

## Fetal cardiac rhabdomyomas as a sonographic sign of tuberous sclerosis complex – a diagnosis not to be missed. A pictorial essay

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### Abstract

Fetal cardiac rhabdomyomas should trigger the awareness of a potential coexisting tuberous sclerosis complex that can lead to a poor neurological outcome. This condition is not only uncommon but can be easily unrecognized prenatally in the absence of a meticulous neurosonogram and MRI. We emphasize that careful consideration of all prenatal facilities is required to confirm the diagnosis of tuberous sclerosis complex as early as possible during pregnancy.

**Keywords:** cardiac rhabdomyomas; tuberous sclerosis; prenatal diagnosis

### Introduction

Fetal cardiac tumors are rare tumors, accounting for 0.11% of all antenatally detected tumors [1]. The histopathologic classification of primitive cardiac tumors includes rhabdomyoma, teratoma, fibroma, hemangioma and myxoma [2].

Cardiac rhabdomyomas (CR) are benign mesenchymal tumors that spontaneously involute in more than 50% of cases in the first three years of life [3]. They are associated with tuberous sclerosis complex (TSC) in 83.3% of cases, especially when they are multiple [4]. CR represent the earliest ultrasonographic sign of TSC that can be detected antenatally [5]. Thus, CR are the ultrasound (US) hallmark that could lead to early diagnosis of TSC. Unfavorable outcome is correlated with their number and size, fetal arrhythmia or hydrops [6]. A recent meta-analysis shows that only 13.7% of cases with CR were detected before 24 weeks of gestation [7].

The incidence of TSC is about 1/10.000 live births/year, with an overall prevalence of 1/6.800-1/7.300 in

general population [8]. The prenatal diagnosis is based on major features according to the 2012 International Tuberous Sclerosis Complex Consensus Conference that can be detected antenatally: cardiac rhabdomyoma, subependymal nodules (SEN) and cortical/subcortical tubers [9]. The cerebral involvement can be detected by US in 86.3% of cases only after 24 weeks of gestation. Cerebral magnetic resonance imaging (MRI) proved greater sensitivity than US and can identify cases declared normal on US [10]. The most common clinical manifestation of the disease is epilepsy, present in 90% of patients in the first year of life and resistant to common antiepileptic drugs [11]. The long-term prognosis of TSC depends on neurological impairment, which is very difficult to anticipate.

In this pictorial review we emphasize that in the paradigm of personalized medicine, careful consideration of all prenatal diagnostic procedures is needed to confirm the diagnosis of TSC as early as possible during pregnancy.

### Cardiac US findings

#### *B mode*

CR appear as round, homogenous, hyperechogenic, intramural or intracavitary masses, often multiple, usually located in the ventricular walls and interventricular septum (movie 1, on the journal site) and occasionally in the atria or pericardium [8]. The tumors are hyperechogenic, well-delineated and round- or oval-shaped (fig 1, 2).

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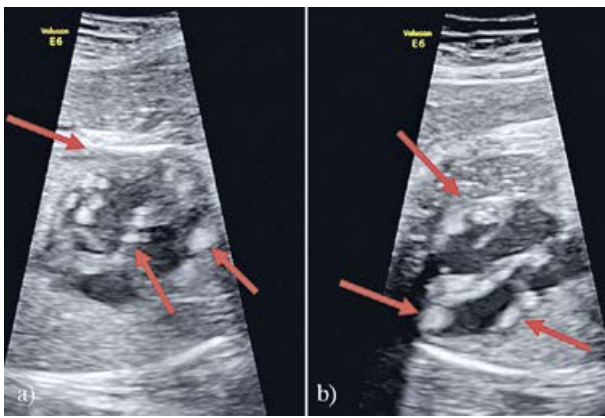
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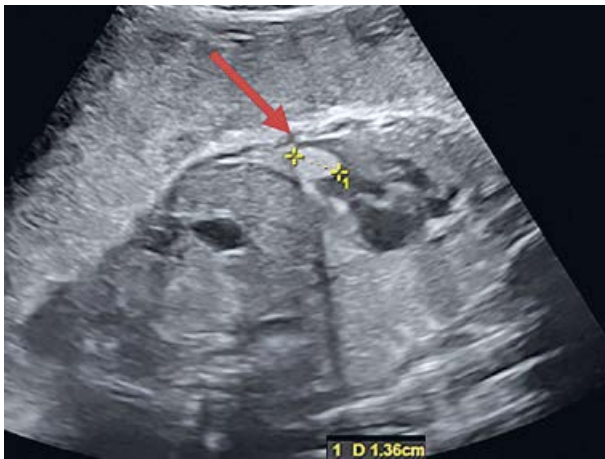
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**Fig 1.** Fetal echocardiography showing multiple masses corresponding to CR located within the myocardium of the ventricular walls, interventricular septum and apex (arrows) at 32 GW (a) and at 35 GW (b).



