Ebstein's Anomaly Associated with Cardiomyopathy and Pulmonary Hypertension

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During the past decade definite progress has been made toward an understanding of the hemodynamic alterations and pathophysiologic aspects of Ebstein's anomaly of the tricuspid valve. Moreover, an increased awareness of the characteristic clinical findings has resulted in an apparent increase in incidence of the disease. Largely as a result of careful pathologic studies, atypical forms of Ebstein's anomaly have been recognized. These include (a) a forme fruste characterized by minor tricuspid valve malformation with mild or clinically inapparent disease and (b) the association of Ebstein's anomaly with a variety of other congenital cardiac lesions. Defects of the atrial septum are common in Ebstein's anomaly and should not be considered associated lesions. Rather they are an integral part of the full-blown syndrome, since they allow shunting of blood away from the poorly functioning right heart. In contrast, ventricular septal defects may be considered associated congenital cardiac lesions, since they have been described in only four patients and markedly alter the clinical findings. Isolated case reports have described the association of Ebstein's anomaly with patent ductus arteriosus, pulmonary stenosis, dilated pulmonary artery, hypoplastic pulmonary artery, corrected transposition of the great vessels with and without ventricular septal defect, hypoplastic aorta with fetal coarctation, pulmonary stenosis with ventricular septal defect and right ventricular hypertrophy, and pulmonary atresia with intact ventricular septum.

Since the clinical features of the atypical forms of Ebstein's anomaly are not characteristic or consistent, the recognition of these patients during life depends upon a high index of suspicion and prudent use of the electrode catheter. In the patient to be described, failure to suspect Ebstein's anomaly led to complications during right heart catheterization so that the procedure had to be terminated prematurely. A second cardiac catheterization, with use of the electrode catheter and left heart measurements, established the correct diagnosis of Ebstein's anomaly associated with a cardiomyopathy. The cardiomyopathy was characterized by marked elevation of the ventricular end-diastolic pressures, prominent "a" wave of the pulmonary wedge pressure pulse, and pulmonary hypertension. These associations are considered worthy of report not only because they are unique but also because the recognition of such atypical forms of Ebstein's anomaly has definite application to clinical diagnosis, cardiac catheterization, and corrective cardiac surgery.

Case Report

M.C., a 20-year-old Caucasian man was admitted to the U. S. Naval Hospital, Portsmouth, Virginia, in September 1963 with the diagnosis of congenital heart disease. A heart murmur was first noted during a hospital admission for appendicitis in 1961. Cardiac roentgenography performed at that time was interpreted as normal. An electrocardiogram, however, was considered to show right ventricular hypertrophy and right atrial enlargement. No follow-up studies were obtained until the cardiac murmur was again noted during a recent preoperative evaluation for an elective herniorrhaphy. The patient was re-
ferred to this hospital for a more precise cardiac evaluation.

The patient was adopted as an infant and little was known concerning his genetic parents. To the best of his knowledge he was a healthy infant and child. His growth and development were normal, and he participated without difficulty in competitive athletics. In retrospect the patient believes that he may have been more dyspneic following strenuous physical exertion than his teammates.

Physical examination revealed a well-developed, well-nourished, Caucasian man. The blood pressure was 110/70 mm Hg; the pulse was 70 per minute and brisk to palpation. An erythematous flush was noted over the malar areas. Examination of the chest revealed an active precordium with a right ventricular heave along the left sternal border. No thrills were palpable. On auscultation a grade-II/VI, rough, systolic murmur of constant intensity was heard along the left sternal border and in the pulmonic area. The second heart sound at the base was loud, narrowly split, and did not seem to vary with respiration. The two components of the second sound were approximately equal in intensity. No gallops or rubs were heard. The remainder of the physical examination including examination of the extremities for clubbing and cyanosis was negative.

