CASE REPORT

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A Suspected Case of Patau Syndrome in an Eight-week-old Male Infant: A Case Report and Review of Literature

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Abstract

Patau syndrome is the third most common autosomal trisomy. It is the least common and most severe of the viable autosomal trisomies. This chromosomal disorder has a characteristic phenotype consisting of multiple congenital anomalies. We report an eight-week-old male infant who is the first child of a non-consanguineous marriage born at term with multiple congenital anomalies. He had an absent left eye and a sunken right eye, a cleft lip, a cleft palate, a mid-facial hypoplasia and a flat occiput. A cranial CT scan showed gross dilatation of both lateral and third ventricles with the absence of the septum pellucidum and fused frontal lobes. There was also marked attenuation of the cortical mantle.

Keywords: Anophthalmus, Congenital Brain Malformations, Hydrocephalus, Patau syndrome, Trisomy 13.

Introduction

Trisomy 13 or Patau syndrome is the third most common autosomal trisomy but it is the least common and most severe of the viable autosomal trisomies.[1] This chromosomal disorder has a characteristic phenotype consisting of multiple congenital anomalies.[2] The incidence of the condition is 1 in 8000-12000 live births with a median survival of 2.5 days and only 1 in 20 surviving longer than six months. In a systematic review and meta-analysis of 60 African studies conducted between year 2000 and 2021, the prevalence of Patau syndrome among babies born with congenital anomalies ranged from 0.26 to 5.8 percent with a pooled prevalence of 0.92 percent.[3,4] The sex ratio of Patau syndrome at birth is skewed toward females, presumably because of decreased survival among males.[2] Central nervous system malformations are important prognostic factors for the survival of a child with Patau syndrome.[5] We report an 8 - week-old infant with suspected Trisomy 13.

Case Presentation

The male patient was the first child in a non-consanguineous marriage. The mother was a 29-year-old who booked the pregnancy at 16 weeks gestational age. She had regular antenatal visits and took the prescribed medications. There was no history of tobacco smoking, consumption of alcohol, or use of herbal medications or anti-convulsant medications during pregnancy. An obstetric ultrasound scan done at 28 weeks gestational age revealed hydrocephalus. The baby

was delivered *per vaginum* and weighed 2.93kg. At birth, he was lethargic and centrally cyanosed. He had abnormal facial features including a small head, ocular hypotelorism, low-set ears, and a flat occiput. He also had a cleft lip, cleft palate, microphthalmos of the right eye, and left-sided anophthalmos. The occipitofrontal circumference (OFC) was 38cm while the body length was 47cm.

The baby was admitted into the Special Care Baby Unit. He developed seizures on the second day of admission. A transfontanelle ultrasound scan revealed hydrocephalus while echocardiogram revealed a structurally normal heart. Requested cranial computerized tomography was not done due to financial constraints. The baby received intravenous antibiotics, acetazolamide and phenobarbitone for seizure control. A multidisciplinary team approach was instituted; this included the neurosurgical, maxillofacial and ophthalmology teams. Seizure control was achieved within the first week of life and he was subsequently discharged on the eighth day of life on oral acetazolamide and phenobarbitone.

When reviewed at the neonatology clinic at eight weeks of age on a follow-up visit, he was noticed to have developed macrocephaly, fever and convulsions which were noticed two weeks prior to presentation. The child cried inconsolably and was highly irritable with craniofacial disproportion in favour of the cranium and a tense anterior fontanelle. The OFC was 40cm (85^{th} centile) and the body weight was 3.4kg. Examination of other systems was essentially normal. A tentative diagnosis of meningitis in a child with suspected Patau syndrome was made.