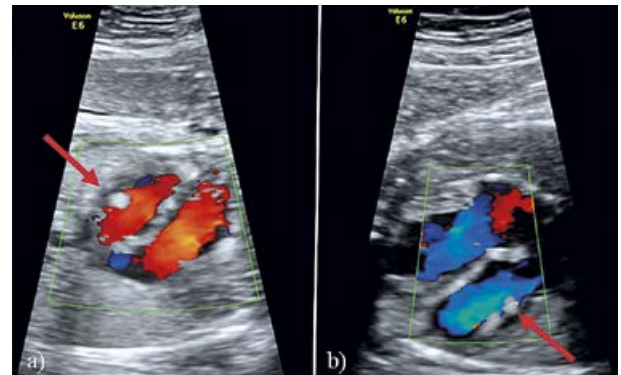
**Fig 2.** Fetal echocardiography at 34 GW revealing a 13.6 mm CR located at the apex of the left ventricle (arrow).

Smaller tumors tend to be multiple and therefore meticulous search for further tumors is recommended when the size of the mass is small [10]. On average, the lesions tend to cluster as a few lesions, grow to a size of 3-25 mm, and are mostly found in the ventricles and along the interventricular septum [12]. An important characteristic is that CR move together with the muscular walls of the heart (movie 2, on the journal site). Postnatally, the apical view of the heart is easy to obtain. Thus, the tumors can be counted and measured and a reliable CR mapping can be provided (movie 3, on the journal site). The tumors may bulge into the cavities of the heart, especially into the ventricles, and they do not have a mass effect if they are small (movie 4, on the journal site).

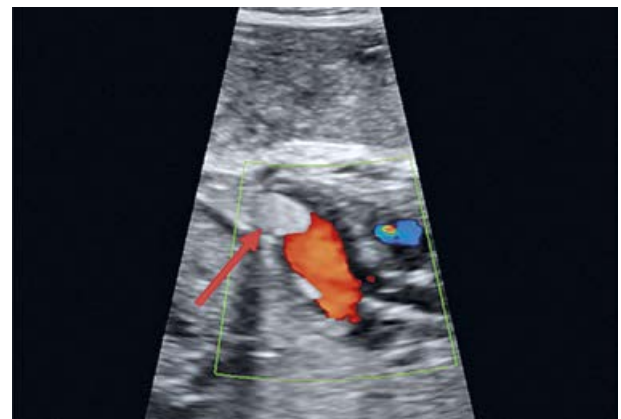
**Doppler mode**

On color Doppler mode subtraction images can be observed on the lateral walls (fig 3), and at the apex of the ventricles (fig 4) corresponding to CR that bulge into

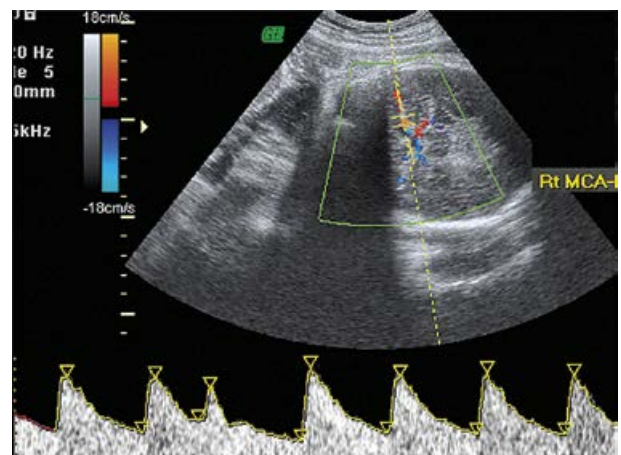
the cavities of the heart (movie 5, on the journal site). Occasionally, cardiac arrhythmia can be documented using Doppler PW mode (fig 5).