Routine laboratory studies including a urinalysis, hemogram, fasting blood sugar, blood urea nitrogen, and serologic test for syphilis were within normal limits. A phonocardiogram (fig. 1) confirmed the auscultatory findings. Chest roentgenograms (fig. 2) showed a globular cardiac silhouette which was at the upper limits of normal in size. The pulmonary vasculature appeared increased. In the right anterior oblique projection the right ventricular outflow tract was prominent and posterior displacement of the barium-filled esophagus suggested left atrial enlargement. Cardiac fluoroscopy confirmed the roentgenographic findings. In addition, there were intrinsic pulsations of the secondary branches of the right pulmonary artery, interpreted as a "hilar dance." The electrocardiogram (fig. 3) showed a QRS interval of 0.11 second, and the terminal QRS forces were directed rightward, superiorly, and anteriorly producing an S wave in lead I and R prime deflections in aV_R and V_1. These findings were interpreted as a variant of incomplete right bundle-branch block. Large R and S waves were recorded in the

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Figure 1

Phonocardiograms, indirect carotid pulse (ICP), and electrocardiogram (EKG) of patient. The upper phonocardiogram was recorded from the second left intercostal space (Lt. 2 ICS), the lower one from the fourth left intercostal space (Lt. 4 ICS). There is a systolic murmur (SM) of constant intensity beginning with the first heart sound (S1) and ending just before the second sound. The aortic (A2) and pulmonic (P2) components of the second heart sound are approximately 0.04 second apart in both inspiration and expiration.

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precordial leads indicating biventricular hypertrophy. The P waves were tall and peaked in the limb leads but in V1 the P wave deflection had a prominent negative component suggesting bialtrial enlargement. A spatial vectorcardiogram obtained with use of the Frank system (fig. 4) confirmed the presence of a counterclockwise QRS loop with terminal forces directed as described.

An atrial septal defect was considered the most likely diagnosis in spite of atypical features, and right heart catheterization was undertaken. After 1 per cent lidocaine was infiltrated for local anesthesia, the patient had a brief tonic convulsion and his mentation became obtunded. The electrocardiogram showed a change to a nodal bradycardia at a rate of 35 beats per minute which was reverted to normal sinus rhythm with intravenous atropine. After complete restoration of the patient’s cerebral function the catheterization was continued. Extensive exploration of the right atrium via a catheter in the right femoral vein revealed a large chamber, but the catheter could not be passed across either an atrial septal defect or the tricuspid valve. Marked cardiac irri-

Figure 2

Chest roentgenograms in the posteroanterior, lateral, and right anterior oblique projections.

Figure 3

Electrocardiogram of patient. Note that precordial leads V5-V6 are recorded at one-half normal standardization.

Figure 4

Spatial vectorcardiogram obtained with use of the Frank system. The sagittal loop is a left sagittal projection.
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Table 1

Cardiac Catheterization Data (Second Procedure)

<table>
<thead>
<tr>
<th>Site</th>
<th>Pressure (mm. Hg)</th>
<th>Mean pressure (mm. Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right atrium</td>
<td>—</td>
<td>(3)</td>
</tr>
<tr>
<td>“a” wave</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Right ventricle</td>
<td>52/0/9</td>
<td></td>
</tr>
<tr>
<td>infundibulum</td>
<td>45/0/7</td>
<td></td>
</tr>
<tr>
<td>Pulmonary artery</td>
<td>45/13</td>
<td>(23)</td>
</tr>
<tr>
<td></td>
<td>57/19*</td>
<td>(39)*</td>
</tr>
<tr>
<td>Pulmonary wedge</td>
<td>—</td>
<td>(16)</td>
</tr>
<tr>
<td>“a” wave</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Left ventricle</td>
<td>131/0/39</td>
<td></td>
</tr>
<tr>
<td>Radial artery</td>
<td>129/70</td>
<td></td>
</tr>
<tr>
<td>Cardiac output</td>
<td></td>
<td></td>
</tr>
<tr>
<td>(dye dilution)</td>
<td>6.4, 5.7 L./min.*</td>
<td></td>
</tr>
<tr>
<td>Nitrous oxide test</td>
<td>4.6 per cent*</td>
<td></td>
</tr>
</tbody>
</table>

* Data from first cardiac catheterization.

