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Original Research Paper

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MATERNAL TUBEROUS SCLEROSIS WITH FETAL CARDIAC RHABDOMYOMA – A CASE REPORT

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ABSTRACT Tuberous sclerosis is a multisystemic, autosomal dominant neurocutaneous disorder of hamartoma formation affecting multiple organ systems and hence adversely affecting the maternal and fetal outcome. We report a case of maternal tuberous sclerosis with fetal cardiac rhabdomyoma detected in utero at 22 weeks but presented at 39 weeks of gestation. We conclude that Maternal or Fetal tuberous sclerosis deserves careful monitoring and evaluation so that the patients can be counselled regarding its life threatening complications to the baby and make informed decision regarding continuation of pregnancy.

KEYWORDS : Maternal Tuberous sclerosis, Fetal cardiac rhabdomyoma , complicated pregnancy

INTRODUCTION:

Tuberous sclerosis complex (TSC) also known as Epiloia or Pringle-Bourneville phacomatosis is an autosomal dominant neurocutaneous disorder of hamartoma formation affecting multiple organ systems.[1,2,3] The name tuberous sclerosis is derived from the characteristic tuber like growth occurring in the brain which calcifies with age and become sclerotic. [4] About 30 percent of cases have Vogt's triad comprising of epilepsy, mental retardation and adenoma sebaceum.[5,6]

It is a rare genetic disease with an estimated incidence of 1 in 6000 to 1 in 10,000 live births.[4,7] Two genetic loci have been identified in Tuberous Sclerosis Complex; tuberous sclerosis complex-1 (chromosome 9q34) and tuberous sclerosis complex-2 (chromosome 16p13). It can also occur through gonadal mosaicism.[1]

Tuberous sclerosis can adversely affect the maternal and fetal outcome by involving cardiac or central nervous system. Pregnant women may have deterioration of renal function, develop preeclampsia, hydrops, intrauterine growth restriction, intrauterine demise and preterm labor.[1,4]

It is observed that up to 80 percent of patients with tuberous sclerosis have cardiac rhabdomyomas.[1] This most commonly diagnosed cardiac tumor represents the earliest and the most important clinical sign of the disease in utero with reported incidence of 0.002–0.25 percent in autopsy series and 0.08 percent in liveborn infants.[1] Although they may regress after delivery, a high rate of intra-uterine demise has been reported [1]

Rhabdomyomas may be visualized as early as 22 weeks of gestation. High gestational hormone concentrations are implicated with rapid intra-uterine cardiac tumor growth.[1] It is observed that most rhabdomyomas undergo spontaneous regression beyond the third trimester or in early postnatal period making post-partum surgery unnecessary in cases of normal cardiac function.[8] But some large masses can cause haemodynamic obstruction, heart failure, cardiac dysrhythmias ultimately resulting in demise.[1,2]

CASE REPORT:

A 27 year second gravida was referred to-Obstetrics casualty GMCH-Nagpur at 39 weeks of gestation with antenatal ultrasonography scan showing fetal cardiac rhabdomyoma with pericardial effusion. Past obstetric history revealed that she underwent caesarean section at 38 weeks for grade 4 placenta previa 1 and 1/2 years back. She had delivered an intrauterine dead baby with no external anomalies. No investigations were done to find the cause of IUD.

Her history revealed that she had 1 episode of convulsions at the age of 11 for which she was on antiepileptic drugs for 3 years. Name of the antiepileptic could not be remembered. Patient had dropped out of school after 7th grade as she could not cope up with academics.

On examination, the patient had multiple easily discernible round to oval, brown, firm papular skin lesions all over her face (adenoma sebaceum). The lesions were not associated with bleeding, itching, pain or change in size.(figure1)She also had 'Shagreen patch' (hyperpigmented plaque) over left lumbar area and subungal fibromas (figure 2). No other family member had similar signs or symptoms and her family was not aware of this condition.

Her Chest and skull radiograph were normal. USG of abdomen revealed multiple small angiomatous lesions in both kidneys with no necrotic changes. Both pelvi-calyceal system, liver, spleen and adrenals appeared normal. Computed tomogram (CT) of brain showed Multiple calcified nodules along the sub ependymal lining of bilateral lateral ventricles without perilesional oedema ,largest measuring 7.5*7.1 mm on right side and calcified granuloma of size 4*4 mm in left medial temporal lobe(figure 3) .Fundoscopy and echocardiography of the mother were normal.

