Cardiovascular manifestations in juvenile-onset Behçet's disease: unusual mode of revelation

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ABSTRACT

Background: Behçet's disease is a systemic vasculitis with unusual thrombosis, especially in children. Intracardiac localization is rare. The site of choice is the right ventricle. It may be isolated, but must necessarily seek other vascular attacks, in particular an aneurysmal pathology of pulmonary arteries. Its clinical expression is not specific.

Case Presentation: An 8-years-old boy was hospitalized for an isolated prolonged fever with marked inflammatory state. No infectious symptoms were identified. Electrocardiogram showed a right branch block and negative T waves in V1-V3 leads. Transthoracic echocardiography revealed multiple right ventricular masses, associated with minimal pericardial effusion. These masses have various sizes and are lining right side of interventricular septum and pulmonary infundibulum without right ventricular outflow tract obstruction. Thoracic computerized tomography scan and cardiac magnetic resonance imaging confirmed that cardiac masses were multiples thrombi filling right ventricle and pulmonary artery. Thrombophilia panel assessment and eye fundus examination were normal. The patient was not a carrier of the *HLA B51* gene. Juvenile Behcet's disease was the final diagnostic. Treated by anticoagulant and corticotherapy, the clinical and ultrasound course of the patient was favorable. A 3-year follow up didn't show a recurrence of these thrombi.

Conclusion: Regression of thrombus under anticoagulant, of fever and inflammatory syndrome under corticosteroid therapy, is a good retrospective diagnostic criterion.

Keywords: Juvenile Behcet's disease, cardiovascular; thrombi.

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Background

Behcet's disease (BD) is a systemic inflammatory disease primarily involving the oral and genital mucosa, skin, and eyes [1]. Pediatric onset is very rare. The onset is insidious with peak age in young adulthood (25-30 years), but also occasionally in children before the age of 16 years [2]. Cardiovascular involvement does not exceed 9% in the various pediatric series [2,3]. Thus, unusual presentations of arterial, venous, and cardiac thrombosis or arterial aneurysm formation should suggest BD as a possible diagnosis [2]. The purpose of this paper is to report an observation of juvenile BD and highlight pediatric spectrum of this disease and its cardiovascular symptoms.

Case Presentation

An 8-years-old boy with no medical history was hospitalized for an isolated prolonged fever progressing for more than 1 month with marked inflammatory state (C-reactive protein at 135 mg/l and high and erythrocyte sedimentation rate at 75 mm). No infectious symptoms were identified. Physical examination was normal and did not find oral or genital aphthosis nor pseudofolliculitis lesions. Electrocardiogram (ECG) showed a right branch block and negative T waves in V1-V3 leads (Figure 1). Transthoracic echocardiography revealed multiple right ventricular masses, associated with minimal pericardial effusion. These masses have various shapes and size, the largest one is 35 mm long. They are lining right side of interventricular septum and pulmonary infundibulum

