Case Report

Fetal valproate syndrome

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Antenatal use of anticonvulsant valproic acid can result in a well-recognized cluster of facial dysmorphism, congenital anomalies and neurodevelopmental retardation. In this report, we describe a case with typical features of fetal valproate syndrome (FVS). A 26-year-old female with epilepsy controlled on sodium valproate 800 mg/day since 3 years, gave birth to a male child with characteristic features of FVS. She also had 3 spontaneous first-trimester abortions during those 3 years. Sodium valproate, a widely used anticonvulsant and mood regulator, is a well-recognized teratogen that can result in facial dysmorphism, craniosynostosis, neural tube defects, and neurodevelopmental retardation. Therefore, we strongly recommend avoidance of valproic acid and supplementation of folic acid during pregnancy.

Key words: Anticonvulsant, pregnancy, sodium valproate

Introduction

There is an increased incidence of major and minor congenital abnormalities in infants born to epileptic mothers (6-7% compared with 2c3% in the general population).[1] Sodium valproate is a popular drug because of its broad range of anticonvulsant effects and relative freedom from sedative and behavioral effects. Exposure to valproic acid during first trimester can result in the constellation of minor craniofacial anomalies and major organ malformations in human fetuses. Here, we report a case of a 3-month-old baby with facial dysmorphism, as a case of fetal valproate syndrome (FVS) based on the phenotype and maternal use of valproic acid during the antenatal period.

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Case Report

A 3-month-old male child admitted with complaints of breathlessness since 3 days with fever. It was a full-term normal delivery with birth weight of 2.5 kg without any postnatal complications. Mother was known case of epilepsy and was controlled on sodium valproate 800 mg/day since 3 years. Before delivering this child mother had three spontaneous abortions within first trimester during those 3 years. On admission, the child was in congestive cardiac failure with heart rate-168/min, respiratory rate - 64/min. There were suprasternal and intercostal retractions. Child had severe failure to thrive with current weight 3.8 kg at 3 months of age despite on exclusive breastfeeding.

Features of facial dysmorphism [Figure 1] such as prominent metopic sutures, trigonocephaly, tall forehead, epicanthal folds, infraorbital groove, and medial deficiency of eyebrows, shallow philtrum, anteverted nares, and broad root of nose, low set ears, thin upper lip, and small mouth were present. Broad hands and feet, loose skin [Figure 2], and hypospadias were other features. Based on facial dysmorphism, congenital heart disease and hypospadias in the setting of maternal valproic acid consumption during antenatal period, diagnosis of FVS was made.

On auscultation, pansystolic murmur with loud pulmonary component of second heart sound were present. Bilateral basal crepitations and hepatomegaly were present due to congestive cardiac failure.

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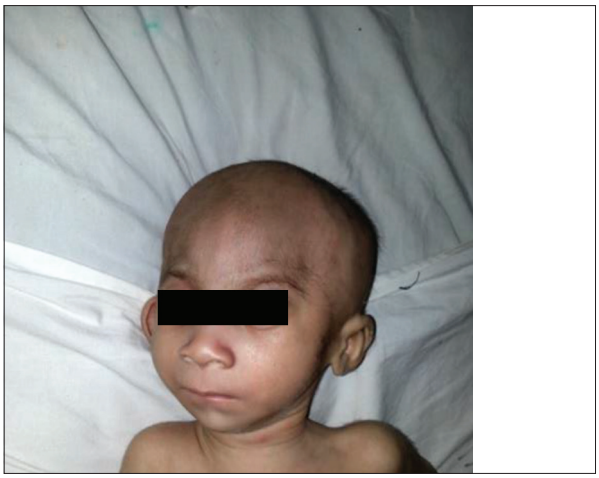

Figure 1: Prominent metopic suture

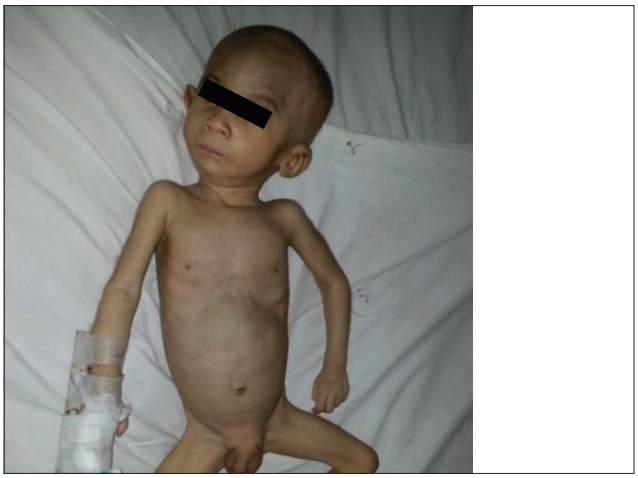

Figure 2: Fetal valproate syndrome

Two-dimensional echocardiography showed moderate atrial septal defect, ventricular septal defect with tiny patent ductus arteriosus with moderate pulmonary hypertension. Ophthal evaluation, ultrasonography abdomen, and X-ray spine were within normal limits.

Discussion

Valproic acid is a mood stabilizer and broad-spectrum anticonvulsant. Valproic acid crosses the placenta and is present in a higher concentration in the fetus than in the mother.[2,3] Complications of epilepsy and antiepileptic drug treatment, include stillbirths, prematurity, low birth weight, major and minor malformations, and cognitive delay later in life.

The term FVS was suggested by DiLiberti *et al.* in 1984, following several other case reports of the teratogenic effects of VPA, all of which documented similar major and minor anomalies.[4] The facial features seen in FVS are trigonocephaly, tall forehead with bifrontal narrowing, epicanthic folds, infraorbital groove, medial deficiency of eyebrows, flat nasal bridge, broad nasal root, antiverted nares, shallow philtrum, long upper lip and thin vermillion borders, thick lower lip, small downturned mouth.[2] Our patient had almost all facial features of FVS that has previously been described in literature.

The timing of exposure and the dose of the drug are important in influencing the outcome of pregnancy. First-trimester exposures are more likely to result in malformations as this is the main period of structural development in the fetus.[5] The efficacy of valproic acid as an antiepileptic drug cannot be disputed, but the extent of its teratogenic effects cannot be under-estimated either. Hence, the balance between the therapeutic effects of this drug and its teratogenic effects is critical in the management of women with epilepsy.[6]

High-dose folic acid (4 mg/day) is recommended during pregnancy,[7] starting at least 6 weeks preconception and continuing through the first trimester. We strongly recommend avoidance of valproic acid and supplementation of folic acid during pregnancy.

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