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Case Report

Cardiac rhabdomyomas and cerebral lesions in 4 pediatric patients with tuberous sclerosis ☆

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ABSTRACT

Rhabdomyoma is the most common primary cardiac tumor in pediatric patients. A strong association exists between cardiac rhabdomyomas and tuberous sclerosis (TS), an autosomal dominant disease, characterized by diffuse lesions in the nervous system, such as cortical-subcortical tubers and subependymal nodules. In TS, cardiac rhabdomyomas typically are diagnosed in childhood, but they could be detected in the neonatal period with echocardiography and magnetic resonance imaging and may precede cerebral lesions. Therefore, the precocious detection of cardiac rhabdomyomas in pediatric patients can suggest the diagnosis of TS and the early detection of cerebral lesions, improving the management of the related symptoms. We reported the cases of 4 pediatric patients, in which the detection of cardiac rhabdomyomas lead to the early discovery of cerebral lesions and the diagnosis of the TS.

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Introduction

Rhabdomyoma is the most common primary cardiac tumor in infants and children, accounting for more than 60% of primary heart neoplastic lesions [1]. A strong association exists between cardiac rhabdomyomas and tuberous sclerosis (TS), a rare genetic autosomal dominant neurocutaneous disorder, also known as “Bourneville disease,” characterized by multiple hamartomas, predominantly in the central nervous system, such as cortical-subcortical tubers, subependymal nodules, and subependymal giant cells astrocytoma [2,3]. The classical clinical manifestation of TS, known as “Vogt triad,” is composed by seizures, intellectual disability, and adenoma sebaceum [4]. The current diagnostic criteria for TS include multiple major and minor criteria established firstly by Roach

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Table 1 – Radiological lesions in tuberous sclerosis.

Site	Lesion
Nervous system	Cortical-subcortical tuber and/or radial migration line
	Subependymal nodule
	Subependymal giant cells astrocytoma
Heart	Rhabdomyoma
Lung	Lymphangioleiomyomatosis
Kidney	Angiomyolipoma
	Cyst

et al. [5] and reviewed and modified by the International Tuberous Sclerosis Complex Consensus group in 2012 and 2021 [6,7], that include lesions that can be detected by radiological exams (Table 1).

In TS, cardiac rhabdomyomas usually appear during fetal or neonatal period preceding cerebral lesions, but they are often detected only in childhood [8,9]. Therefore, the precocious detection of cardiac rhabdomyomas could lead to the early diagnosis of the brain lesions related to the TS, improving the management of the related symptoms [10].

We reported the cases of 4 pediatric patients, in which the early detection of cardiac rhabdomyomas have led to the diagnostic suspicion of the TS with the early diagnosis of cerebral lesions.

Case reports

Patients' presentations

Four neonates, 2 males and 2 females, with ages comprise between 14-day-old and 43-day-old, were hospitalized to the pediatric department of our hospital for sudden dyspnea and arrhythmia. They have had a regular mean gestational age. All neonates except one were delivered vaginally, with average weight and blood pressure within normal limits and they underwent echocardiographic examination.

Echocardiography

The echocardiographic examination was performed using an EPIQ ultrasound (Philips HealthCare Medical Systems, USA) with a dedicated transthoracic transducer. Two- and three-dimensional echocardiographic evaluation and speckle tracking echocardiography were performed in each patient using cardiac planes (2 chambers, 4 chambers, short-axis, and 3 chambers). Multiple solid hyperechoic masses within the myocardium were detected in all patients, with a significant regional reduction of the longitudinal and circumferential strain. The masses were suspicious for rhabdomyomas. Therefore, cardiac magnetic resonance imaging (MRI) was performed in all 4 patients to a better evaluation of these lesions.

Cardiac MRI

A 1.5 Tesla MRI scanner (Achieva, Philips Healthcare, The Netherlands) was used. Balanced steady-state free precession, T1-weighted (T1w) and T2-weighted (T2w) sequences were acquired in the short-axis, 2-chamber, and 4-chamber views. The cardiac masses were isointense compared to myocardium on T1w images and hyperintense on T2w images. The diagnosis of cardiac rhabdomyomas was confirmed in all patients. The location and the dimension of each rhabdomyomas were reported. Multiple cardiac rhabdomyomas were detected in each patient, with a combined total of 12 lesions in the 4 patients. Eight of the lesions were extramural and 4 intramural within the interventricular septum (Table 2). Next, brain MRI was performed in all patients to detect possible cerebral lesions.