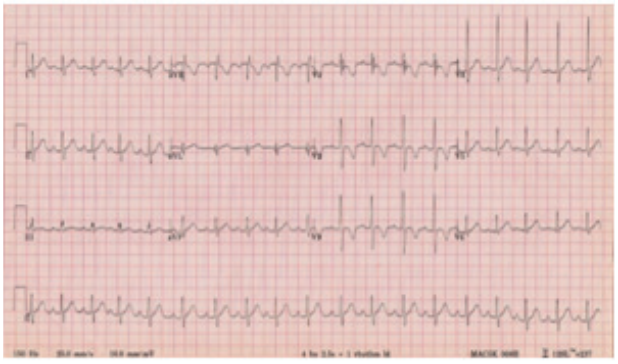

Figure 1. *ECG recording right branch block and negative T waves from V1 to V3.*

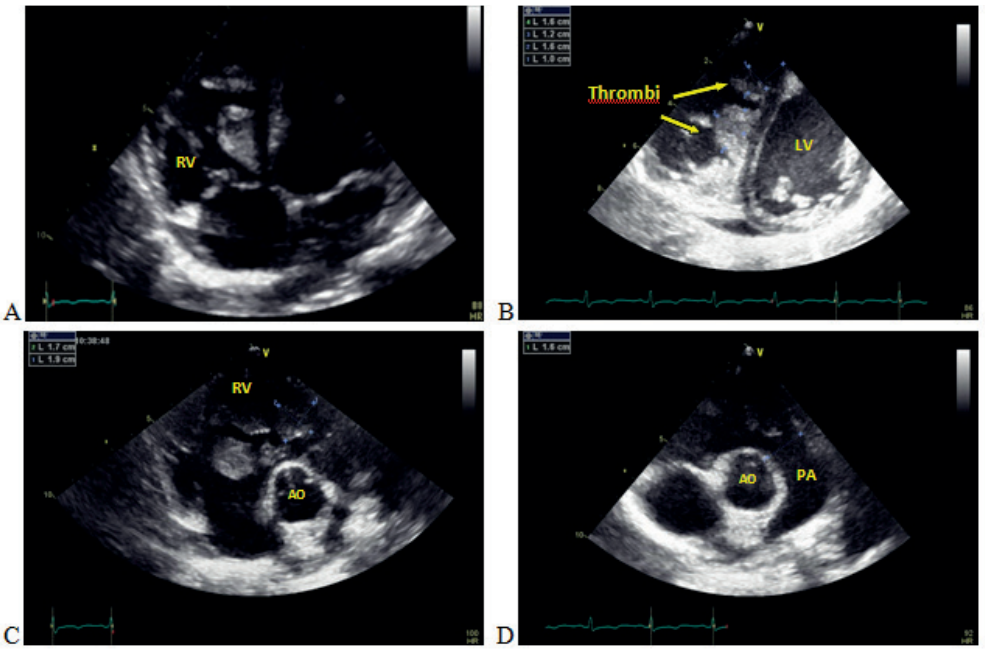

Figure 2. *(A) Apical four-cavity view echocardiography visualizing different masses with various shapes and size within right ventricle. (B) Short axis view echocardiography showing an interventicular septum lined with masses. (C) Pulmonary artery infundibulum filled with rounded formations. (D) Non-dilated pulmonary artery trunk measuring 16 mm. RV = right ventricle; LV = left ventricle; PA = pulmonary artery; AO = aorta.*

