Severe congenital tricuspid regurgitation in the newborn

A rare form with myxomatous valvular incomplete development[1]

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A case of congenital tricuspid insufficiency in the newborn secondary to myxomatous degeneration of the tricuspid valve is described. There were myxomatous changes of the pulmonary and aortic valves. The mitral valve was normal. Histologic study showed an increased amount of glycosaminoglycans and a decreased amount of mature collagen of the tricuspid, aortic, and pulmonary valves. The etiology of congenital tricuspid insufficiency of the newborn can be expanded to include failure of the tricuspid valve leaflets to develop normally, a condition that is histologically similar to myxomatous degeneration in the adult.

Index terms: Heart defects, congenital • Tricuspid valve insufficiency

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Congenital tricuspid insufficiency is an uncommon but recognized cause of neonatal congestive heart failure, cyanosis, and death.[1–9] The tricuspid regurgitation may be secondary to (1) dysplastic tricuspid leaflets or chordal attachments without displacement,[1] (2) dysplastic and displaced leaflets (Ebstein's anomaly),[1] (3) tricuspid regurgitation secondary to pulmonary atresia with an intact ventricular septum, and (4) a form of transient regurgitation associated with neonatal stress and hypoglycemia.[2–9] A small group of the latter infants has died and the postmortem examination demonstrated necrosis of the distal portion of the anterior papillary muscle of the tricuspid valve while the mitral valves have been normal.[8] It has been suggested that the tricuspid valve regurgitation was the result of infarction of the papillary muscles secondary to neonatal stress and hypoxia.

Few reports have described myxomatous degeneration of the tricuspid valve and we found no report of associated severe tricuspid valve regurgitation in the newborn with myxomatous changes of both the pulmonary and aortic valves. We describe a newborn infant who presented with severe tricuspid regurgitation and died soon after birth. There were marked myxomatous degenerative changes in the tricuspid, pulmonary, and aortic valves without evidence of systemic collagen disease and with a normal-appearing mitral valve.

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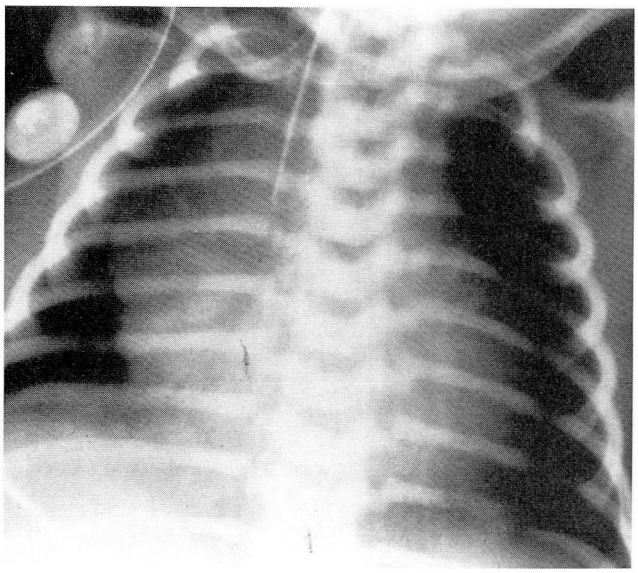

Fig. 1. Anteroposterior chest radiograph demonstrating cardiomegaly with decreased pulmonary vascularity. The endotracheal tube is in place.

Case report

The patient presented to the Cleveland Clinic Foundation Hospital as a 30-hour-old, 2550-gram infant who was the product of a 31-year-old gravida 3, para 3 female who had no problems during pregnancy, labor, or delivery. The infant was full term by dates. Apgar scores were 8 at one and five minutes. The patient was noted to be "dusky" at birth and a heart murmur was noted shortly after delivery. The patient was treated with 30% oxygen. A chest radiograph showed markedly increased heart size. Shortly thereafter, the infant suffered a cardiac arrest. No heart beat or blood pressure was obtainable for 25 to 40 minutes. The pupils were fixed and dilated with arterial pH ranging from 6.6 to 6.9. Prior to transfer to another regional hospital the patient had been noted to have bloody stools and seizures. Cardiac catheterization was done and suggested severe pulmonary stenosis and an intact ventricular septum. The infant was treated with intravenous prostaglandin (PGE_1) and transferred to the Cleveland Clinic Foundation.