Cranial CT scan revealed hypoplasia of cerebral hemispheres with the fusion of both frontal lobes. The septum pellucidum and the majority of the body and rostrum of the corpus callosum were absent. There was marked dilatation of the fused lateral ventricles and bifrontal subdural CSF hygroma. The fourth ventricle was normal. A radiological diagnosis of holoprosencephaly (alobar) and non-communicating hydrocephalus was made. An ocular scan showed microphthalmos of the right eye and anophthalmus of the left eye with features of persistent hyperplastic primary vitreous on the right eye. CSF analysis showed a relative hypoglycorrhachia. Karyotyping was not done due to lack of funds. Percutaneous ventricular decompression using a 21 G needle was done and CSF samples were sent for analysis. Intravenous Ceftriaxone was commenced, and acetazolamide and phenobarbitone were continued as previously prescribed. Further options of management including CSF diversion by the neurosurgical team and ocular prosthesis by the ophthalmologist were discussed with both parents. Genetic counselling was carried out and the parents were informed of the poor prognosis. The parents ultimately refused surgery and the patient was discharged home on the tenth day of admission to be followed up at the various clinics.

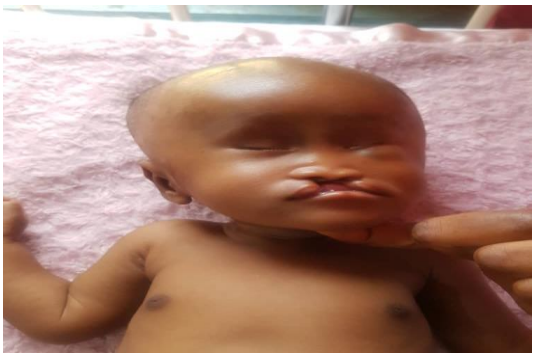

Figure 1: The patient demonstrating the ocular anomalies and cleft deformity at eight weeks.

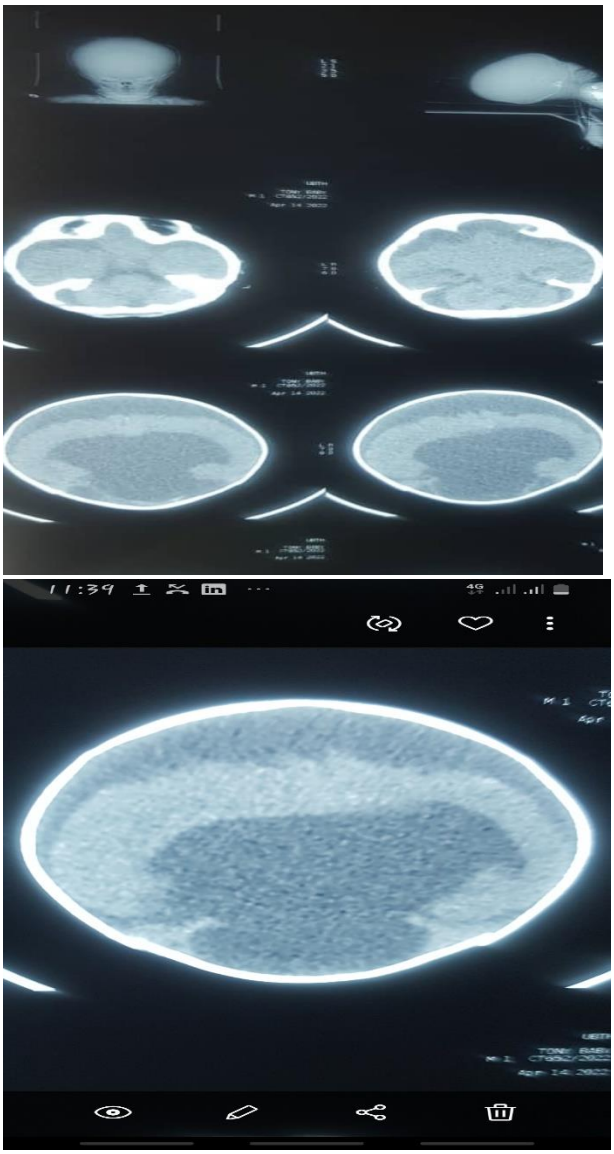

Figure 2: Imaging of the brain (CT scan) showing dilatation of both lateral and the third ventricles, hypoplastic cerebral hemisphere with the fusion of both frontal lobes.