tability was encountered during manipulations of the catheter. A forward dye curve from the superior vena cava with indocyanine green indicated that there was no right-to-left shunt. A second catheter was inserted into the right antecubital vein and after repeated attempts it was possible to catheterize the pulmonary artery. Moderately severe pulmonary hypertension was noted (table 1). Administration of 100 per cent oxygen during continuous monitoring of pulmonary artery pressure caused no change in pressure during an observation period of 10 minutes. Normal oxygen saturations, a nitrous oxide test, and forward dye curves militated against the presence of a left-to-right shunt. During an attempt to wedge the catheter in a branch of the right pulmonary artery a twisted loop developed in the right atrium, presumably because of a lack of fulcrum in this chamber. Further manipulation only caused the catheter to twist once more upon itself. A pullback from the pulmonary artery was performed in anticipation that the loops would unravel themselves. Instead, the tip of the catheter fell through one of the loops in the right atrium and a loose knot developed. After careful manipulations of the catheter the knot was “untied.” The catheterization, which had consumed 4 hours, was terminated. In spite of the pulmonary hypertension a diagnosis of Ebstein’s anomaly was entertained because of the catheter coiling in the large right atrial chamber, the difficulty in crossing the tricuspid valve, and the marked cardiac irritability.

A week later a second cardiac catheterization was undertaken. Again following instillation of 1 per cent lidocaine the patient developed sinus bradycardia, which was reverted by intravenous atropine. Retrograde left ventricular catheterization revealed marked elevation of the ventricular end-diastolic pressure (fig. 5). The pullback of the catheter across the aortic valve showed that there was no gradient. Right heart catheterization was accomplished via the left antecubital vein. With this approach it was less difficult to cross the tricuspid valve and catheterize the pulmonary artery. Pulmonary hypertension was again demonstrated, and when the catheter was advanced to the pulmonary wedge position, an elevated pressure with a prominent “a” wave was observed (fig. 6). An angiocardiogram with injection into the pulmonary artery was performed in order to rule out obstructive lesions of the left atrium or pulmonary veins. The injection was

Figure 5

Left ventricular (LV) and radial artery (RRA) pressures recorded simultaneously. Note the marked elevation of left ventricular end-diastolic pressure indicated by the arrow.
repeated in the left anterior oblique position during the exposure of a cineangiogram. Both studies showed normal filling of the pulmonary arteries and veins, left atrium, and left ventricle; the only demonstrable abnormality was increased thickness of the left ventricular wall (fig. 7). The pullback of the catheter from the pulmonary artery to the right ventricle showed a small systolic pressure gradient in the region of the right ventricular infundibulum and an elevated ventricular end-diastolic pressure. The right ventricle was irritable and tended to “eject” the catheter into the right atrium, where a prominent “a” wave was noted. Finally an electrode catheter was employed in order to record simultaneously the intracavitary electrocardiogram and pressure during passage of the catheter from the right atrium into the right ventricle. An intermediate “chamber,” with an atrial pressure pulse and intracavitary electrocardiogram similar to that in the right ventricle, was demonstrated (fig. 8). These findings were reproducible upon repeated manipulations of the catheter.

Discussion

The clinical findings in patients with Ebstein’s anomaly of the tricuspid valve are sufficiently distinctive that the diagnosis may be suspected with a high degree of accuracy during life. An awareness that the severity of symptoms and degree of incapacity are highly variable is essential for correct diagnosis. A few patients are cyanotic from birth and have a rapidly progressive clinical course. In the majority, however, dyspnea, easy fatigability, and cyanosis develop gradually during childhood or adolescence. Some patients remain asymptomatic until the third or fourth decades and, in rare instances, throughout life. Paroxysmal tachycardia may occur at any age and eventually affects at least one fourth of all patients with Ebstein’s anomaly.² On physical examination an unusual facial erythema or violaceous hue may be noted.³ Most patients are cyanotic, and clubbing is present in those with long-standing
cyanosis. Although the heart is usually enlarged to percussion, the cardiac pulsations are minimal. Almost all patients have a moderately loud systolic murmur, which is accompanied by a diastolic murmur in somewhat less than half. A triple rhythm frequently occurs, and occasionally a quadruple rhythm is noted. The second sound at the pulmonic area is usually increased, and some authors have emphasized the diminished intensity of the first heart sound. A globular cardiac silhouette, with a prominent right heart border, narrow base, small aorta, and clear lung fields is the classical roentgenographic finding. Moderate to marked cardiomegaly is almost always present. The pulmonary vascular markings are either normal or decreased. A “boxlike” contour to the cardiac silhouette is frequently observed and is said to be diagnostic of this disorder. The electrocardiogram in Ebstein’s anomaly has several characteristic features. In Vaccaro’s review of 86 electrocardiograms, three fourths showed right bundle-branch block, often
atyphical; two thirds had large P waves; and in one quarter there was prolongation of the PR interval. The QRS complexes are often splintered, notched, or shuffled, and the R prime deflections in the right precordial leads may be "dwarfed."4, 5 Such variants of right bundle-branch block combined with large P waves should alert one to this diagnosis. Six of 23 patients reported by Schiebler4 had type-B Wolff-Parkinson-White pattern. The finding of tall peaked P waves and the Wolff-Parkinson-White syndrome strongly suggests Ebstein's anomaly. Those episodes of paroxysmal tachycardia that are documented electrocardiographically are almost always supraventricular in origin.

