INTRODUCTION

Ohtahara syndrome (OS) or early infantile epileptic encephalopathy (EIEE) is a rare age related epileptic syndrome, starting in the first 3 months of life. The main seizure type consists of tonic spasm. EEG demonstrates a characteristic suppression burst (SB) pattern in both sleep and awake states (1,2,3,4).

OS has multiple presumed etiologies, although it is considered to be predominantly secondary to structural lesions of the cerebral cortex, particularly asymmetric lesions. The prognosis is poor with intractable seizures, psychomotor retardation and evolution to West syndrome (1,2,3).

I report a male infant with OS and asymmetric structural brain abnormalities. The infant was conceived through in vitro fertilization (IVF).

Case Report

This male infant was the only child of healthy non-consanguineous parents with an unremarkable family history. He was conceived through IVF after 18 years of infertility. Delivery was at 35 weeks of gestation via Caesarean section because of premature rupture of membranes and fetal bradycardia. Although the fetus passed meconium, Apgar scores were good. The initial physical examination was normal and he was not dysmorphic. Birth weight was 2250 gr and head circumference (HC) was 33 cm. At 3 hours of age the attacks began with slight jerking and stiffening of limbs and cyanosis. Recurrent attacks persisted for 48 hours. He was discharged after 14 days with phenobarbital but satisfactory control was not achieved. Persistence of seizures 10-20 times per day resulted in a new admission at 2.5 months of age. He had head lag with a HC of 36.5 cm. His plasma electrolytes, sugar, calcium, magnesium, BUN and liver function tests were normal. Blood ammonia, blood and urine aminoacids, arterial blood gas and TORCH study were normal. EEG demonstrated SB pattern (Figure 1). Brain CT scan demonstrated CNS dysgenesis and asymmetry of two hemispheres (Figure 2). Phenobarbital, phenoxytoin, nitrazepam and prednisolone were unsuccessful in complete seizure control, and ten days later he was discharged with primidone. Vit B6 and phenytoin. At 4.5 months of age his developmental progress had remained static. Seizures persisted and were characterized by head and eye deviation to right or left, cyanosis and tonic stiffening of limbs, then clonic movements of upper limbs especially on the right side. At the end of the attack, flexion of head and trunk like a sleep seizure occurred. He was again admitted. EEG demonstrated paroxysmal activity of high voltage slow wave discharges with intermittent normal background and no SB pattern (Figure 3). MRI and brain CT scan demonstrated diffuse white matter disorder in both hemispheres in T2, cortical atrophy and mild hemimegalencephaly (Figure 4).

Fig. 1. Suppression burst pattern at 2.5 months of age EEG; while asleep.
In addition to primidone and phenytoin, Vigabatrin (zorbil) was started that resulted in a decrease of seizures frequency. At 10 months of age, seizures of mixed types especially tonic spasm of limbs persisted. He had complete head lag and was severely hypotonic with exaggerated deep tendon reflexes. He had slight eye following movements. HIC was 44 cm and weight was 8700 gr. Brain sonography at 10 months of age demonstrated asymmetry of lateral ventricles (Figure 5).

Fig. 2. Brain CT scan at 2.5 months of age. UNS dygenesis and asymmetry is demonstrated.

Fig. 3. Normal background with intermittent high voltage slow wave discharges at 4.5 months of age EEG.

Fig. 4. Axial T2 - weighted magnetic resonance imaging at 4.5 months. Cortical atrophy and mild megalencephaly are demonstrated.

Fig. 5. Brain sonography at 10 months. Asymmetry of lateral ventricles is demonstrated.
DISCUSSION

In 1976, Ohtahara described an epileptic syndrome with an onset before 3 months of age. It is the earliest age dependent epileptic encephalopathies, which includes early infantile epileptic encephalopathy with SB (Ohtahara syndrome), West syndrome and Lennox-Gastaut syndrome (1,2).

No sex difference has been observed (1). The onset of seizure is early. Intrauterine onset of seizure has been reported (5). The main seizure type is tonic spasm, in addition partial seizures and hemiconvulsion are observed. Myoclonic seizures are rare. The most characteristic EEG finding in the SB pattern (1-4). SB is seen in both awake and sleep EEG. SB pattern is characterized by high voltage bursts alternating with nearly flat patterns at an approximately regular rate (Figure 3).

Neuroimaging reveals abnormal findings especially symmetric lesions. Phrenoplasty, cerebral dysgenesis, hemimegalencephaly, olivary interstitial dysplasia (2), pachygyria (6) may be observed, and metabolic screens are usually normal but a case of OS with cytochrome oxidase deficiency (8) and a case with glycine encephalopathy (9) was reported. The diagnosis of OS in this case was based on seizures during the neonatal period and refractoriness to antiepileptic therapy, SB pattern at EEG and the predominant tonic nature of the infant’s seizures. In early myoclonic epilepsy (EME) a major differential diagnosis of OS, the predominant seizure is fragmentary myoclonus and SB pattern persistence for a prolonged period (1-3). In this case SB pattern was not found at 4.5 months of age (Figure 3). In addition neuroimaging is normal at the beginning in most cases of EME and underlying pathologies are inborn error of metabolism especially nonketotic hyperglycemia (1,2). In this case metabolic screen was normal and imaging showed structural brain abnormalities from the early onset of disease. An interesting finding was history of IVF in this case, that has been reported in other case from Miller, SP and co-workers (7).

A relation between IVF and later occurrence of OS needs further observation. Seizures of OS are very intractable. Two cases are severely handicapped and many cases died in the early stages of the disease (1-4).

REFERENCES