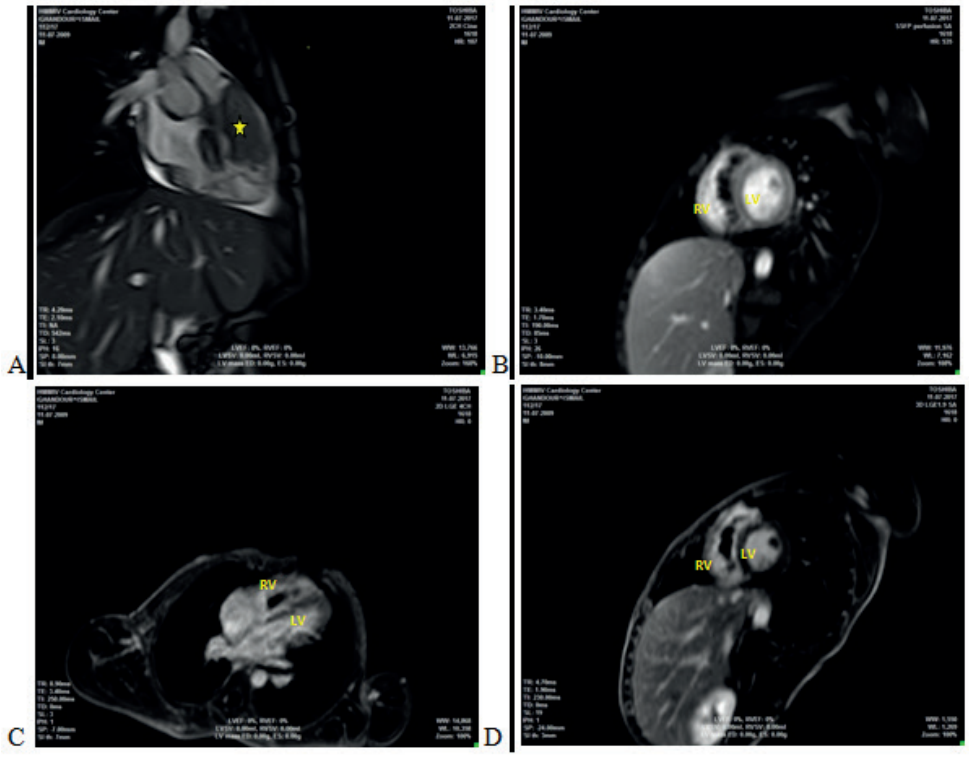

Figure 3. *Cardiac MRI. (A) MRI Cine SSFP sequence, two right-chamber view visualizing multiple thrombi of the right ventricle and pulmonary artery. (B) gadolinium perfusion sequence showing no early enhancement of right ventricle thrombus. (C, D) MRI sequences of late enhancement in four-chamber view (C) and short axis (D), absence of late gadolinium enhancement of right ventricle mass attesting the diagnosis of intracardiac thrombus. ★ = thrombus; RV = right ventricle; LV= left ventricle.*

without right ventricular outflow tract obstruction, suggesting either tumors or constituted thrombi (Figure 2). Thoracic computerized tomography scan (CT scan) and cardiac magnetic resonance imaging (MRI) confirmed that cardiac masses were multiples thrombi filling right ventricle and pulmonary artery (Figure 3).

Thrombophilia panel assessment was normal; especially, no C and S protein deficiency, antiphospholipid, and antinuclear antibodies were negative. The patient was not a carrier of the human leukocyte antigen (*HLA*) *B51* gene and eye fundus examination was normal.

Table 1. *International classifications criteria for BD [3]-Pediatric criteria for BD 2015.*

ITEM	VALUE/ITEM	DESCRIPTION
Recurrent oral aphtosis	1	At least three attacks/year
Genital ulceration	1	Typically with scar
Skin involvement	1	Necrotic folliculitis, acneiform lesions, erythema nodosum
Ocular involvement	1	Anterior or posterior uveitis, retinal vasculitis
Neurological signs	1	With the exception of isolated headaches
Vascular signs	1	Venous thrombosis, arterial thrombosis, arterial aneurysm

Three of six items are required to classify a patient as having pediatric BD.

In the absence of a patent etiologic diagnosis of this extensive cardiac thrombosis, and due to the frequency of BD among the Maghreb Mediterranean population, diagnosis of angio-Behcet was highly presumed. Thereby, the patient was treated by anticoagulant and corticotherapy, heparin initially then relayed by vitamin K antagonist for 6 months associated to prednisone at a dose of 1 mg/kg/day in gradual decrease in addition to potassium and calcium supplementation. The clinical and ultrasound course was favorable. A 3-year follow-up did not show a recurrence of these thrombi.

