Contemp Pediatr* 2021;8:941-3.