At cardiac catheterization the distinctive features of Ebstein's anomaly are a markedly enlarged right atrium in which the catheter tends to coil and displacement of the tricuspid valve to the left of the spine. As a result, the catheter tip can be advanced far to the left in the cardiac silhouette and still record an atrial pressure pulse. In addition, it is difficult to pass the catheter across the tricuspid valve, and cardiac irritability including bouts of supraventricular tachycardia may result from such manipulation. The right atrial pressure is usually elevated. An atrial septal defect is sometimes demonstrated by direct catheterization of the defect or more often by evidence of a right-to-left shunt. There may be a pressure gradient across the tricuspid valve, suggesting tricuspid stenosis, or a pressure pattern in the right atrium simulating tricuspid insufficiency.4 Although the findings enumerated above suggest the diagnosis of Ebstein's anomaly, the electrode catheter is considered essential for confirmation of the diagnosis. The characteristic changes in the intracavitary electrocardiogram have been extensively described by Hernandez and his co-workers.17 The increased risk of cardiac catheterization has been stressed in several reports,7, 9, 18, 28 and some authors28 believe that this procedure should not be performed except under special circumstances. Other investigators, however, have not encountered arrhythmias or complications during catheterization of large numbers of these patients.4

The reasonably distinct set of clinical and laboratory findings described above as characteristic of Ebstein's anomaly will necessarily be altered by the presence of associated cardiac lesions. In retrospect, however, our patient did show some typical features. The facial erythema described by Schiebler4 was present. The auscultatory findings did include a systolic murmur along the left sternal border and a moderately loud second heart sound at the pulmonic area. The chest roentgenogram showed a globular cardiac silhouette, which was at the upper limits of normal in size. The right atrial enlargement demonstrated at cardiac catheterization was not obvious fluoroscopically except in retrospect. Left atrial and right ventricular enlargements, not characteristic of Ebstein's anomaly, were observed roentgenographically and probably resulted from the cardiomyopathy and pulmonary hypertension. The increase in pulmonary vascular markings was also attributed to pulmonary hypertension. The electrocardiogram showing a variant of incomplete right bundle-branch block and large peaked P waves was typical of Ebstein's anomaly. In addition, there was marked splintering of the QRS complexes. The prominent negative deflection of the P wave in V1, the increased voltage across the left precordium, and the T-wave vector directed away from the left ventricle were attributed to the cardiomyopathy. Cardiac hyperirritability, well known in patients with Ebstein's anomaly, was a persistent problem during the catheterization of our patient. In addition, the coiling of the catheter in the dilated right atrium resulted in the development of a knot in the catheter, which fortunately was resolved. The moderately severe pulmonary hypertension, which has not previously been described in Ebstein's anomaly,7, 15 was considered to be a manifestation of the underlying cardiomyopathy.

