Review

Cardiac rhabdomyomas in tuberous sclerosis patients: A case report and review of the literature

Rhabdomyomes cardiaques chez les patients avec sclérose tubéreuse de Bourneville : un cas et revue de la littérature

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Summary Rhabdomyomas are the most common benign cardiac tumours. They are often associated with tuberous sclerosis and can be diagnosed antenatally and postnatally by echocardiography. Rhabdomyomas tend to regress spontaneously and are not usually operated upon, unless they become obstructive or cause severe arrhythmias. We describe the case of a child with tuberous sclerosis who was admitted for the resection of a subependymal giant cell astrocytoma, in whom cardiac rhabdomyomas in the right ventricular outflow tract were diagnosed. These two kinds of tumours are well known in the setting of tuberous sclerosis.

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Résumé Les rhabdomyomes cardiaques sont les plus fréquentes des tumeurs cardiaques bénignes. Ils sont souvent associés à la sclérose tubéreuse de Bourneville et peuvent être diagnostiqués avant et après la naissance, par échographie. Ils ont une tendance spontanée à la régression et ne sont pas conséquents habituellement pas opérés, sauf s’ils se compliquent d’arythmies sévères ou d’obstruction intracardiaque. Nous rapportons le cas d’une enfant porteur d’une sclérose tubéreuse de Bourneville avérée, admise dans notre établissement pour résection d’un astrocytome épénydymaire à cellules géantes, et chez laquelle l’échographie

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Background

Tuberous sclerosis is an autosomal dominant syndrome with variable penetration, characterized by hamartomas in numerous organs, including the heart [1]. The overall prevalence of tuberous sclerosis found in a study carried out in Scotland in 1986 was one in 27,000 but for children under 10 years of age it was one in 12,000 [2]. Two genes implicated in tuberous sclerosis have been identified: the tuberous sclerosis 1 (TSC1) hamartin gene on chromosome 9 (9q34) and the tuberous sclerosis 2 (TSC2) tuberin gene on chromosome 16 (16p13.3) [3]. Hence, first-degree relatives of a tuberous sclerosis patient should be investigated with ophthalmological examination, skin examination, cerebral computed tomography scan, chest X-ray, kidney examination, and echocardiography. However, in up to 60% of cases, the disease is related to de novo mutations [2].

Around 60% of children with tuberous sclerosis have been reported to have cardiac rhabdomyomas, whereas they only affect around 20% of adults with tuberous sclerosis [4]. These benign tumours seem to originate from embryonic myocytes, representing hamartomas. The involution may be related to the inability of the tumours to divide while the heart chambers grow.

Cardiac rhabdomyomas were first diagnosed by histological examination of surgical or postmortem specimens but are now generally diagnosed by echocardiography. Rhabdomyomas are usually highly reflective tumours, arising from the myocardium, but may be intramural, complicating the diagnosis. If a patient with tuberous sclerosis has multiple cardiac tumours on echocardiography, they are generally considered to be cardiac rhabdomyomas [5]. Furthermore, in view of the high frequency of rhabdomyomas in infants with tuberous sclerosis, echocardiography has been proposed by some as a diagnostic tool when tuberous sclerosis is suspected in infants, even in the absence of other clinical signs, which is common at this age [4].

The advent of echocardiography has increased the number of reported cases of rhabdomyomas. However, the association between cardiac rhabdomyomas and tuberous sclerosis remains insufficiently recognised by adult cardiologists.

Case report

Herein, we describe the case of a 10-year-old girl who had been diagnosed with tuberous sclerosis using the current diagnostic criteria [6]. She was found to have premature beats at auscultation and therefore underwent Holter monitoring and echocardiography prior to resection of an intracranial tumour.

Holter monitoring for 24 hours recorded numerous atrial premature beats without atrial fibrillation and transthoracic echocardiography revealed two non-obstructive masses in the right ventricular outflow tract (Fig. 1). These multiple, homogeneous and echodense tumours on echocardiography were thought to be congenital cardiac rhabdomyomas, as these are common among patients with tuberous sclerosis. As the cardiac tumours did not affect her cardiac output, the cerebral surgery was performed under general anaesthesia and was uneventful. The resected cerebral tumour was diagnosed as a subependymal giant cell astrocytoma.

