

Uhl's Anomaly: 10 Years of Follow-Up of an Unoperated Patient



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INTRODUCTION

Uhl's anomaly is characterized by the absence of myocardium in the right ventricle (RV). It was described by Henry Uhl in 1952 after performing an autopsy on an 8-month-old infant.¹

In Uhl's anomaly, the RV free wall is extremely thin and consists only of epicardium and endocardium, with no evidence of myocardium as in a normal right ventricle or fat infiltration, inflammation, and necrosis present in other pathologies. There is marked RV dilatation and failure, with preservation of interventricular septum, septo-marginal band, and normal tricuspid valve insertion.² The main hemodynamic consequence of Uhl's anomaly is inadequate or absent RV contraction, which acts as a passive systemic conduit through which the blood of the right atrium is channeled into the pulmonary circulation. The left ventricle is morphologically normal.³

In the past century, fewer than 100 cases of Uhl's anomaly have been reported. As an extremely rare entity, its prevalence is not yet estimated. It usually occurs in childhood as an isolated cardiopathy, with equal gender distribution. In most cases, no family history is reported, but there have been descriptions in twins.^{2,4,5}

The exact cause of Uhl's anomaly is unknown. It was originally attributed to an embryologic failure of right cardiogenic fold development, leading to a congenital absence of the RV myocardium.^{6,7} Another hypothesis is the selective but uncontrolled apoptosis of RV myocytes during the perinatal period, after complete cardiac development.^{3,7}

This disease leads to progressive right heart failure (HF), with death occurring mostly in infancy. The diagnosis is made by typical findings on echocardiography and cardiac magnetic resonance imaging. Surgical options have been described that include cardiac transplantation, but this disease is still associated with poor prognosis and a high mortality rate.²⁻⁵

We describe the case of a 31-year-old man with echocardiographic and cardiac magnetic resonance imaging findings typical of Uhl's anomaly, with progressive worsening HF, who had 10-year survival after diagnosis, without surgical intervention or heart transplantation.

CASE PRESENTATION

A 20-year-old Caucasian man was admitted to the emergency department with abdominal pain and worsening dyspnea, with 6 months of symptom evolution. He was usually in New York Heart Association functional class I or II, with no history of chest pain, palpitations, or syncope.

He had no relevant medical history and an unknown family history because he was adopted.

Physical examination revealed tachypnea with peripheral cyanosis, a pulse rate of 100 beats/min, normal blood pressure, afebrile, and oxygen saturation of 95% on room air. The patient had jugular venous distension of about 8 cm at 45°, with hepatojugular reflux. Pulmonary auscultation was normal, and a grade VI holosystolic murmur in the left sternal margin was present on cardiac auscultation. The abdomen was diffusely painful, and the liver edge was palpable 5 cm below the right costal margin.

Chest radiography showed cardiomegaly with a normal pulmonary vasculature pattern.

Electrocardiography revealed sinus rhythm, signs of right atrial anomaly, and low QRS complex voltage in leads V₁ to V₃, with changes in RV repolarization (Figure 1).

Transthoracic echocardiography showed severe right chamber dilatation with a thin RV free wall and severely reduced RV function. Left chambers and left ventricular function were normal. There was tricuspid valve annular dilatation and severe tricuspid regurgitation without signs of significant pulmonary hypertension (Figures 2 and 3).

The patient was admitted for further investigation. He underwent cardiac magnetic resonance imaging, which showed marked right chamber dilatation with thinning of the RV free wall with no fat infiltration. Dimensions and function of the left ventricle were normal, and the tricuspid valve had normal insertion. A medium-volume pericardial effusion was visualized (Figures 4 and 5). A genetic study to screen for arrhythmogenic RV dysplasia (ARVD) was performed, with a search for mutations in the *PKP2* gene, which was negative.

The diagnosis of Uhl's anomaly was established, and the patient started diuretics with reasonable control of HF symptoms. However, during the 3 years after diagnosis, he presented multiple decompensations of HF, requiring hospitalization (Videos 1 and 2). Additionally, he was diagnosed with atrial fibrillation and thrombus in the right atrium and ventricle (Videos 3 and 4).

Because there was progressive clinical worsening with multiple hospitalizations, the patient was referred for heart transplantation or eventual palliative surgery at a tertiary center, but he was refused for both procedures because of the absence of social conditions and intellectual limitation.

During follow-up, no sustained ventricular arrhythmia was ever documented, and he maintained New York Heart Association

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VIDEO HIGHLIGHTS

Video 1: Transthoracic echocardiography performed 3 years after the diagnosis of Uhl's anomaly. Subcostal view showing severe right chamber dilatation with a thin RV free wall and severely reduced RV function. Left ventricular function was normal. Normal insertion of tricuspid valve with annular dilatation and severe tricuspid regurgitation. Large-volume pericardial effusion.

