Definitive Antenatal Diagnosis of Tuberous Sclerosis in Fetus -A Case Report

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ABSTRACT

Tuberous sclerosis (TSC) is a rare genetic disease that causes benign tumors to grow in the brain and on other vital organs. It commonly affects the central nervous system (CNS). In addition to the benign tumors that frequently occur in TSC, other common symptoms include seizures, mental retardation, behavioral problems and skin abnormalities. TSC may present at birth, but signs can be subtle and full symptoms may take some time to develop. Definitive antenatal diagnosis is very rare.

Keywords: Tuberous Sclerosis Complex, Bourneville Disease, Epiloia

INTRODUCTION

Mrs. BS a 24 yr old G3P1L1A1 (gravida 3 para1 living 1 abortion1) presented for antenatal care with 9 months of amenorrhea. Her general & physical examination findings were normal. Uterus was term size with single live fetus in longitudinal lie with cephalic presentation. Routine level II ultrasound examination revealed normal fetal biometry with presence of multiple focal hyper echoic cardiac lesions involving right ventricle & right atrium of the fetus (picture1). Diagnostic consideration of rhabdomyoma of the heart was made. She was referred for level III fetal ultrasound. It showed borderline symmetric macrosomia, unilateral left lateral ventriculomegaly & fetal color duplex Doppler echocardiography revealed normal fetal chambers with normal function & showed the presence of a 1.7 X 1.1 cm hyper echoic, solid space occupying lesion in the apex of the right ventricle . Possibility of tuberous sclerosis was considered with these findings. Fetal / neonatal magnetic resonance imaging (MRI) was suggested. After taking informed consent from the patient & relatives fetal brain MRI was done. Multiple different sized circumscribed discoid areas of hypo intensities were noted outlining the lateral

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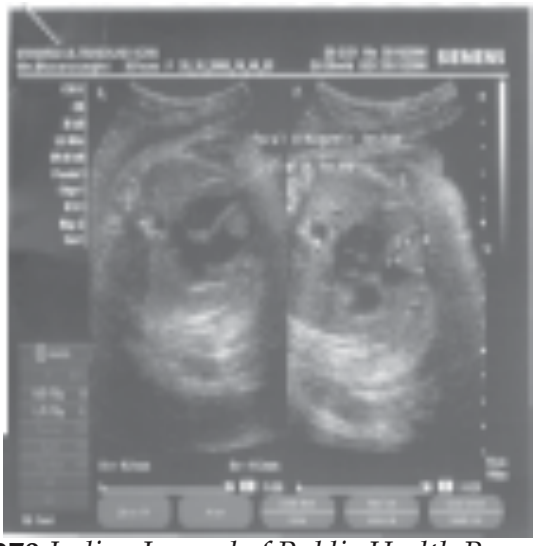
ventricles & projected into them from their lateral ependymal silhouettes (picture3&4). A solitary focal lesion across the left fronto parietal sub cortical region was also noted. The cerebrum was otherwise normal. Final diagnosis of Tuberous sclerosis was made based on the USG & MRI findings .Mrs. BS underwent emergency Lower segment cesarean section (LSCS) for cephalo pelvic disproportion (CPD). A live term male weighing 3.5 kg was extracted on 14/11/06 (picture2). Baby cried well after birth. Baby was seen both by pediatric cardiologist & neurosurgeon who advised regular follow up of the baby. Baby was doing fine till 9 months with normal milestones. Baby developed generalized tonic clonic seizures at 10 months.MRI brain was done which showed the same findings as that of antenatal MRI of fetal brain. Baby died at the age of 13 months.

Fig. 1. USG showing rhabdomyoma in the apex of Rt ventricle



 DISCUSSION

Fig. 2. New born fetus without any cutaneous TSC stigmata

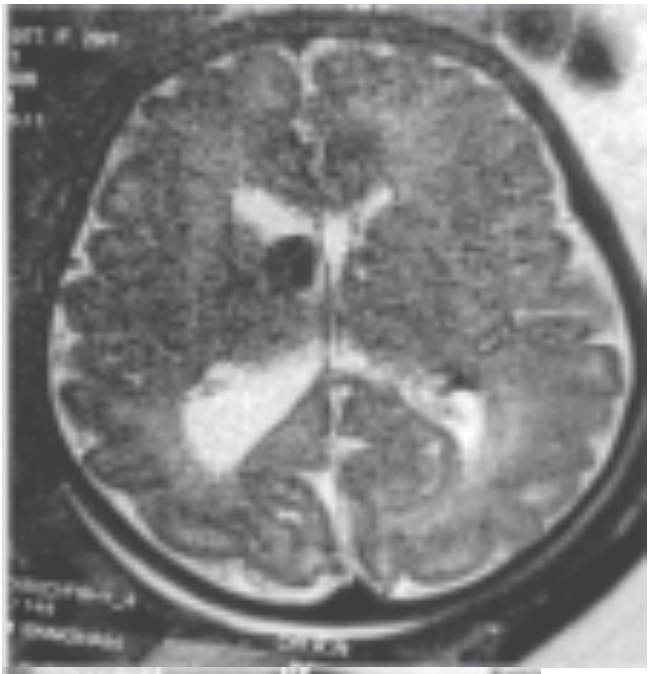
Fig. 3. MRI fetal brain showing subependymal nodules