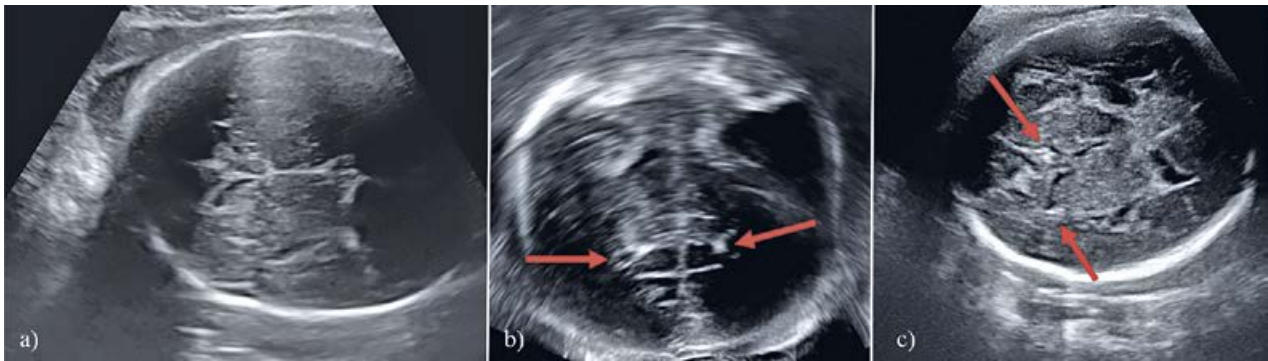
**Fig 3.** Fetal echocardiography showing subtraction images (arrows) in the lateral wall of the left ventricle at 32 GW (a), and at 35 GW (b), in keeping with multiple CR.



**Fig 4.** Fetal echocardiography at 34 GW revealing subtraction image at the apex of the left ventricle (arrow), corresponding to CR.



**Fig 5.** Doppler PW of the middle cerebral artery at 38 GW, fetus with multiple CR and cardiac arrhythmia.



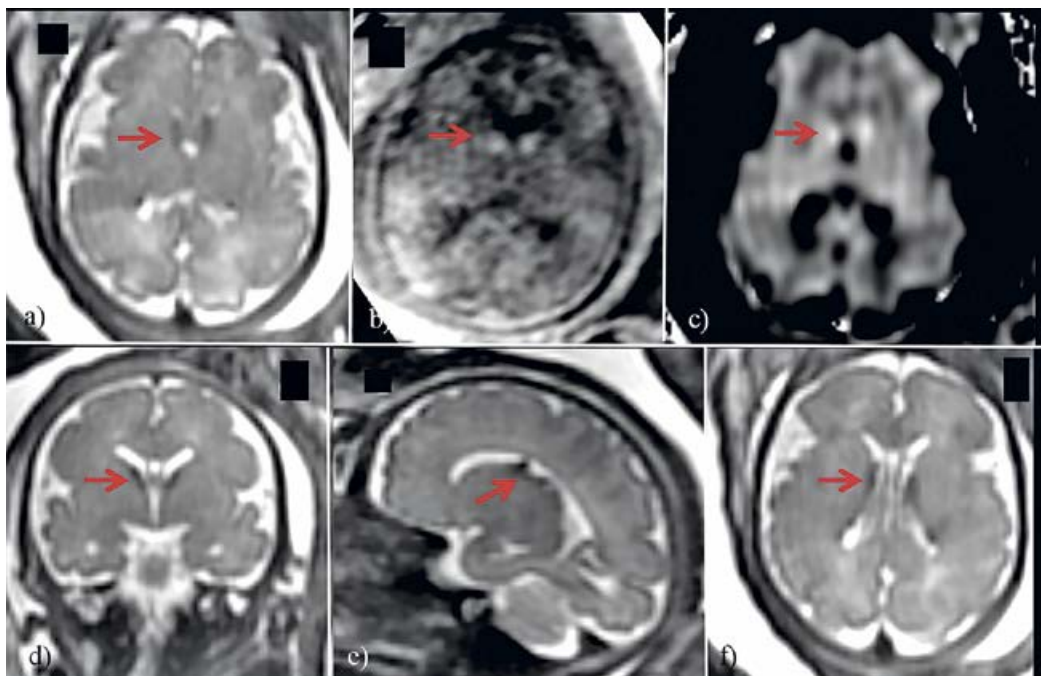
**Fig 6.** Fetal cerebral ultrasound of a fetus with multiple CR. At 35 GW (a) no images of cortical tubers or SEN were detected at the transabdominal scan. At 37 GW echogenic foci (arrows) within the walls of the anterior horns of the lateral ventricle are seen at the transvaginal scan (b), which are better visualized on a transabdominal scan at 39 GW (c), in keeping with SEN.