Video 2: Transthoracic echocardiography performed 3 years after the diagnosis of Uhl's anomaly. Parasternal short-axis view showing systodiastolic retilinization of the interventricular septum.

Video 3: Transthoracic echocardiography performed 6 years after the diagnosis of Uhl's anomaly. Modified parasternal view showing exuberant auto contrast in the right chambers.

Video 4: Transthoracic echocardiography performed 6 years after the diagnosis of Uhl's anomaly. Modified parasternal view showing presence of thrombus in the right atrium.

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functional class II or III, requiring frequent hospitalization for intravenous diuretic by anasarca.

Ten years after the diagnosis, the patient experienced sudden death in his home. An autopsy was not performed.

DISCUSSION

Uhl's anomaly is an extremely rare entity, characterized by isolated RV dilatation and failure, with almost complete absence of RV myocardium.

The most common presentation, as in this case, is right HF, but the severity of clinical manifestations varies from premature death in childhood through rare reports of asymptomatic adult patients.⁸ Reports of palpitations, syncope, arrhythmias, and sudden death are infrequent.² This fact is probably due to the lack of muscle tissue and foci of abnormal electrical conduction in the right ventricle.

In the past, the diagnosis of Uhl's anomaly was made only on autopsy. Currently, the development of cardiac imaging allows early and accurate diagnosis of this disease, including in fetal life.^{7,9}

Echocardiography shows marked RV dilatation with thin walls (1–2 mm in almost all regions) and significant depression of its contractility. Right atrial enlargement is also observed, as well as hypertrophy with normal left chambers. The tricuspid valve has normal morphology and implantation.^{6,10,11}

Cardiac magnetic resonance imaging reveals an extremely thin-walled right ventricle with almost complete absence of free wall myocardium and with scarce apical trabeculations. There is no fibrofatty infiltration, with RV systolic dysfunction.^{11,12}

In 1979, Fontaine *et al.*¹³ described ARVD, characterized by fibrofatty replacement of the RV myocardium. In 1993, Gerlis *et al.*¹⁴ concluded that many cases of ARVD were incorrectly classified as Uhl's anomaly, and these two entities had to be distinguished.^{9,14}

Both ARVD and Uhl's anomaly produce a thin-walled dilated right ventricle, but in ARVD, differently from Uhl's anomaly, the myocardium is progressively replaced by fibrofatty tissue. It has also been linked to mutations in the genes encoding plakoglobin and desmoplakin. Moreover, the left ventricle may also be affected.

Uhl's anomaly affects both genders, and it is typically found in childhood with congestive HF. Usually, there is no family history of sudden death, and there is no knowledge of specific mutations causing the disease. By contrast, patients with ARVD are diagnosed in adolescence or adulthood, with a 3:1 male predominance. A family history of the disease and sudden death induced by physical effort is frequent, as it is inherited as an autosomal-dominant trait with variable penetrance and clinical expression (Table 1).^{6,14,15}

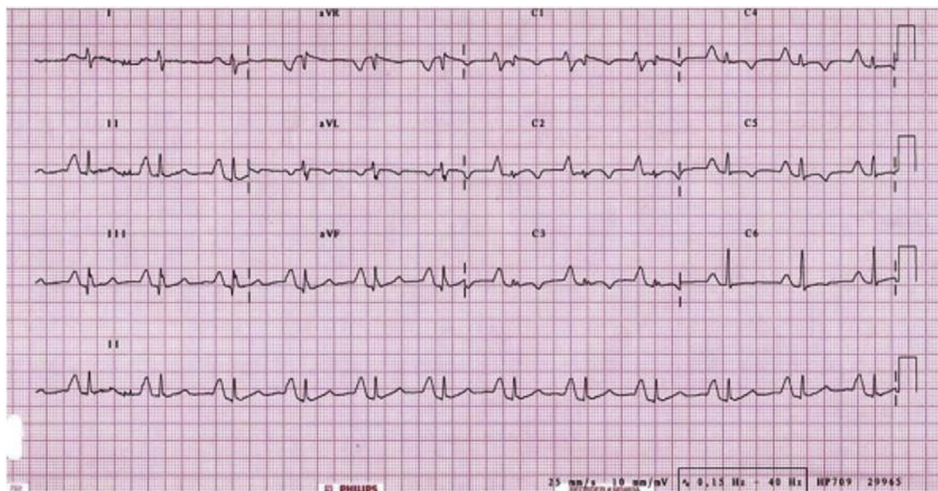


Figure 1 Electrocardiogram.