Discussion

Trisomy 13 (Patau syndrome) is an important cause of aneuploidy characterized by multiple congenital anomalies with a cardinal triad of orofacial clefts, microphthalmia, and postaxial polydactyly of the limbs. It has an estimated worldwide liveborn prevalence (after the advent of prenatal diagnosis) of 1/8000 – 1/10000.[6] African studies report prevalence ranging between 0.26% and 5.8%.[3] The majority of cases (80%) are caused by the presence of an additional chromosome 13 due to non-disjunction in maternal meiosis.[1] Between 10% and 20 % of cases are due to unbalanced Robertsonian translocation.[7] Normal development requires two copies of most of the human genome and the presence of a third copy of an autosome is generally lethal to the developing embryo.

The chromosomal anomalies severely disrupt normal development resulting in miscarriages, stillbirth or early neonatal deaths. Structures such as the central nervous system and the heart are sensitive to chromosomal imbalance. The clinical features widely vary with severe mental deficiency as a consistent feature. Growth deficiency is also common and is related to aneuploidy as well as to poor feeding associated with orofacial clefts, gastrointestinal malformations and gastro-oesophageal reflux. Structural malformations of the central nervous system (CNS), including the holoprosencephaly spectrum, cerebellar hypoplasia and hypogenesis of the corpus callosum are known and occur in 76% of patients.[5] The presence of CNS malformations results in facial defects such as cleft lip and palate, microphthalmia, anophthalmia, and hypotelorism. Cardiac malformations are present in up to 80% of patients with atrial septal defect, patent ductus arteriosus and ventricular septal defect reported as the most common anomalies.[5,6] Abnormal cysts in the kidneys may also be seen.[8] Other anomalies include limb defects (postaxial polydactyly, oligodactyly, omphalocele, and cutis aplasia of the scalp.[5] Central apnoea, related or unrelated to CNS malformations, may explain the increased mortality rate, with 90% of affected patients succumbing to the condition before one year of age.[6]

The index patient had some of the classical triad of cleft lip and palate, and microphthalmia. Other features seen included ocular hypotelorism, low-

set ears, and holoprosencephaly. The presence of a CNS malformation portended a poor prognosis in this case. This patient had a cleft lip and cleft palate, as individuals with CNS abnormalities typically have facial deformities. Studies have suggested that patients with combined CNS and heart defects have worse outcomes. Cytogenetic studies are important to confirm the diagnosis of a child with suspected Patau Syndrome and to aid genetic counseling.[9] However, this intervention was not done in the index patient due to parental financial constraints. A prenatal ultrasound scan may identify congenital malformations *in-utero* which can aid genetic counselling and assist the parents with making a decision on the option of termination of pregnancy. However, the birth of a child with a congenital anomaly not previously identified from prenatal ultrasound can cause severe distress and psychopathology to the mother and other members of the family. Hence early clinical recognition of Trisomy 13 at birth is essential to optimize guidance for the care of the child and the family. Avoiding expensive therapeutic or diagnostic interventions may be essential in our environment where access to medical care and investigations is limited by funds as seen in the index patient.

There is no specific treatment for Patau syndrome and it is managed on a case-by-case basis. Surviving beyond the first few days of life is dependent on their specific symptoms and needs. Genetic counselling is beneficial in terms of understanding the diagnosis and its implications as well as supporting the family in making particularly difficult decisions for future care and family planning. Intensive therapy is controversial due to the universal poor prognosis of patients despite treatment. The cause of death in Patau syndrome may be primary apnea, regardless of the presence of a CNS abnormality. Recurrent apnea may be related to the common occurrence of a cyanotic heart defect, pulmonary hypertension, congestive heart failure and aspiration pneumonia. It is, therefore, recommended that facilities for postoperative ventilation should be made available when these patients undergo surgery. Multiple studies have detailed a poor prognosis with a median survival of 7 – 10 days in live-born patients and 90% do not survive to one year. Survival is often attributed to mosaicism and the absence of severe presence of malformations.[10] Mosaicism of Trisomy 13 is a rare genetic variant with milder features and hence longer survivals. Patients with Patau Syndrome who make it past infancy usually have seizures, severe psychomotor dysfunction, failure to thrive, and intellectual incapacity.[11]

Conclusion

Trisomy 13 can be clinically diagnosed based on the clinical phenotype of the affected infant. Referral to a genetic counselling clinic is advocated whenever possible, although care of the affected infant and support for the family can and should be offered by all healthcare practitioners.

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