### Cerebral US findings

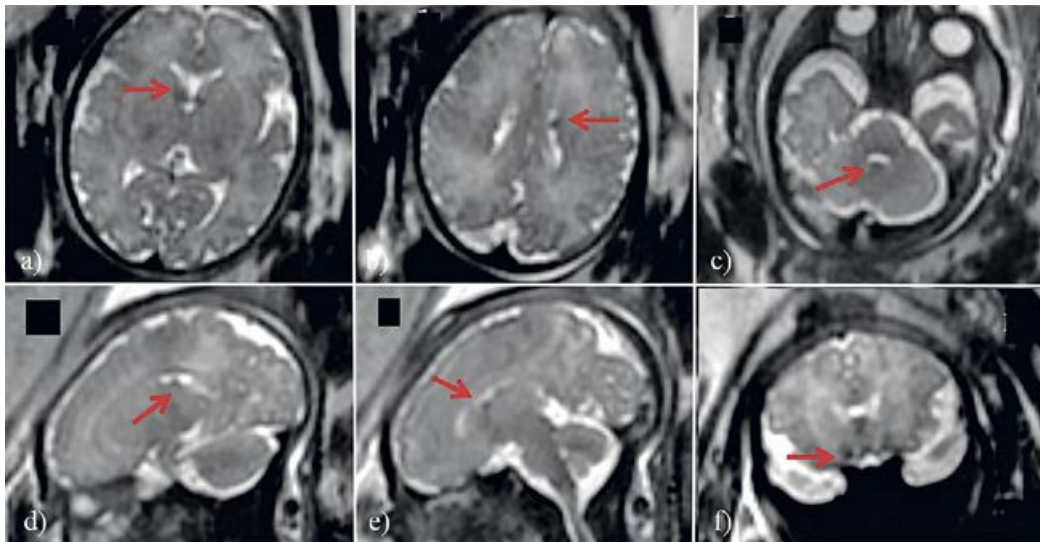
The prenatal US signs of cerebral involvement in TSC include mixed iso- and hyperechoic nodular lesions which vary in size. They are located in the cerebral lobes (cortical/subcortical tubers) or along the walls of the lateral ventricle (SEN) (fig 6). SEN occasionally may protrude into the cavity of the lateral ventricle. Multiple vague hyperechoic lesions may also be seen in bilateral subcortical white matter regions, especially at the frontal lobes [13].

### Cerebral MRI findings

Single-shot fast spin-echo T2-wi in three planes is the standard sequence for evaluation of the fetal brain with fast sequences used to scan the moving fetus. SEN and cortical/subcortical tubers are typically T2-wi hypointense and T1-wi hyperintense (fig 7, 8); the former are more clearly identified on fetal imaging than the latter and cortical tubers are occasionally detected only on the postnatal MRI of the brain [14]. The cortical/subcortical tubers are surrounded by an unmyelinated white matter



**Fig 7.** A 32 GW fetus with multiple CR and cerebral nodules. Plain T2-wi axial (a, f), coronal (d) and sagittal (e) MRI images of the brain show multiple T2-wi hypointense nodules along the walls of the lateral ventricles bilaterally (arrows), in keeping with SEN. Plain axial MRI image of the brain shows corresponding T1-wi hyperintense nodules (arrow in panel b) and eADC hyperintense nodules (arrow in panel c) in the walls of the anterior horns of the lateral ventricles bilaterally.