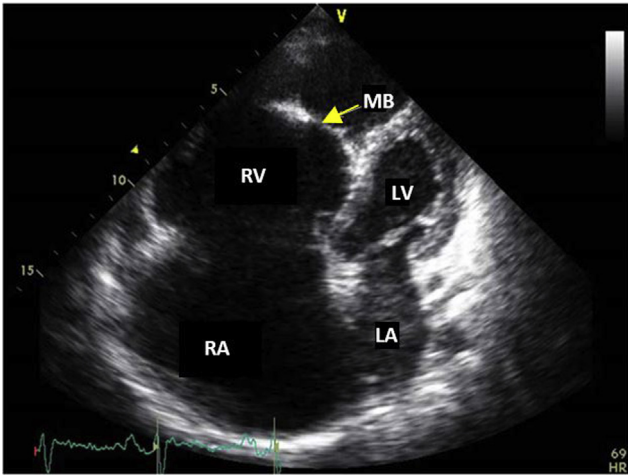


Figure 2 Transthoracic echocardiogram, apical four-chamber view in diastole, showing marked right atrial and right ventricular dilatation. A moderator band (MB) and thin right ventricular walls were observed. LA, Left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

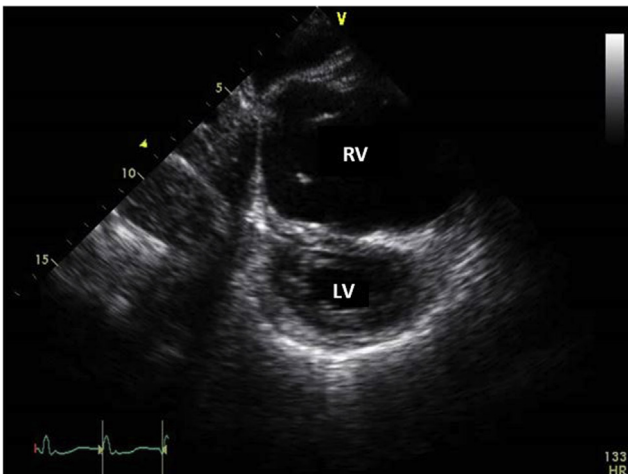


Figure 3 Transthoracic echocardiogram, parasternal short-axis view in diastole, showing marked right ventricular dilatation with thin walls and interventricular septum flattening. LV, Left ventricle; RV, right ventricle.

Ebstein's anomaly should also be considered in the differential diagnosis. In Uhl's disease, the tricuspid valve hinges normally and is not dysplastic.¹²

The treatment of Uhl's anomaly is still controversial and usually palliative. The initial medical approach for HF, as in this case, has a poor response.²

The principle of surgical management of Uhl's anomaly is total or partial exclusion of the right heart with some form of cavopulmonary connection (bidirectional Glenn or Fontan). The "one and a half" ventricular repair surgery is a reduction plasty of the right ventricle com-

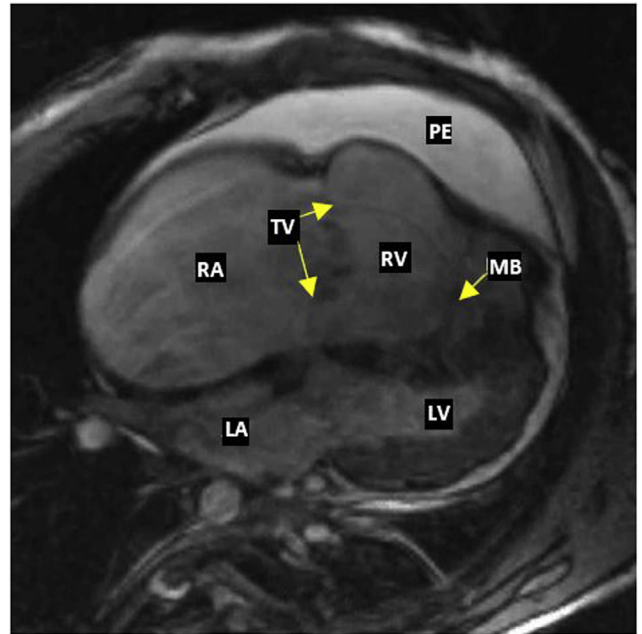


Figure 4 Cardiac magnetic resonance, in steady-state free precession, four-chamber sequence showing marked right chamber dilatation. The tricuspid valve (TV) has normal positioning. A moderator band (MB) and a medium-volume pericardial effusion (PE) are visualized. LA, Left atrium; LV, left ventricle; RA, right atrium; RV, right ventricle.

bined with bidirectional Glenn, and this procedure allows better left ventricular adaptation to the new physiology. Heart transplantation is also possible.^{9,10,16}

Although the surgical procedures for Uhl's provide reasonable short-term clinical improvement, the long-term outcome remains uncertain, and the prognosis is still adverse with high mortality.^{2,16}

There is no indication for primary prevention of sudden death in the presence of Uhl's anomaly. However, if secondary prevention is indicated, a subcutaneous implantable cardioverter-defibrillator is probably the most appropriate approach, given the risk for RV rupture.