Discussion

Rhabdomyomas in children should be differentiated from other cardiac tumours, such as cardiac myxoma (usually located in the atria, inserted on the interatrial septum), teratoma (located in the pericardium), haemangiomia and fibroma. Cardiac magnetic resonance imaging may be
helpful but is not mandatory for the diagnosis of cardiac rhabdomyomas in the setting of tuberous sclerosis.

Cardiac rhabdomyomas have been reported to regress spontaneously in the first years of life, although the regression mechanism is not yet well understood. Recently, in a series of 154 patients with tuberous sclerosis, partial regression of the cardiac rhabdomyomas was reported in 50% of cases and complete resolution in 18% [7]. An earlier report found regression rates of 60% in preadolescent tuberous sclerosis patients and 18% in adult tuberous sclerosis patients [8]. An age range during which rapid versus protracted regression of cardiac rhabdomyomas could be anticipated has been identified by DiMario et al. [9]. They reported that early complete regression occurs before the age of 6 years. However, it should also be noted that cardiac rhabdomyomas have been reported to grow or to appear de novo in 4% of patients with tuberous sclerosis [7].

Cardiac rhabdomyomas are typically asymptomatic and are therefore usually not operated upon unless they are obstructive, cause heart failure or are complicated with severe intractable arrhythmias [10]. Also, they can be difficult to remove completely, because they are often located in the deep myocardium. No embolic events have been reported and there is no need for oral anticoagulation in the absence of a specific indication (for example, atrial fibrillation). Although there are no consistent guidelines, cardiac monitoring may be proposed for all tuberous sclerosis patients with rhabdomyomas, with serial annual or biannual echocardiograms to detect haemodynamic compromise and annual Holter monitoring to detect severe arrhythmias, even if most patients are usually free from cardiac symptoms. When symptoms are present, they are generally related to the size of the tumours and their location.

Despite the potentially favourable prognosis of patients with cardiac rhabdomyomas, their presence should be sought (by echocardiography) in patients with tuberous sclerosis, especially when extracardiac surgery is planned. It should also be noted that symptomatic patients generally have a poorer prognosis than those who are asymptomatic [5].

A review of all papers on cardiac rhabdomyomas published up to 1990 is available [11]. At least 51% of tumours were associated with tuberous sclerosis and this rose to 86% if all patients with a possible diagnosis of tuberous sclerosis were included [11]. We reviewed the English-language literature (included in Pubmed) on cardiac rhabdomyomas in tuberous sclerosis patients diagnosed after birth, published after 1990 and up to March 2011. We deliberately excluded rhabdomyoma cases diagnosed before birth, as this involves antenatal ultrasonography, which is a very specialized field. Cardiac rhabdomyomas can be identified prenatally as early as 20 weeks gestation [12].

We found 322 patients with tuberous sclerosis and cardiac rhabdomyomas (Table 1, Supplementary data). We looked at the age of patients with rhabdomyomas when this information was available. Of the 164 patients whose age was clearly mentioned, 131 were aged < 6 years (79.9%) and 33 were aged ≥ 6 years (20.1%). Among 189 patients in whom multiplicity was mentioned, 108 had multiple rhabdomyomas (57.1%) and 81 had solitary rhabdomyomas (42.9%). Symptoms (Wolff-Parkinson-White syndrome, heart failure or arrhythmias) were present in 48 of the 134 patients in whom symptoms were mentioned (35.8%) while 86/134 patients (64.2%) were asymptomatic (nothing, heart murmur or irregular heartbeats). Eleven patients died: nine from cardiac complications of the rhabdomyomas, one from aortic dissection and one from congenital dextrotransposition of the great arteries. Of 12 patients who underwent rhabdomyoma surgery, one died on the operating table and one had a heart transplantation after resection failure.

Conclusions

Cardiac rhabdomyomas are the most frequent benign cardiac tumours and are often associated with tuberous sclerosis. They must be investigated by echocardiography in this setting. They are often asymptomatic but can cause heart failure, arrhythmias and obstruction. In these cases, they must be operated upon. In other cases — and because of their tendency to regress spontaneously — these tumours are simply monitored by echocardiography and Holter recording, in addition to usual clinical examinations.

Disclosure of interest

The authors declare that they have no conflict of interest concerning this article.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.acvd.2012.01.009.

References