The physical examination demonstrated a cyanotic infant who was intubated and ventilated. The heart rate was 180 per minute with sinus rhythm. The blood pressure was 50–60 mmHg systolic in both the upper and lower extremities. Head, ears, eyes, nose, and throat examinations were within normal limits. The chest was clear. The first heart sound was normal. The second heart sound was split with an increased pulmonary component. There was a Grade II/VI systolic murmur at the left upper sternal border and a Grade II/VI long blowing systolic murmur at the right midsternal border that varied with respiration. The liver was palpable

A, B

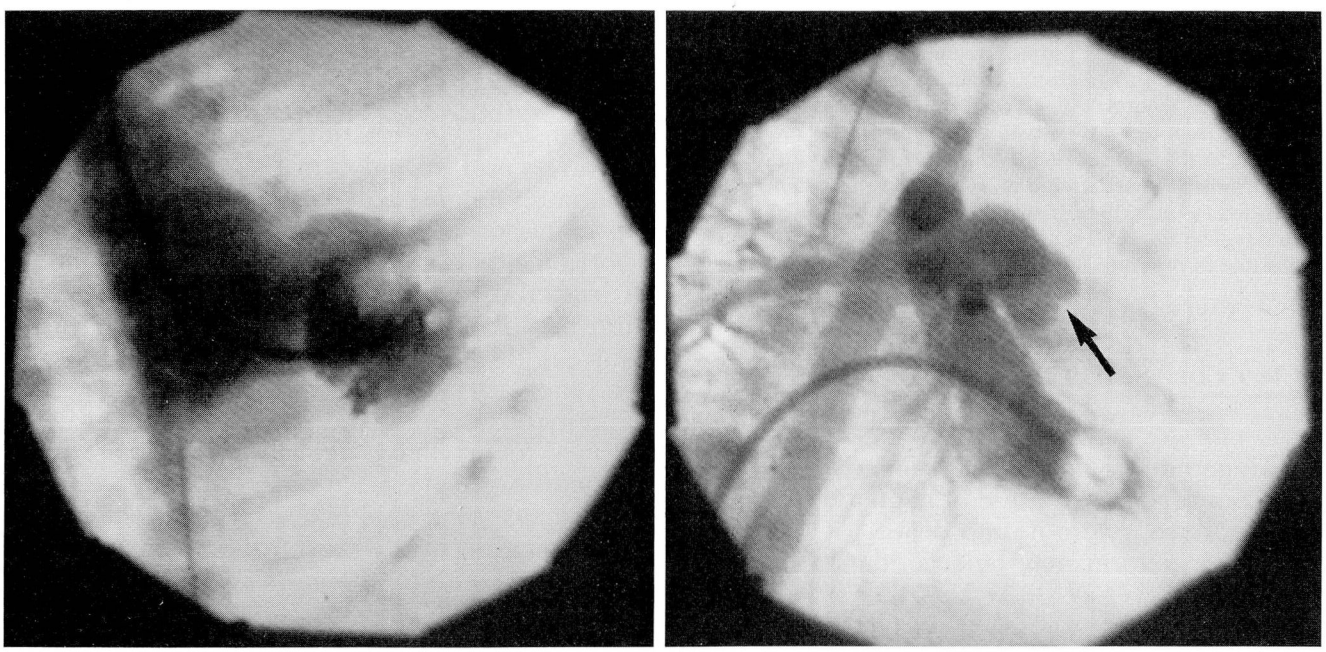

Fig. 2. A. Right ventricular angiogram, right anterior oblique view, with a catheter in the midportion of the right ventricle, demonstrating severe tricuspid regurgitation with contrast material passing into a huge right atrium. No right ventricular outflow tract is seen in this view.

B. Left ventricular angiogram, shallow right anterior oblique view, with the balloon catheter at the apex of the left ventricle, demonstrating flow out the left ventricle into the descending aorta. The pulmonary artery is visualized *via* flow from the patent ductus arteriosus and the arrow points to a somewhat thickened but definitely present pulmonary valve.

5 cm below the right costal margin. The peripheral pulses were 2+/4+ with no brachial-femoral pulse delay.

The chest radiograph demonstrated cardiomegaly with decreased pulmonary vascularity (*Fig. 1*). The electrocardiogram showed sinus rhythm with mild right ventricular hypertrophy and right atrial enlargement. The angiograms from the other institution revealed severe tricuspid regurgitation and a dilated right atrium (*Fig. 2A*). The systolic right ventricular pressure measured at catheterization was 26 mmHg and the left ventricular systolic pressure was 50 mmHg. There was an intact ventricular septum. On the left ventricular angiogram, there was filling of the aorta and a patent ductus arteriosus. The pulmonary artery and pulmonary valve were visualized *via* the ductus arteriosus. A well-defined pulmonary valve was visualized, which was mildly thickened (*Fig. 2B*). Based on the angiograms, the diagnosis of neonatal tricuspid insufficiency secondary to perinatal stress was made. The decreased pulmonary blood flow on the chest radiograph and the angiogram was secondary to the marked degree of tricuspid regurgitation with right-to-left shunting at atrial level. Treatment with tolazoline was begun, but it became apparent over the next 24 hours that the infant had already suffered severe neurologic stress, shown by fixed dilated pupils, posturing, and an EEG that showed very low amplitude and was almost flat. The patient was also noted to have severe renal failure. Thirty-six hours following admission, the infant suffered a severe episode of bradycardia and was not responsive to any resuscitative measures.