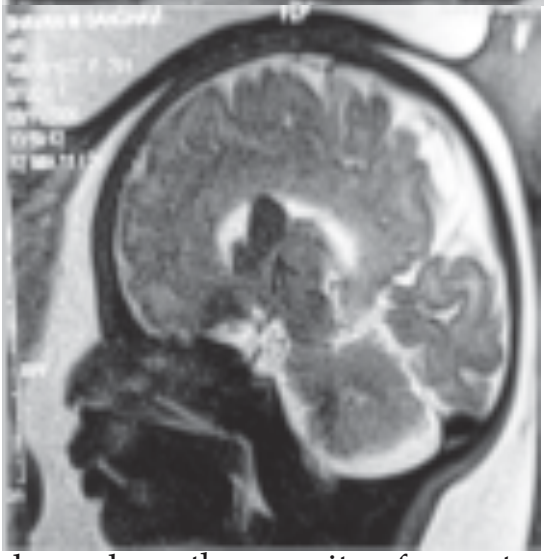
Fig. 4. Sagittal fetal MRI brain showing lateral ventriculomegaly with nodules

Tuberous sclerosis is a genetic disorder with an autosomal dominant pattern of inheritance, and penetrance is variable. A 1998 study estimated total population prevalence between about 7 and 12 cases per 100,000.More than half of these cases go undetected.[1] So far it has been mapped to two genetic loci,TSC1 and TSC2. TSC1 encodes for the protein hamartin located on chromosome 9q34 and was discovered in 1997.[2] TSC2 encoding for the protein tuberin is located on chromosome16p13.3 and was discovered in 1993.[3] TSC2 has been associated with a more severe form of TSC.[4] It affects cellular differentiation and proliferation, which results in hamartoma formation in many organs (eg, brain, skin, eye, kidney, heart). Von Recklinghausen first described tuberous sclerosis in 1862. Bourneville coined the term sclerose tuberuse. It commonly affects the CNS. In addition to frequently occurring benign tumors, other common symptoms include seizures, mental retardation, behavior problems and skin abnormalities. The term tuberous sclerosis complex (TSC) is now widely used, emphasizing the variegated nature of its manifestations. TSC may be present at birth, but signs of the disorder can be subtle & full symptoms may take some time to develop. Some individuals are severely affected & some have very few features. No racial & sex predilection has been noted. Most patients are diagnosed between 2 & 6 years of age. Most individuals present with parental concern about small raised tumors on the child's face.

The criteria for diagnosing TSC have recently been revised. Diagnostic Criteria for Tuberous Sclerosis Complex[5] - Major features are facial angiofibroma, non traumatic ungula/periungual fibromas, hypomaelanotic macules, shagreen patch, multiple retinal nodular hamartoma, cortical tubers, subependymal nodule, giant cell astrocytoma, cardiac rhabdomyoma, lymphangiomyomatosis& renal angiomyolipoma. Minor features are multiple randomly distributed pits in dental enamel, hamartamatous rectal polyps, bone cysts, cerebral white matter radial migration lines, gingival fibromas, non renal hamartoma, retinal achromic patch, confetti skin lesions & multiple renal cysts. The definite TSC is diagnosed by the presence of 2 major features or 1 major plus 2 minor features. Preimplantation diagnosis is not widely available.

There is no cure for TSC. Treatment is mainly symptomatic. The prognosis for individuals with TSC





depends on the severity of symptoms, which range from 2. mild skin abnormalities to varying degrees of learning disabilities and epilepsy to severe mental retardation, uncontrollable seizures, and kidney failure. However, with appropriate medical care, most individuals with 3. the disorder can look forward to normal life expectancy.[6] In 2002, treatment with rapamycin was found to be effective at shrinking tumours in animals.

This has led to human trials of rapamycin as a drug to 4. treat several of the tumors associated with Tuberous Sclerosis. It has shown to decrease the size of astrocytomas associated with TSC[7]. It is hoped current research will improve the genetic test for TSC and lead

to new avenues of treatment, methods of prevention, 5. and ultimately, a

cure. This case is reported as Tuberous Sclerosis Complex is rare & very rarely definitive antenatal diagnosis of TSC is made. 6.

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