A Report of Uhl's Disease in Identical Adult Twins*

Evaluation of Right Ventricular Dysfunction with Echocardiography and Nuclear Angiography

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The first example of Uhl's disease affecting identical adult twins is reported, offering support for the contention that a congenital developmental defect or hereditary tendency is the responsible cause. In one case, echocardiography and nuclear angiography proved to be valuable in making the diagnosis. Uhl's disease in the adult should be suspected among cases of isolated right ventricular enlargement and failure complicated by ventricular dysrhythmias. The diagnosis may be made using a combination of noninvasive tests, obviating the need for cardiac catheterization.

Uhl's disease is an uncommon cardiac disorder characterized by varying degrees of replacement of the right ventricular myocardium by fibrous and adipose tissue in the presence of normal tricuspid and pulmonic valves. Like Ebstein's disease and right ventricular infarction, it is a cause of isolated right ventricular dilatation and failure. The postulate that Uhl's disease may be a result of abnormal embryologic development is supported by this report of the anomaly affecting identical adult twin brothers, both of whom died because of ventricular dysrhythmias. One patient's condition was investigated with M-mode and two-dimensional echocardiography combined with nuclear angiography. The findings are illustrated and these suggest that the identification of the cause of isolated right ventricular failure may not require cardiac catheterization and angiography.

Case Reports

Case 1

This patient had suffered episodes of palpitations associated with lightheadedness since the age of 20 years. At the age of 35, he was admitted to the hospital with ventricular tachycardia which was converted to sinus rhythm with quinidine sulfate. Physical examination at this time was normal apart from mild elevation of the jugular venous pressure. Following conversion to sinus rhythm, the ECG demonstrated left anterior hemiblock and T wave inversion in leads V_{2} to V_{6}.

Over the ensuing years, episodes of ventricular tachycardia became more frequent despite intensive medical therapy, necessitating repeated electrical cardioversion. In 1978, he was successfully resuscitated from ventricular fibrillation by paramedics and transferred to the hospital. On this admission, frequent ventricular ectopic beats and episodes of ventricular tachycardia were controlled with a combination of orally administered disopyramide and propranolol. Physical examination was again unremarkable apart from mild elevation of the jugular venous pressure. In comparison to previous films, the chest roentgenogram demonstrated an increase in heart size.

M-mode echocardiography demonstrated a right ventricular dimension of 4.8 cm and a left ventricular dimension of 3.4 cm. The interventricular septal motion was normal. The tricuspid, aortic, mitral, and pulmonary valve echoes were normal. Specifically, the tricuspid valve echo was identified in the normal position with a normal E-F slope and time of closure (C point), and presystolic opening of the pulmonic valve was not found (Fig 1). Two-dimensional echocardiography confirmed the markedly increased right ventricular dimension and normal position of the tricuspid valve (Fig 2). Images of the first pass of the radio-indicator (^{99m}Tc
technetium, 20 mCi) were obtained as two second frames on x-ray film. The right ventricular ejection fraction was measured employing the count-rate method, as described by Tobinick et al.\footnote{1} Ungated cardiac blood pool imaging in the anterior and modified 40° LAO projections was made by collecting 500,000 counts in each image. Multiple gated scintigraphy was then performed using ^{99m}Tc
technetium labeled red blood cells in the left anterior oblique projection (Fig 3). These techniques demonstrated a prolonged right heart transit time (in excess of 18 seconds), marked enlargement of the body of the right ventricle and its infundibulum, an enlarged slowly-emptying right atrium, and an unmeasurable right ventricular ejection fraction. The left ventricular ejection fraction was 67 percent.

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Figure 1. Echograms of case 1. Top left, enlarged right ventricular cavity (RV). Top right and bottom right, tricuspid valve closure (TC) follows mitral valve closure (TC) by 10 msec. Bottom left, normal pulmonic valve echogram.

Right heart catheterization performed with a Swan-Ganz catheter demonstrated the following pressures (mm Hg): right atrium, 11 (A wave = 14); right ventricle, 34/8-14; pulmonary artery, 32/16; pulmonary artery wedge, 18; and brachial artery, 132/90. The cardiac output obtained by dye curve technique was 4.3 L/min. The pulmonary arteriolar and systemic resistances were within normal limits.

Following discharge, the patient did well on the combination of orally administered disopyramide and propranolol for approximately six months. In August 1978, he suffered a second episode of ventricular fibrillation at home and attempts at resuscitation were unsuccessful.

Figure 2. Two-dimensional echocardiogram. Systolic apical four chambered view showing mitral and tricuspid valves in same plane, a dilated right ventricle (RV) in comparison to left ventricle (LV), and dilated right atrium (RA). Solid arrow indicates tricuspid valve, and open arrow indicates anterior leaflet of mitral valve.
At necropsy, the heart weighed 550 g. The right atrium was hypertrophied, and the right ventricle was strikingly dilated. The tricuspid orifice was normally positioned and the leaflets normal. The pulmonary valve was normal. An atrial septal defect was not present. Several areas of the right ventricular wall were paper thin, but other areas appeared to be of normal thickness. Sections of the right ventricle taken from the apex to its base showed extensive replacement by fatty and dense collagenous tissue with small islands of surviving muscle fibers (Fig 4). Numerous mural thrombi were attached to subjacent fibrotic areas of the endocardium of the right ventricle. A small area of focal fibrosis was present in the anterolateral wall of the left ventricle, but there was no evidence of recent myocardial infarction. The aortic and mitral valves were intrinsically normal. A significant degree of atherosclerosis affected all three coronary arteries.