Brain MRI

A 1.5 Tesla MRI scanner (Achieva, Philips Healthcare, The Netherlands) was used. T1w, T2w, and T2 fast field echo (FFE) sequences were acquired in axial, sagittal, and coronal planes. The type, the number and the location of celebral lesions were reported. Cortical-subcortical tubers and radial migration lines were identified in 4 patients and subependymal nodules in 3 patients. Cortical-subcortical tubers and radial migration line were hyperintense on T1w images and hypointense on T2w images. Subependymal nodules were hyperintense on T1w images and hypointense on T2w images, with hypointense areas on T2 FFE images due to calcifications. In all patients coexisted 2 or more cerebral lesions (Table 2).

Tuberous sclerosis diagnosis

According to the Tuberous Sclerosis Diagnostic Criteria [7], TS was diagnosed in all patients and the management for the prevention of cerebral symptoms has been started (Figs. 1-4).

Table 2 – Cardiac rhabdomyomas and cerebral lesions in four pediatric patients.

Patient's characteristics		Cardiac rhabdomyomas (number and site)	Cerebral lesions (type and number)
Age (day)	Sex		
14	Male	1 RA – 1 LV – 1 IVS	17 CT – 5 RML – 6 SN
20	Female	2 LV	4 CT – 3 RML – 2 SN
27	Male	1 RV – 1 LV – 1 IVS	4 CT – 5 RML – 1 SN
43	Female	2 LV – 2 IVS	8 CT – 5 RML

RA, right atrium; RV, right ventricle; LV, left ventricle; IVS, intraventricular septum; CT, cortical-subcortical tubers; RML, radial migration line, SN, subependymal nodules.

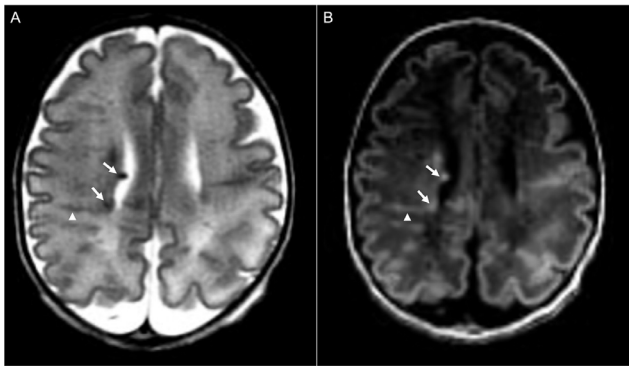

Fig. 1 – A 14-day-old female patient. Brain MRI axial T2w sequence (A) shows 2 hypointense subependymal nodules (white arrows) and 1 hypointense radial migration line (white arrowhead) that appear hyperintense on axial T1w sequence (B).

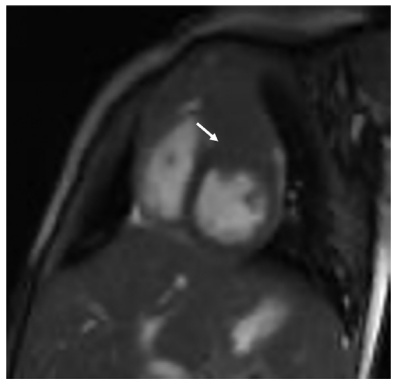

Fig. 3 – A 27-day-old female patient. Cardiac MRI balanced steady-state free precession sequence in short-axis shows an exophytic left ventricular cardiac rhabdomyoma (white arrow).

One-year follow-up examinations

No patients developed any neurologic symptoms during 12 months. All neonates underwent to cardiac MRI and brain MRI 12 months after the first examination. At cardiac MRI, the rhabdomyomas remained stable. At brain MRI, in 2 of 4 patients was found a better definition of celebral lesions.

Discussion

Rhabdomyomas are the most common cardiac pediatric tumors. They are strongly associated with TS, a rare genetic syndrome, characterized by multiple hamartomas especially in the nervous system [11]. In TS, cardiac rhabdomyomas usually appear before cerebral lesions and could cause the first recognizable manifestation such as atrial or ventricular arrhythmias, sinus node dysfunction, left ventricle outflow obstruction, and heart block. Rhabdomyomas are often multiple, forming a cluster, with different dimensions. They usually regress within 3 years of life [12]. On echocardiography, they appear as round, homogeneous, hyper-echogenic, intramural or intracavitary masses, predominantly localized within ventricles, and can cause a reduction of the longitudinal and circumferential strain [13]. Cardiac MRI has a complementary role, and it is recommended when the diagnosis is unclear or when additional information for operative planning in symptomatic patients are necessary [14]. Rhabdomyomas appear isointense on T1w images and isointense to mildly hyperintense on T2w images. They show minimal or no enhancement on postcontrast images [15].

