

Fetal Hydantoin Syndrome: A Case Report

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Abstract

A term baby born to an epileptic mother who was treated with Phenytoin until 10 weeks of pregnancy was born with multiple congenital anomalies and diagnosed to have Fetal Hydantoin Syndrome. Infants of mothers who have taken hydantoin during pregnancy have been found to have broad multisystem patterns of abnormalities, including mental retardation, craniofacial anomalies, nail and digital hypoplasia and prenatal onset of growth deficiency. The discussion aims to bring to attention the potential hazard of the use of hydantoin drug during reproductive age to all medical practitioners.

Key words: Congenital anomalies, epilepsy, fetal hydantoin syndrome, phenytoin.

The Case

A full term baby (41wks) was born to a G₃P₂L₁ mother with polyhydramnios having seizure disorder and was on Phenytoin for the last eighteen (18) months and which was continued till ten (10) weeks of pregnancy. Once pregnancy was confirmed, it was switched over to Carbamazepine. She was seizure free throughout the pregnancy.

The live born 3.6 kg male neonate was noted to have webbed-short neck with slanted palpebral fissures, a depressed nasal bridge, coarse profuse scalp hair, short nose with bowed upper lip and ocular hypertelorism (Fig. 1). The baby also had widely spaced small nipple with absent areola along with hirsutism. Further examination revealed a cleft palate, hypoplasia of nails (Fig. 2), hypoplasia of distal phalanges, abnormal palmar crease, and a single umbilical artery, depressed skin on sacral region, hypospadias and cryptorchidism. As suggested from the maternal history and the features of the newborn, the diagnosis of Fetal Hydantoin Syndrome was made. However, baby went into respiratory distress due to moderate birth asphyxia and expired on the 3rd day of life.



Fig. 1: Dysmorphic facies in Fetal Hydantoin Syndrome

Discussion

Phenytoin, formerly called diphenylhydantoin, was first discovered in 1938¹. It is an effective anti epileptic drug used in suppressing tonic-clonic and partial seizures in the adult age group. It is preferred to other anticonvulsant drugs due to its well defined therapeutic level in serum than other anticonvulsants, easier withdrawal, no addiction liability and no drug antagonism.



Fig. 2: Hypoplastic nails in Fetal Hydantoin Syndrome.



Fig. 3: Fetal Hydantoin Syndrome

Its teratogenic effects were first recognized in 1968². Phenytoin may induce folic acid deficiency in the epileptic patient by impairing GI absorption or by increasing hepatic metabolism^{3,4,5}. Therefore, the risk for having a baby with a spinal abnormality is increased. Some reports have shown that phenytoin is a transplacental carcinogen⁶. Tumors were reported to occur after in utero exposure to phenytoin in a few cases. Drug is thought to deplete already low levels of fetal vitamin K therefore suppressing the vitamin K-dependent coagulation factors. Taking oral vitamin K during last 2 months of pregnancy and the administration of Vit K to the newborn is proposed for the risk of hemorrhagic incidents⁷. In a study conducted from 1985 to 1992, 332 newborns exposed to phenytoin during the 1st trimester were studied. A total of 15 (4.5%) had major birth defects, including cardiovascular, spina bifida and hypospadias⁷. It is also known to cause cleft lip and cleft palate⁷.

Fetal Hydantoin Syndrome is characterized by broad nasal bridge, wide anterior fontanelle, low hairline, broad alveolar ridge, short neck, hypertelorism, microcephaly, cleft lip/palate, low set ears, epicanthal folds, ptosis, coloboma and coarse scalp hair. The limbs may have small or absent nails, hypoplasia of distal phalanges, altered palmar crease, digital thumb and dislocated hip¹. Mild to moderate growth deficiency, usually prenatal in onset is usually observed in children with the syndrome. Occasional borderline to mild mental deficiency is observed. However performance in childhood is usually better than that predicted in infancy⁸. Occasional cardiovascular abnormalities such as aortic valvular stenosis, coarctation of aorta, PDA, and septal defects and GI abnormalities such as pyloric stenosis, duodenal atresia and anal atresia as well as small widely spaced nipples, umbilical and inguinal hernia have been reported¹. Risks of delivering a child with congenital

defects are 2-3 times greater for women taking dilantin than for the general population. Increased risk could be caused by epilepsy, the drugs, or a combination of the two. It is thought that the drugs are the causative factor. Risks of child having full syndrome is about 10% and the risk for having some of the effects of the disorder is an additional 33%^{9,10}. However, a pregnant woman not taking Phenytoin or other antiepileptics have an increased risk of seizures during the period and risk fetal hypoxia.

Conclusion

Due to the documented pattern of malformations with the use of hydantoin, it is evident that the drug be discontinued when possible. But due to lack of evidence that other anti convulsants are any safer in pregnancy, it is important that the women of reproductive age group on hydantoin or any other anti convulsants be properly counseled about the risks of continuing the drug during pregnancy and the risk benefit be analyzed before any decision is taken.

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