An Unusual Case of Perinatal Tuberous Sclerosis

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ABSTRACT

We report a case of a neonate who presented to us with multiple rhabdomyomas of heart, cortical tubers in the brain and skeletal anomalies such as Pierre Robin sequence, bilateral clubfoot and lower small bowel obstruction. Though a diagnosis of neonatal tuberous sclerosis was made, the association of skeletal anomalies and intestinal obstruction was a rare and unusual finding.

Key words:
Neonate, Pierre Robin sequence, rhabdomyoma, tuberous sclerosis complex

INTRODUCTION

Rhabdomyoma is the most common cardiac tumor in fetal life, though a rare condition.[1,2] Cardiac rhabdomyomas (CR) are closely associated with tuberous sclerosis complex (TSC). Tuberous sclerosus (TS) is an autosomal dominant condition involving multiple organs such as heart, brain, eye, kidney and skin. CRs may precede the skin, neurological and radiological signs of TSC by months or even years.[3] Our case had cardiac and neurological manifestations. However, association of craniofacial malformation such as Pierre Robin sequence (PRS), clubfoot and intestinal obstruction with TS has not been described earlier. This is probably the first case where TS and PRS have been described in the same patient and that too in a neonate.

CASE REPORT

The present case report is about a 3-day-old late preterm (36 weeks of gestational age at birth) male neonate, who was referred to us from an outside institution with complaints of bilious vomiting and antenatally detected multiple cardiac tumors. The baby was born out of a non-consanguineous marriage to a 29-year-old primigravida. The mother had received regular antenatal care. Antenatal ultrasonography done at 30th week was essentially normal except for bilateral clubfoot. Routine obstetric examination done on 35 6/7 week revealed fetal bradycardia. Fetal echo study was done which showed multiple cardiac tumors suggestive of rhabdomyomas. Two homogenous echogenic tumors of size 7 mm and 4.5mm were noted in the ventricular septum. Other locations were medial papillary muscle of mitral valve and right ventricular free wall. The tumors were non-obstructive. Emergency cesarean section was done and a male baby weighing 2.5 kg was delivered. Apgar scores were normal at birth. However, feeds could not be started as he developed abdominal distension and bilious vomiting on day 1. The infant was transferred to us on day 3 for further management. Physical examination was remarkable for the presence of PRS (micrognathia, glossoptosis and cleft palate). Furthermore, bilateral clubfoot was noted [Figure 1]. Two-dimensional echocardiogram confirmed antenatal echo findings [Figure 2a]. Further, multiple ectopic beats were noted during echocardiography. Clinically, bradycardia and irregularly irregular heart rate was present (heart rate varying between 80 and 110/min). Premature atrial complexes were seen on the electrocardiogram. Interestingly, cardiac rhythm became regular by day 9 without any intervention. X-ray erect abdomen showed multiple air-fluid levels suggestive of lower small bowel obstruction and a barium enema study revealed microcolon probably indicating an atretic lesion in the distal small bowel. The infant developed multifocal clonic seizures on day 5. Nature of convulsions became mixed on day 6 with predominantly myoclonic type and was controlled with phenobarbitone and levetiracetam. Computed tomography scan - brain showed subependymal nodules and cortical tubers [Figure 2b]. A diagnosis of TS was made in view of CR and cortical tubers in brain.

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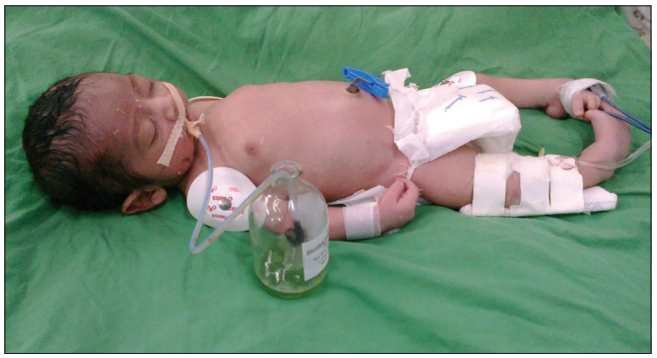

