CASE REPORT

Neonate Presenting with Multiple Cardiac Masses

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ABSTRACT

This is a case of a neonate with multiple cardiac masses causing right ventricular outflow tract obstruction. Further work-up revealed presence of subependymal hamartoma, subependymal giant cell astrocytoma, cortical tubers and retinal astrocytic hamartoma in the right eye. Upon fulfillment of a set criteria, the patient was diagnosed with Tuberous Sclerosis Complex.

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INTRODUCTION

Tuberous sclerosis complex is a disease characterized by presence of benign hamartomas in multiple organs, cortical tubers, subependymal giant cell astrocytomas and renal angiomyolipomas [1]. It occurs in 1 in 6000 live births [2]. In utero, the earliest sign of tuberous sclerosis is rhabdomyoma. Cardiac rhabdomyoma is the most common pediatric cardiac tumor and 51–86% of cases are associated with tuberous sclerosis [1]. The presentation and clinical manifestations of tuberous sclerosis complex are diverse. Patients may be asymptomatic or present with intellectual disabilities and seizures [3].

THE PATIENT

This is a case of a neonate with multiple cardiac masses initially found during prenatal ultrasound and fetal 2D echocardiography. Patient was then worked up after delivery.

Patient was born via normal spontaneous delivery at 37 3/7 weeks of gestation with a normal birthweight and with an APGAR score of 7,9. Physical examination showed no head abnormality, acyanotic with good cry, and normal neurologic examination including reflexes. A grade 2 holosystolic murmur was identified at the second left intercostal space. No heredofamilial disease was noted.

Echocardiography was done revealing multiple homogeneous soft tissue masses within the right ventricular cavity and right ventricular lateral wall. There is also a 1.2 x 1.8 cm mass at the right ventricular outflow tract, partially obstructing the pulmonary outflow by more than 50%. Multiple similar masses are also detected at the left ventricular cavity, interventricular septum, and left ventricular lateral wall. The findings were suggestive of rhabdomyomas (Fig. 1).

The patient was referred to a pediatric neurologist and a cranial magnetic resonance imaging (MRI) was done revealing subependymal nodules/hamartomas, presumed subependymal giant cell astrocytoma, cortical/subcortical tubers, and obstructive hydrocephalus (Fig. 2). Referral to an ophthalmologist was also done wherein retinal astrocytic hamartoma was identified in the right eye.

A whole abdominal ultrasound was also performed with no remarkable findings.

The constellation of findings fulfilled the criteria for a diagnosis of Tuberous Sclerosis Complex.

DISCUSSION

Tuberous sclerosis complex, also known as tuberous sclerosis or Bourneville Disease, is an inherited autosomal dominant disease with a broad clinical spectrum [3]. Symptoms vary from severe intellectual impairment and uncontrollable epilepsy to normal intelligence and

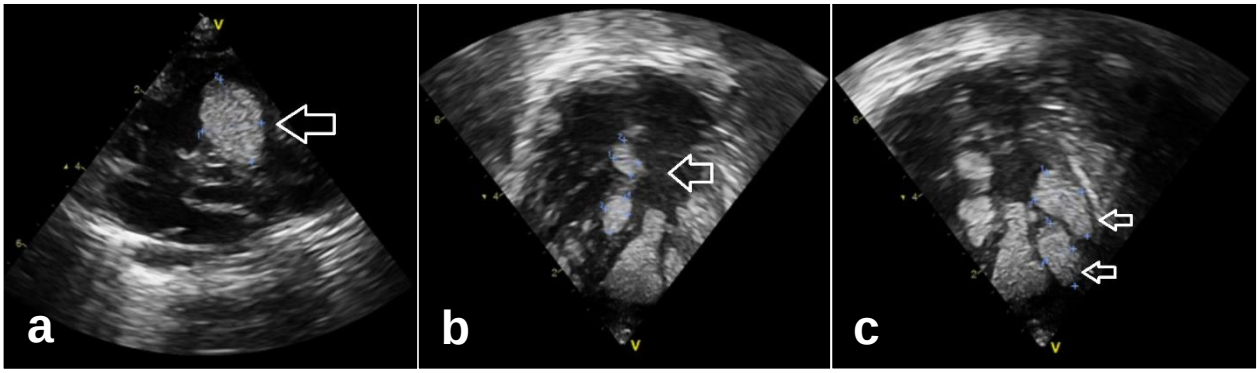

Fig. 1a-c Echocardiography revealed a homogeneous echogenic soft tissue masses (arrows) in the right ventricular outflow tract (**a**), interventricular septum (**b**) and left ventricle (**c**)

without seizures [3]. It is a multi-organ disease characterized by presence of hamartomas, cortical tubers, subependymal giant cell astrocytomas, and renal angiomyolipomas [1]. Its occurrence is attributed to mutation of the tumor suppressor genes TSC1 or TSC2, which encodes the proteins hamartin and tuberin, respectively, and affects 1 in 6,000 newborns [3]. There is few information on the disease's regional prevalence or trends but is perceived to be a rare disease by clinicians in Asia-Pacific countries [4].

According to the updated International Tuberous Sclerosis Complex Diagnostic Criteria and Surveillance and Management Recommendations [5], definite diagnosis of tuberous sclerosis complex is made when at least 2 major or one major plus two minor features are present (Table 1).