In retrospect, the three-vessel coronary artery disease aids in the explanation of both the elevated pulmonary artery wedge pressure and the deterioration of the patient's chronic paroxysmal ventricular tachycardia into ventricular fibrillation in the final year of his life.

CASE 2

The identical twin brother to patient 1 had suffered episodes of paroxysmal ventricular tachycardia since the age of 18 but had refused medical treatment. Physical examination and chest roentgenography were apparently within normal limits. In 1959, an ECG was normal apart from occasional unifocal ventricular ectopic beats and deeply inverted T...
waves in leads 3, aVF, and V1 to V6. He died suddenly at the age of 37 years during a game of softball.

Autopsy demonstrated a markedly dilated, transparent right ventricle covered with adipose tissue. The dilation involved the entire chamber but was particularly prominent in the infundibular region. Microscopic examination showed that the right ventricular myocardium was virtually totally replaced by adipose tissue without fibrosis or evidence of inflammation. Some surviving myocardial fibers showed focal fragmentation. The left ventricle was normal; the coronary arteries were free of atherosclerosis, and the atrioventricular and semilunar valves were intrinsically normal.

Family Studies

The son of case 2 presented in 1978 with a history of palpitations, and an ECC documented frequent premature ventricular contractions. These were somewhat suppressed during exercise testing, but couplets were noted in the postexercise period. Physical examination was unremarkable. An echocardiogram demonstrated only mild enlargement of the right ventricular internal dimension. Propranolol therapy satisfactorily suppressed the premature beats. Although a definitive diagnosis could not be made in this case, certain features were suggestive of a mild form of Uhl's disease.

Echocardiograms of two other asymptomatic siblings were normal.

DISCUSSION

Forty-nine cases of Uhl's disease have been documented in the world literature, and 21 of these patients survived to adult life.5-20 It would appear that longevity is related to the extent of right ventricular involvement. Characteristically, the severe form presents in infancy with intractable congestive cardiac failure. The hemodynamic findings reflect right ventricular pump failure, and the right atrium is responsible for maintaining the pulmonary circulation. The right atrial "a" wave may be transmitted to the right ventricle and pulmonary artery producing diastolic opening of the pulmonary valve. Cyanosis may be present, resulting from a right-to-left shunt at the atrial level. With lesser degrees of right ventricular dysfunction, longer survival is possible and only elevated right ventricular filling pressures may be observed, as in our case 1. This relatively benign course in adults is, however, complicated by the occurrence of malignant ventricular dysrhythmias in two-thirds of the reported cases6,18 and an occasional conduction defect.17

Although Uhl's disease is distinctly uncommon, it forms with Ebstein's disease and right ventricular infarction part of the differential diagnosis of isolated right ventricular enlargement and failure. Noninvasive echocardiography and scintigraphy play an important role in this differentiation, because cardiac catheterization may be hazardous when Uhl's disease is complicated by ventricular dysrhythmias. Markedly compromised right ventricular function may be recognized echocardiographically by finding a dilated right ventricle and diastolic opening of the pulmonary valve preceding tricuspid valve closure.18 Even when the latter finding is absent with milder degrees of right ventricular dysfunction, echocardiography and scintigraphy are helpful in excluding Ebstein's disease and right ventricular infarction. The tricuspid echogram in Ebstein's disease is located in an abnormally leftward position, and has a decreased E-F slope, an increased excursion in diastole, and follows mitral valve closure by 40 to 100 msec, features which are absent in Case 1.18 Additionally, the scintigrams show a normally situated tricuspid valve and absence of reflux into the inferior vena cava. Healed right ventricular infarction may also be associated with features similar to Uhl's and Ebstein's disease. Isner and Roberts22 demonstrated "a" wave transmission to the pulmonary artery seven years after the acute infarction and stressed the frequency of a dilated right ventricle. Multiple gated blood pool imaging is helpful in the diagnosis of right ventricular infarction by demonstrating segmental areas of hypokinesis and dyskinesia rather than global right ventricular and infundibular dysfunction.23 Left-to-right intracardiac shunts (eg, atrial septal defect) and other right ventricular volume overload states (eg, tricuspid insufficiency) may also provide an echocardiographic pattern of isolated right ventricular enlargement. However, in these conditions, the interventricular septal motion is characteristically paradoxical (in the absence of pulmonary hypertension). Moreover, the physical examination, ECG, and chest roentgenogram usually offer important clues in the differential diagnosis.

The cause and nature of the defect in Uhl's disease is unknown. Recently, Bharati et al19 postulated that the abnormality of the right ventricle may occur because of faulty fusion of the descending proximal and distal portions of the bulboventricular loop. The occurrence of the disease in our identical twin patients and one of their siblings lends support to the thought that an embryologic or hereditary fault may be operative.

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REFERENCES

2 Segall H: Parchment heart (Osler). Am Heart J 1950; 70:948-50
3 Castleman B, Towne VW: Case records of the Massachu-
9 Cote M, Davignon A, Fourier JC: Congenital hypoplasia of the right ventricular myocardium (Uhl's anomaly) associated with pulmonary atresia. Am J Cardiol 1973; 31:658-61
10 Obma R, Perry LW, Scott LP: Uhl's anomaly of the heart with atrial septal defect and valvular pulmonary stenosis. Med Ann DC 1974; 43:413-18
11 Esposito L, Nobili B: A case of progeria associated with Uhl's syndrome. Pediatr (Napoli) 1975; 83:326-43
21 Kotter MN, Tabatznik B: Recognition of Ebstein's anomaly by ultrasound technique. Circulation 1971; 44 (suppl 2):34