Figure 1: Bilateral club foot and bilious gastric aspirates

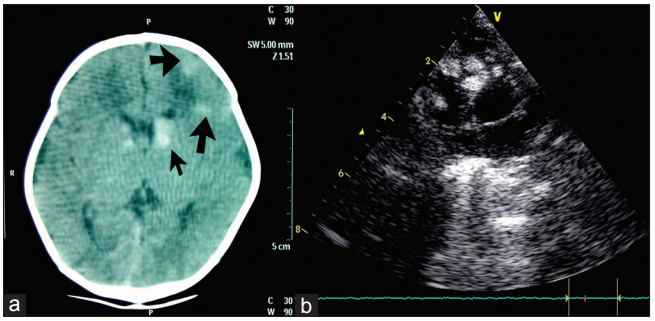

Figure 2: Apical four chamber view of two-dimensional echocardiogram showing multiple rhabdomyomas of heart in the mid and apical interventricular septum (a). Multiple subependymal nodules and cortical tubers (shown by black arrows) in computed tomography scan of brain (b)

However, no family history of TS was forthcoming. There were no skin lesions. The parents did not give consent for explorative laparotomy and took discharge against medical advice on day 10 of life. Lack of facilities and logistic reasons precluded the genetic work-up of our patient.

DISCUSSION

Fetal CR is a rare condition, but the most common cardiac tumor in fetal life accounting for 60-86% of fetal cardiac tumors.[1,2] Though CRs have a natural history of spontaneous regression, prognosis is guarded as it is very frequently associated with TS which is inherited as an autosomal dominant trait with variable penetrance and prevalence of 1/6,000 people.[4] Clinical manifestations include seizures, skin lesions and hamartomas affecting multiple organs such as heart, brain, eye and kidneys.

The first signs of TS can be picked up on routine prenatal ultrasound screening where lesions are found in heart (rhabdomyomas) and brain (cortical tubers, subependymal nodules and subependymal giant cell astrocytoma).[5] With advancement in fetal echo and magnetic resonance imaging, prenatal diagnosis can be made earlier. The exact incidence of CRs coexisting with TS in fetuses is unknown. A recent meta-analysis showed that the incidence of TS was 64% in fetuses with CRs.[5] Furthermore, a positive family history of TS and multiple cardiac tumors were more likely to be associated with TS. A 42 year retrospective review of 70 patients consisting of 43 fetuses and 27 neonates with TS showed that CRs comprised 33% of pathological findings, those of central nervous system origin 47% and renal cystic disease 13%.[6] Skeletal anomalies like clubfoot and cleft palate are not usually associated with TSC and have been reported in isolated cases.[7,8] Our case is unusual in having bilateral congenital talipes equino varus along with PRS and small bowel obstruction. PRS has been associated with nearly 40 varieties of syndromes and chromosomal anomalies, but the underlying pathogenesis of this disease has still remained enigmatic.[9] Recently a genetic association has been identified between a neurocutaneous syndrome (neurofibromatosis type 2) and PRS.[10] The present case is also a neurocutaneous syndrome with PRS as an additional finding, but genetic work-up could not be done.

When TS is diagnosed in the perinatal period, it is associated with high incidence of morbidity and mortality. However, it is observed that survival rates of patients diagnosed antenatally was practically the same as for those after birth.[6] CR are known to have a benign course. It has been reported that more than 80% of CRs have complete resolution within infancy and early childhood.[11] However unlike CRs, cerebral lesions do not regress, but instead progressively increase in size and number. Our knowledge of natural history of CRs in utero is limited and meta analytical approach to the prenatal management of TS is lacking.

The age-dependent nature of the characteristic features of TSC has presented challenges for the diagnosis in the first year of life.[12] Hypomelanotic macules may be present in infancy, but facial angiofibromas and Shagreen patches usually do not occur until puberty and renal angiomyolipomas occur in adults. Cortical and subcortical tubers develop before birth and are responsible for the epilepsy. CRs may be the earliest finding of TSC in utero and may precede the detection of the brain or kidney lesions and can be symptomatic in the fetus and newborn. Fetal rhabdomyoma can become a prenatal echo marker of TS.[11,13]

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