The patient was registered at 15 weeks in a nearby PHC where she underwent routine blood investigations. She had a Level II ultrasonography done at 22 weeks which raised the suspicion of a fetal cardiac tumor (echogenic lesion involving interventricular septum and lateral wall of left ventricle) with no haemodynamic changes. She was explained about the rhabdomyoma and she chose to continue this pregnancy. No chromosomal tests were done in this pregnancy. Another scan done at 36 weeks showed this tumour of 38*34mm involving left ventricular wall and intraventricular septum. Colour Doppler did not suggest any obstruction in the outflow pattern of left ventricle. No other gross fetal anomalies like cerebral lesions were noted in the antenatal USG. She was referred to GMCH-Nagpur for further management where she was evaluated and an elective caesarean section was done at 39 weeks 4 days of gestation. She delivered a live female baby weighing 2,800 g. There were no intrapartum or peripartum complications.

The baby was evaluated further and the cardiac tumor was confirmed by a postnatal echocardiography to be a rhabdomyoma along with trivial MR and TR.(figure 4) USG abdomen of baby was not significant and no cerebral hamartomas were detected in neuro-sonography. However

the baby developed distress and cyanosis on day 8 and was admitted to NICU. Baby went into cardiorespiratory arrest due to congestive cardiac failure and died on day 11. The mother was discharged in a stable condition on day 12.

We report this case of maternal tuberous sclerosis diagnosed clinically and radiologically with associated fetal complication of cardiac rhabdomyoma to reveal the complex nature of the this disease and its impact on fetal outcome so as to help in the earliest diagnosis and management during pregnancy.

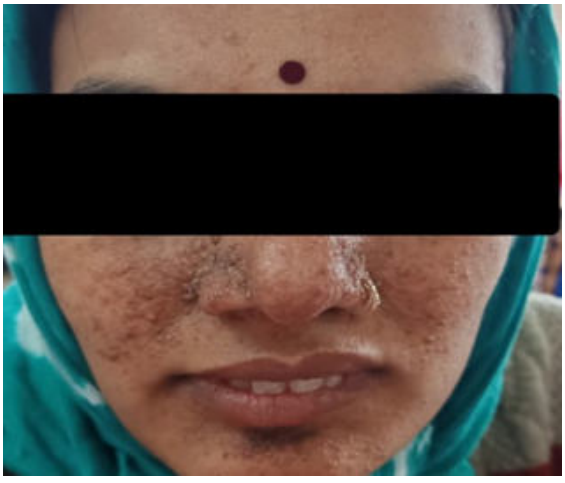

Figure 1:Adenoma sebaceum in a patient with tuberous sclerosis complex

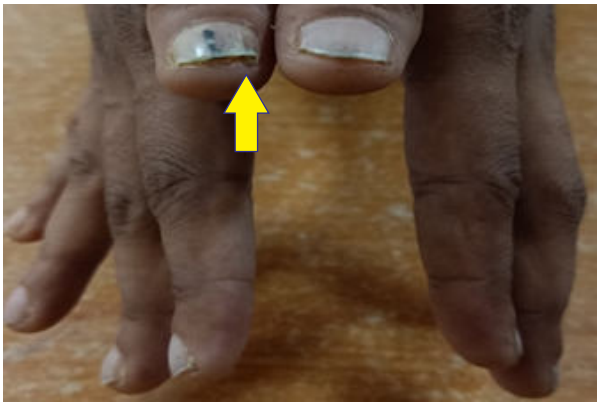

Figure 2:Subungual fibroma on the thumb of a patient with tuberous sclerosis complex

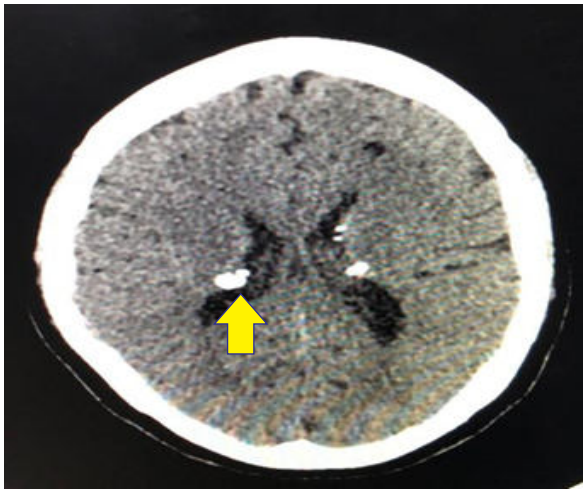

Figure 3:Calcified nodules along the sub ependymal lining of bilateral lateral ventricles

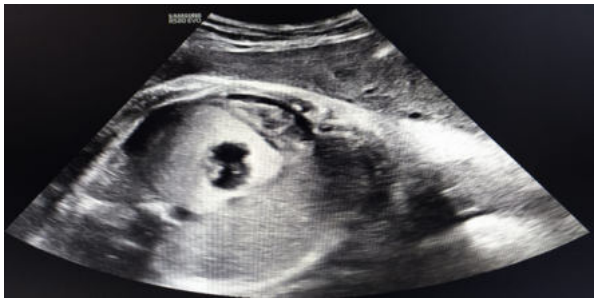

Figure 4:Cardiac Rhabdomyoma involving left ventricle and septum

DISCUSSION:

In 2012, the second International tuberous sclerosis complex consensus conference held in Washington, Surveillance and management of TSC patients published new diagnostic criteria for diagnosis of tuberous sclerosis.[3,4]

Major features

1. Hypomelanotic macules (3, at least 5-mm diameter)
2. Angiofibromas (3) or fibrous cephalic plaque
3. Ungual fibromas (2)
4. Shagreen patch
5. Multiple retinal hamartomas
6. Cortical dysplasias
7. Subependymal nodules
8. Subependymal giant cell astrocytoma
9. Cardiac rhabdomyoma
10. Lymphangioleiomyomatosis (LAM)
11. Angiomyolipomas ((≥2)

Minor features

1. "Confetti" skin lesions
2. Dental enamel pits (>3)
3. Intraoral fibromas (2)
4. Retinal achromic patch
5. Multiple renal cysts
6. Nonrenal hamartomas

Definite diagnosis: Two major features or one major feature with 2 minor features.

Possible diagnosis: Either one major feature or two minor features.

Accordingly our patient had 4 major criteria and was considered as Tuberous Sclerosis Complex. The most common neurologic symptom of TSC are Seizures(90%) followed by mental retardation (70%)[4] which was seen in our patient along with adenoma sebaceum thus completing the vogt's triad.

The earliest skin finding is multiple hypopigmented macules (Ashleaf spots). Angio-fibromas (adenoma sebaceum) are hamartomas composed of connective and vascular elements forming discrete pink papules on the malar region of the face in 70% of TSC patients.[2,6]

Patients with TSC can develop a `number of renal lesions, the most common being angiomyolipomas and cysts.[4] They may enlarge, rupture and bleed which can cause retroperitoneal haemorrhage and death. Ultrasonography plays a role in monitoring these patients.[6]Although our patient had renal angiomas, no complications were noted in this pregnancy.

The intracranial features of TSC are cortical or subcortical tubers, subependymal nodules, subependymal giant cell astrocytomas and white matter radial migration lines.[4] Our patient showed evidence of Multiple calcified nodules along the sub ependymal lining of bilateral lateral ventricles.

Ophthalmic features associated with TSC can be retinal lesions like astrocytic hamartomas and Non retinal lesions like coloboma, angoifibroma of the eyelid and papilledema.[4] Our patient did not have any ocular complaints.

Multiple bony changes like sclerotic lesions, Hyperostosis of inner table of skull, periosteal new bone formation, scoliosis and bone cysts have been described.[4] Our patient did not have any evident bony lesions.

Cardiac rhabdomyoma can be discovered using echocardiography in approximately 50% of TSC patients. A case study by Gupta et al done at Delhi detected fetal cardiac tumor by echocardiography in a pregnant TSC woman at 26 weeks of gestation.[2] Similarly in our case the presence of this large cardiac rhabdomyoma detected at 22 weeks raised the suspicion of tuberous sclerosis.

Giant cell astrocytoma is a path gnomic feature of this disease but like most other cerebral and renal lesions it goes undetected by prenatal/fetal ultrasound. MRI helps to assess these extra-cardiac manifestations of tuberous sclerosis. It also indicates the prognosis in severe infantile spasms and epilepsy.[1,2,7] In our case MRI could not be performed .

Tuberous sclerosis can lead to intrauterine fetal death. Agrarwal et al at Amravati [6] reported a case of stillbirth at 27 weeks of gestation in TSC patient and of the 19 TSC pregnancies reviewed by Bader et al [9] there was one spontaneous IUD and seven fetuses required either medical or surgical intervention. Similarly in our case the previously undiagnosed IUD could have been for the same reason.

There is no specific treatment for this disease. The seizures can be treated with antiepileptics. Surgical decompression can be tried for renal angiomyolipomas and ungual fibromas can be excised with Laser, cautery and diathermy. Dermabrasion can be used for adenoma sebaceum and shagreen patch.[6] Use of mTOR inhibitors (affecting mTOR pathways involved in hamartoma formation) is well-tolerated in patients including infants and has shown clinical improvements in young TSC patients with different types of tumors.[3,7,10]

Identifying the manifestations of this disease in early life especially in-utero is limited[6,7] thus making it difficult to assess the severity. Hence the present report emphasizes the importance of a detailed multi-organ investigation along with genetic testing of the fetus of a TSC mother. It also encourages the need for counselling and regular antenatal follow ups when the patient conceives.

CONCLUSION

A pregnancy complicated by Maternal or Fetal tuberous sclerosis deserves careful monitoring and complete prenatal evaluation so as to determine the prognosis and prevent any untoward complications in the baby and mother.

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