The practical problem of planning cardiac catheterizations and anticipating complications that might arise during this procedure...
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makes it imperative to have a high index of suspicion for the atypical forms of Ebstein's anomaly. An electrode catheter should be readily available, if not routinely used, during the cardiac catheterization of all patients with congenital heart disease. The increasing number of associations of Ebstein's anomaly with other congenital cardiac defects also has surgical ramifications. Operative closure of atrial septal defects, which carries a mortality of 1 to 2 per cent in most medical centers,\(^{19}\) has had a staggering mortality of three deaths in four patients with Ebstein's anomaly.\(^{20-22}\)
The one patient with a ventricular septal defect, pulmonic stenosis, and Ebstein's anomaly\(^{15}\) who had corrective surgery did not survive.\(^{4}\) Numerous other patients with Ebstein's anomaly have died during induction of anesthesia,\(^{23}\) at thoracotomy,\(^{8,9,12,25,26}\) cardiac catheterization,\(^{7,9,27,28}\) angiocardiology,\(^{7,29}\) sympathectomy,\(^{30}\) and lung resection.\(^{31}\) The experience cited above makes it clear that these patients are poor candidates for surgical as well as diagnostic medical procedures. The benefits to be gained from such procedures must be weighed against the very real possibility of sudden death. In spite of the increased surgical risk, those patients who are markedly cyanotic and deteriorating rapidly may benefit from anastomosis of the superior vena cava to the right pulmonary artery. Experience from four different institutions\(^{32-36}\) in seven such patients indicates definite clinical improvement in five; however, there were two postoperative deaths.

The nature of the patient's cardiomyopathy remains obscure. The clinical and laboratory findings are not unlike those described by Braunwald\(^{37}\) in a group of patients with "idiopathic myocardial hypertrophy without congestive heart failure or obstruction to blood flow." The points of similarity include electrocardiographic features of left ventricular hypertrophy with a wide QRS-T angle, elevated ventricular end-diastolic pressures, prominent "a" waves in the atrial pressure pulses, and increased thickness of the left ventricular wall. As in Braunwald's patients, the elevated left ventricular end-diastolic pressure was the result of a prominent atrial contraction wave transmitted into the ventricle. In addition, our patient showed a gradient across the right ventricular outflow tract in the region of the infundibulum suggesting muscular obstruction. No gradient was demonstrable, however, across the left ventricular outflow tract. In retrospect, the administration of isoproterenol, which increases the obstruction in patients with hypertrophic subaortic stenosis,\(^{38}\) may have been illuminating in the further classification of this patient's cardiomyopathy.

**Summary**

A patient is described with cardiomyopathy and intracavitary electrocardiographic findings typical of Ebstein's anomaly of the tricuspid valve. The cardiomyopathy was characterized by extreme thickness of the left ventricular wall on angiocardiology, elevated end-diastolic pressures of the ventricles, and prominent "a" waves in the atrial pressure pulses. Moderately severe pulmonary hypertension, which has not previously been described in Ebstein's anomaly, was also attributed to the cardiomyopathy. This case illustrates the increasing number of associations with which Ebstein's anomaly has been reported and emphasizes the importance of considering this diagnosis in planning the cardiac catheterization of patients with congenital heart disease. The necessity of demonstrating coexisting Ebstein's anomaly in patients with congenital heart disease is indicated by the formidable mortality of such patients at surgery.

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References
Marcello Malpighi: 1628-1694

When Malpighi submitted his doctor's thesis, in which he made condemning remarks about Galen and the great Arab physicians Avicenna and Rhases, the thesis was not accepted. At the second attempt he fared no better, although he had modified the text considerably.

When there was nothing left which could be considered offensive, the thesis was finally accepted. In fact, it had been somewhat embarrassing to twice fail the most brilliant student. The other students were in sympathy with Malpighi—they knew that the reason for his failures certainly was not the poor opinion held of the candidate's abilities.

However, Malpighi was not to rejoice for long. Some of the professors were not reconciled to the fact that the tranquility of one of Europe's most ancient universities should be disturbed by an inquisitive, doubting doctor who harbored suspicions against the ancient philosophers.

They succeeded in having his diploma taken away from him. He was only able to get it back after a lengthy struggle.—TIBOR DOBY, M.D. Discoverers of Blood Circulation. From Aristotle to the Times of Da Vinci and Harvey. New York, Abelard-Schuman, 1963, p. 223.
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