Unfortunately, in this case, the social conditions of the patient limited the therapeutic interventions. This case represents the longest follow-up of a symptomatic patient with an unoperated Uhl's anomaly.

CONCLUSION

Uhl's anomaly is an extremely rare entity. Despite being known for a long time, it does not have a defined etiology, and it is often confused with ARVD. Recent advances in cardiac imaging allow its early diagnosis. Most patients are diagnosed prenatally or in infancy and rarely survive to adulthood. In a patient with RV morphologic derangements and intractable HF, it is important to consider this disorder.

Optimal treatment of these patients is not defined, and its prognosis is usually poor, particularly if not operated.

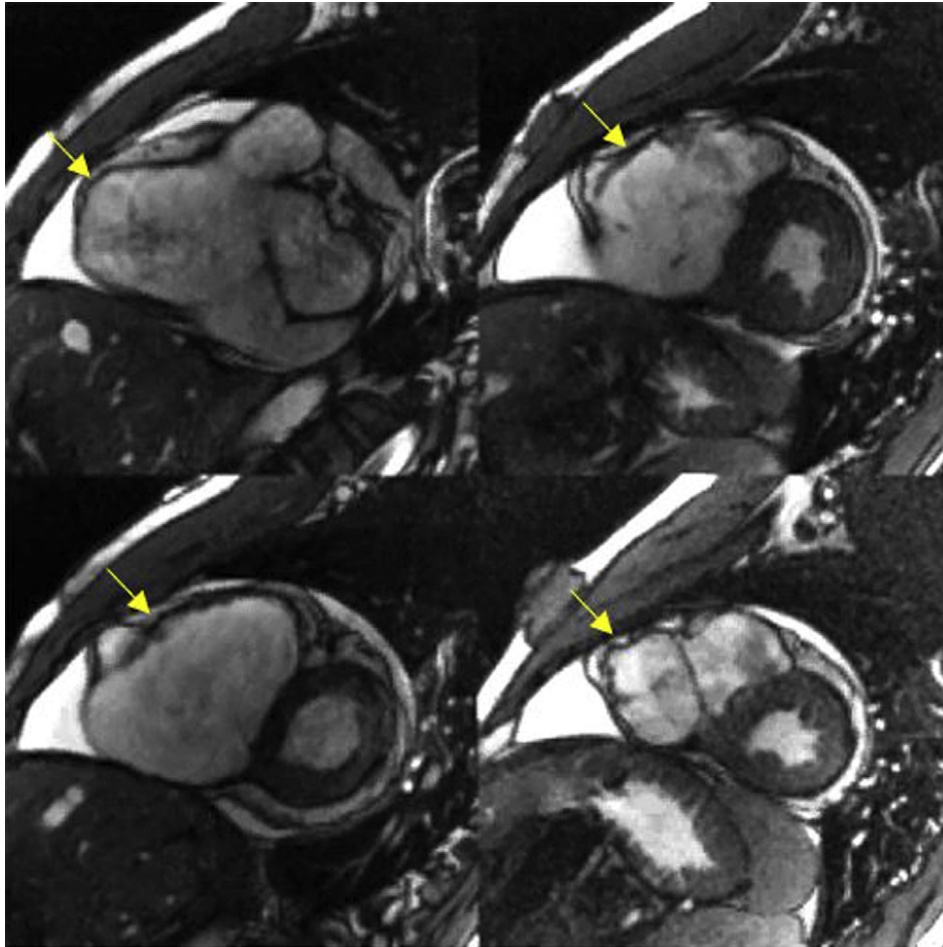


Figure 5 Cardiac magnetic resonance, in steady-state free precession, short-axis sequence showing normal left ventricular size, and the obvious thinning of the RV free wall (arrows).

Table 1 Differential diagnosis of Uhl's anomaly and ARVD^{5,12,15}

Features	Uhl's anomaly	ARVD
Morphology	RV myocardial absence	Fibrofatty replacement of RV myocardium
Distribution	Generalized	Localized
Age of presentation	Childhood	Adolescence and adulthood
Gender	Indifferent	More common in men (3:1)
Family history	No	Usual
Usual mode of presentation	Heart failure	Arrhythmias, syncope, or sudden death
Risk for sudden death	Low	High
Electrocardiography	Uncharacteristic	Localized QRS enlargement (>110 msec) in right precordial leads (V ₁ –V ₃) and epsilon waves

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.case.2020.05.014>.

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