The hallmark of tuberous sclerosis complex is the involvement of the central nervous system [3]. Cortical tubers are characteristic brain lesions and are best seen on MRI [6]. Its appearance on MRI varies in age. In neonates and young children, these lesions are hyperintense to premyelinated white matter on the T1-weighted (T1W) sequence as in this case and hypointense on the T2-weighted (T2W) scans. In older children and adults, the lesions are iso-to hypointense on T1W and hyperintense to both gray and white matter on T2W images. Enhancement occurs in less than 5% of patients [7].

Aside from cortical tubers, subependymal nodules or hamartomas are also found in 95% of patients with tuberous sclerosis complex. They appear as irregular nodules protruding into the CSF-filled ventricles. In neonates, they usually appear hyperintense to adjacent unmyelinated white matter on T1W images [7].

Table 1 Diagnostic criteria for Tuberous Sclerosis. Adapted from the Updated International Tuberous Sclerosis Complex Diagnostic Criteria and Surveillance and Management Recommendations [5]. * These are present in this case

Major Criteria	Minor Criteria
Hypomelanotic macules (≥3; at least 5 mm in diameter)	"Confetti" skin lesions
Angiofibroma (≥3) or fibrous cephalic plaque	Dental enamel pits (≥3)
Ungual fibromas (≥2)	Intraoral fibromas
Shagreen patch	Retinal achromic patch
Multiple retinal hamartomas	Multiple renal cysts
Multiple cortical tubers and/or radial migration lines*	Nonrenal hamartomas
Subependymal nodule (≥2)*	Sclerotic bone lesions
Subependymal giant cell astrocytoma*	
Cardiac rhabdomyoma*	
Lymphangiomyomatosis (LAM)	
Angiomylipomas (≥2)	

Subependymal giant cell astrocytomas (SGCA) are also seen with an incidence of 15% in patients with tuberous sclerosis. They are located at or near the foramen of Monro and appear heterogeneous on cross-sectional imaging. They tend to enlarge and are associated with obstructive hydrocephalus [7].

White matter lesions presenting as straight or curvilinear bands, extending from the ventricle through the cerebrum toward the cortex, wedge-shaped lesions, nonspecific tumefactive or conglomerate foci or cerebellar radial

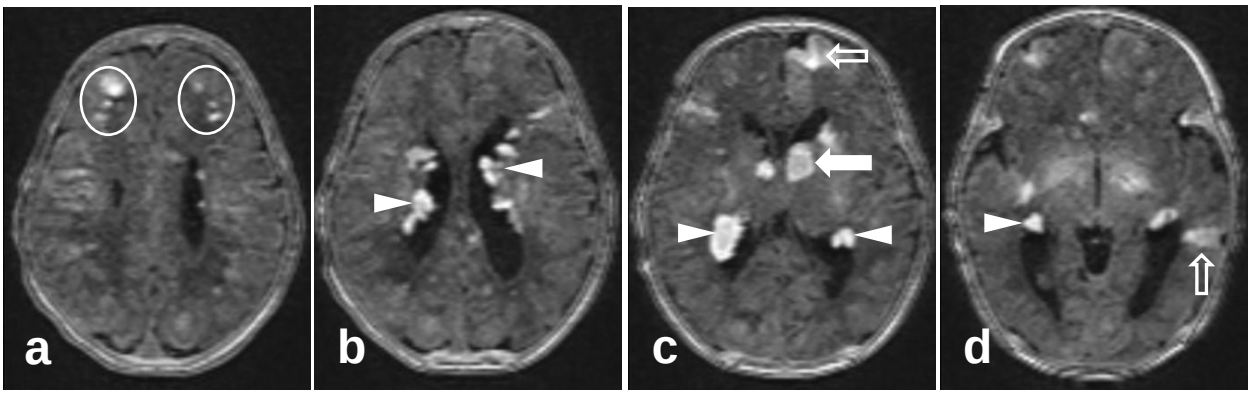

Fig. 2a-d Axial T1-weighted magnetic resonance images of the brain show white matter lesions (encircled), subependymal nodules (arrowheads), cortical tubers (open arrows) and subependymal giant cell astrocytoma (arrow)

bands can also be seen. In infants, they also appear as hyperintense lesions on T1W image and hypointense to unmyelinated white matter on T2W studies. In older children and adults, they are typically iso- to hypointense to white matter on T1W images and hyperintense to both gray and white matter on T2W scans. Twelve percent of the lesions show enhancement after contrast administration [7].

Another presentation of tuberous sclerosis is the presence of cardiac rhabdomyomas. Cardiac rhabdomyoma is the earliest clinical sign of tuberous sclerosis in utero. In ultrasound, it appears as rounded, homogeneous, hyperechoic areas within the myocardium. In contrast-enhanced CT, it is identified as low-density masses. Variable signal characteristics are seen on MRI but are often isointense or minimally hyperintense to the myocardium on T1W images and hyperintense on T2W images. Cardiac rhabdomyomas tend to increase in size until 32 weeks of gestation and progressively regress with observance of complete regression by 6 years of age [1].

Other lesions associated with tuberous sclerosis include presence of retinal hamartomas, vascular abnormalities such as aneurysm formation, skin lesions, renal angiomyolipomas and lymphangioleiomyomatosis [3].

CONCLUSION

Tuberous sclerosis complex is a rare multi-organ disease with a wide clinical spectrum that includes neurologic and cardiac manifestations. In this case, the earliest sign was the presence of cardiac rhabdomyoma. Through the aid of various imaging techniques, the diagnosis of tuberous sclerosis was made. Imaging played an integral role in the appropriate diagnosis and evaluation of the disease.

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