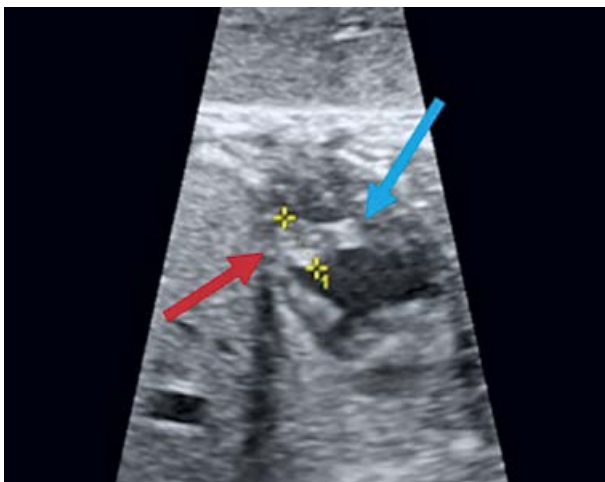


**Fig 8.** A 34 GW fetus with multiple CR and cerebral nodules. Plain T2-wi axial (a and b) and sagittal (d and e) MRI images of the brain reveal hypointense T2-wi lesions (arrows) along the walls of the lateral ventricles bilaterally, in keeping with SEN. Plain T2-wi axial MRI image of the posterior fossa (c) shows a T2-wi hypointense lesion (arrow) in the roof of the 4<sup>th</sup> ventricle. Plain T2-wi coronal MRI image of the brain (f) reveals ill-defined T2-wi hypointense lesions (arrow) within the hippocampus, in keeping with subcortical tubers.

which is T1-wi hypointense. Linear T1-wi hyperintense foci can be seen radiating from periventricular to subcortical white matter which are suggestive of radial migration lines [13].

### Differential diagnosis

Normal cardiac structures such as papillary muscle i.e., moderator band or chordae tendineae could be misdiagnosed as CR but they move independently from the myocardium (fig 9, movie 6, on the journal site).



**Fig 9.** Fetal echocardiography of the right ventricle at 36 GW showing a hypertrophied papillary muscle (red arrow) and the moderator band (blue arrow).

Other cardiac tumors i.e., fibroma (usually unique, within atria), myxoma (within atria), teratoma (within pericardium) and hemangioma (with inhomogeneous echogenicity) could mimic CR (multiple and hyperechogenic).

Care should be taken not to mistake SEN as a hemorrhage or calcifications especially if there has been a history of fetal distress and prematurity [13]. Other potential cerebral lesions that present as hyperechoic images and could be mistaken for cerebral tubers are subependymal giant cell astrocytoma, subependymal grey matter heterotopia and subependymal/germinal matrix hemorrhage.

### Conclusion

TSC is not only uncommon but can be easily unrecognized prenatally in the absence of a meticulous neurosonogram and a cerebral MRI. The CR seen with TSC are of paramount value, as their presence hallmarks the diagnosis in a considerable number of cases.

Prenatal diagnosis of cerebral lesions is important for confirmation of TSC diagnosis and further counseling the parents regarding its future prognostic implications and the usual poor neurological outcome. Comprehensive care and multidisciplinary management of these cases, as well as appropriate postnatal nursing are mandatory if the parents accept the baby.

**Conflict of interest:** none

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## Captions for the movies uploaded to the journal site

**Movie 1.** Fetal echocardiography of a 32 GW fetus with multiple CR that move together with the ventricular walls. Cardiac arrhythmia can be observed.

**Movie 2.** Fetal echocardiography of a 35 GW fetus with multiple CR dispersed into the ventricular walls, interventricular septum, apex of the left ventricle, and anterior cuspid of the mitral valve. Cardiac arrhythmia can be noticed.

**Movie 3.** Echocardiography performed on the 1-day-old newborn using a superficial probe detected the occupying masses dispersed into the ventricular walls and interventricular septum, bulging into the ventricular cavities.

**Movie 4.** Fetal echocardiography of a 34 GW fetus with multiple CR, one of them is floating freely in the cavity of the left ventricle.

**Movie 5.** Fetal echocardiography at 34 GW, oblique image of the right ventricle showing the inlet with the tricuspid valve and the outlet with the pulmonary valve in a fetus with multiple CR.

**Movie 6.** Fetal echocardiography at 36 GW showing a hypertrophied papillary muscle within the right ventricle.