All neonates underwent brain MRI because common manifestations of TS include central nervous system lesions, such as cortical-subcortical tubers, radial migration line, and subependymal nodules [16]. Cortical-subcortical tubers and radial migration line are benign lesions. Cortical-subcortical tubers may be epileptogenic foci, presenting with seizures, and they may also contribute to cognitive defects or autistic traits in some patients. In neonatal period, they appear hypointense on T2w images and hyperintense on T1w im-

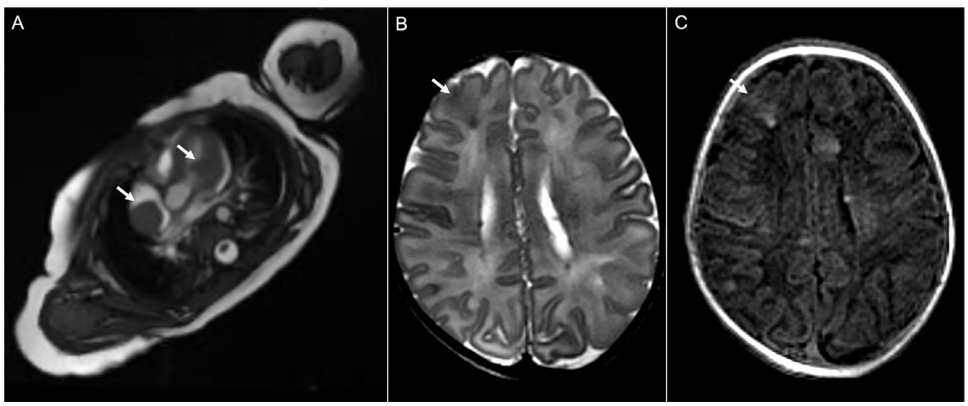

Fig. 2 – A 20-day-old male patient. Cardiac MRI balanced steady-state free precession in 4-chamber view (A) shows 2 cardiac rhabdomyomas: one in right atrium and one in left ventricle (white arrows). Brain MRI axial images (B, C) show a cortical-subcortical tuber (white arrow) in right frontal lobe that appear hypointense on T2w sequence (B) and hyperintense on T1w sequence (C).

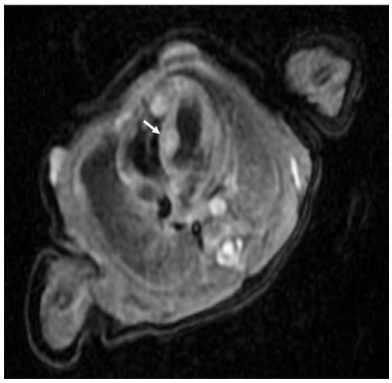

Fig. 4 – A 43-day-old male patient. Cardiac MRI T1 double-IR sequence in 4-chamber view shows an intraventricular septum cardiac rhabdomyoma (white arrow).

ages compared to the surrounding unmyelinated brain; differently, in adults, no calcified cortical-subcortical tubers are hyperintense on T2w images and hypointense on T1w images. In some cases of medically refractory epilepsy, cortical-subcortical tubers may be surgically removed [17] and the early detection of celebral lesions is necessary due to the strong association between a greater burden of cortical-subcortical tubers and worse neurological outcomes [18].

Subependymal nodules are hamartomas located along the ventricles and are mostly asymptomatic. They grow at the same rate of the surrounding tissues. On brain MRI, they are small intraventricular masses with variable signal, frequently hyperintense compared to gray matter on T1w images and hypointense on T2w images with marked hypointense areas secondary to calcifications. Moreover, the subependymal nodules, near to the interventricular foramen, may progress to subependymal giant cell astrocytoma, and follow-up is recommended [19].

Cardiac rhabdomyomas, cortical-subcortical tubers, radial migration line, and subependymal nodules are considered major criteria for diagnosis of TS, according to the Tuberous Sclerosis Diagnostic Criteria [6], and the tumor findings of our cases are comparable to those presented in the recent literature [19,20].

In conclusion, we reported the cases of 4 pediatric patients with TS, in which the detection of arrythmia secondary to cardiac rhabdomyomas allowed the early diagnosis of cerebral lesions improving the therapeutic management and reducing the onset of neurological symptoms. For this reason, the presence of cardiac symptoms should not be underestimated in pediatric patients; on the contrary, it is necessary to investigate the reasons because they could be the initial presenting symptoms of TS.

Patient consent

Informed written consent was obtained from the patient for examination and publication of this report and any accompanying images.

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