Discussion

The definition of BD is difficult and relies only on clinical features. Koné-Paut et al. [4] recently published provisional classification criteria from the largest prospective cohort ever reported for BD in children (Table 1). This classification has been proposed for the main purpose of clinical research. Indeed, in children; the number of symptoms may be too few to apply any classification to a single patient. Therefore, in most cases; the diagnosis is made provisionally on the basis of physician's expertise [4]. The prevalence of BD in children is unknown but it is probably very low, as a range of 3.3%–26% of cases has been reported [5]. The time to diagnosis is long between 3 and 5 years taking into account the rarity of symptoms [2]. BD includes a vasculitis affecting all sizes of vessels but prominently the veins, and was recently classified as "variable" vasculitis [1]. Venous lesions are more common than arterial occlusions and arterial aneurysm. The main pathologic feature is an inflammation of the vessel wall leading to thrombus formation, and many patients may accumulate other associated factors of thrombophilia such as anticardiolipin antibodies and protein C deficiency [1]. Cardiac involvement is particularly rare, as it affects about 6% of the patients with BD [6]. Most common cardiac manifestations are pericarditis (29%), endocarditis (mainly aortic insufficiency) (25%), intracardiac thrombosis (29%), myocardial infarction (15%), endomyocardial fibrosis (8%), and left ventricular aneurysms (4%). Coronary artery aneurysms have also been described [7]. Male patients are predominantly affected. Intracardiac thrombosis mainly affects the right heart and is very often associated with other venous thromboses (pulmonary embolism in 60% of the cases), or pulmonary aneurysms [6]. Also, increased ventricular arrhythmias, dispersion of ventricular repolarisation, and conduction defects have been described in BD [7]. Echocardiography is a useful non-invasive diagnostic tool for the detection of cardiac involvement in BD. Cardiac thrombosis is a rare finding of this disease. Therefore, differential diagnosis with intracardiac tumors is very difficult, justifying the use of cardiac MRI which has better specificity and sensitivity in cardiac thrombosis. It is a relevant technique for studying cardiac mass due to its high signal resolution. In particular, by looking for specific components in the lesion (fat), studying its mobility with cine MRI sequences, and analyzing its dynamic and late enhancement. CT scan offers a lower tissue contrast but because of its high spatial resolution, it is possible to better define the anatomical relationships of a lesion. These two examinations can thus be complementary [8]. In children, the treatment of BD follows the 2008 international recommendations [9]. However, none of these treatments have been currently approved. The use of anticoagulants in treating BD thromboses is still controversial and no studies have demonstrated their efficacy in comparison to immunosuppressive treatment [10]. Some authors did not recommend anticoagulating these patients, arguing the predominant role of inflammation in the genesis of lesions [9], the potential hemorrhagic risk in patients have associated aneurysmal affections (in particular pulmonary) and the supposed low emboligenic risk of venous thromboses due to their great adherence to the wall [9]. However, in the largest cohorts of patients with venous disease, the majority of patients were anticoagulated and hemorrhagic complications were very rare (2%) [11]. The course of BD is recurrent and unpredictable. In children, the disease remains often active with new symptoms appearing with time. In a cohort of 817 children and adults, the mortality rate was 5%, and death was associated with younger age, male sex, arterial involvement, and a high number of flares [12].

Conclusion

Diagnosis of BD is difficult in children, especially in the absence of its primary criteria. Cardiac involvement during this disease is rare and underestimated. Thus, any discovery of an intracardiac mass in a child should evoke the diagnosis of cardiac thrombus and BD; therefore, its management must be as early as possible given the long duration of development.

What is new?

Behcet's disease is a systemic vasculitis with unusual thrombosis, especially in children. Intracardiac localization is rare. The site of choice is the right ventricle. It may be isolated, but must necessarily seek other vascular attacks, especially pulmonary artery aneurysms. We report the case of juvenile BD revealed by thrombi within the right ventricle, diagnosed by multimodal imaging. Such patients are a diagnostic challenge. The purpose of this paper is to shed light on the disease, especially in its pediatric population and its cardiovascular symptoms.

List of Abbreviations

BD	Behcet's disease
ECG	Electrocardiogram
CT scan	Thoracic computerized tomography scan
MRI:	magnetic resonance imaging
HLA	human leukocyte antigen
RV	right ventricle
LV:	left ventricle.
PA	pulmonary Artery
AO	aorta

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None.

Conflict of interests

The authors declare that there is no conflict of interest regarding the publication of this article.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Ethical approval

Ethical approval is not required at our institution for publishing a case report in a medical journal.

Author details

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Summary of the case

1	**Patient (gender, age)**	Male, 8-year-old
2	**Final diagnosis**	BD
3	**Symptoms**	Fever, multiple thrombi of right ventricle and pulmonary artery
4	**Medications**	Anticoagulants and corticosteroids
5	**Clinical procedure**	Heparin initially then relayed by vitamin K antagonist for 6 months associated to prednisone at a dose of 1 mg/kg/day in gradual decrease
6	**Specialty**	Cardiology/internal medicine