Pathologic findings

Except for acute renal infarction with hemorrhage bilaterally, the abnormalities in this patient were confined to the cardiovascular system. There was no evidence histologically or grossly that the infant had a major collagen or systemic illness. The heart weighed 28.5 grams. The coronary arteries were normal. The right and left ventricular walls were markedly hypertrophic. The tricuspid ring was dilated, with the cusp held in an open position by markedly shortened chordae tendineae. The tricuspid valve ring measured approximately 1.1 × 0.65 cm. The pulmonary valve ring measured 0.4 cm in diameter; the valve was tricuspid but floppy (*Fig. 3*). The mitral valve was grossly normal. The aortic valve was also tricuspid and without fusion of commissures. The aortic valve leaflets, however, grossly resembled the pulmonary valve leaflets in that they were slightly thickened and floppy. There was a patent foramen ovale and a patent ductus arteriosus.

Microscopic sections of the myocardium of the right and left ventricle showed small immature myofibrils consistent with a newborn infant with focal vacuolization. There was slight interstitial edema, but no evidence of infarction.

Multiple microscopic sections were obtained through all four cardiac valves. The tricuspid, pulmonary, and aortic valves showed incomplete and immature development. The fibrosa, which normally forms the structural backbone of the valves, was present only in the base of each valve. The major portion of each valve consisted of loose, uniform myxoid tissue, rich in glycosaminoglycans without mature collagen (*Figs. 4–6*), an appearance suggestive of primitive mesenchyme and consistent with an immature valve. The annulus of the pulmonary and aortic valves showed focal dystrophic calcification adjacent to the valvular insertion. A section of papillary muscle of the left ventricle showed focal basophilic necrosis adjacent to the insertion of the chordae tendineae. Otherwise, the papillary muscles were unremarkable. The shape of the valves was unremarkable, without nodularity and with only slight thickening. Thus, the most prominent findings were an increase in the loose connective tissue rich in glycosaminoglycans and lacking mature collagen and a fibrosa in the tricuspid, pulmonary, and aortic valves (*Figs. 4–6*).

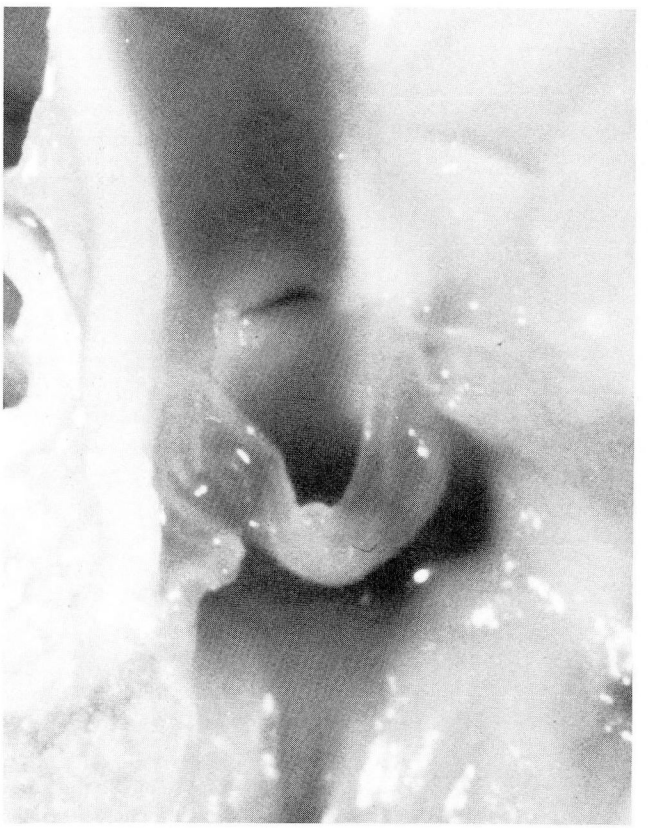

Fig. 3. Anatomic specimen demonstrating a dilated pulmonary valve ring with floppy pulmonary valve tissue.

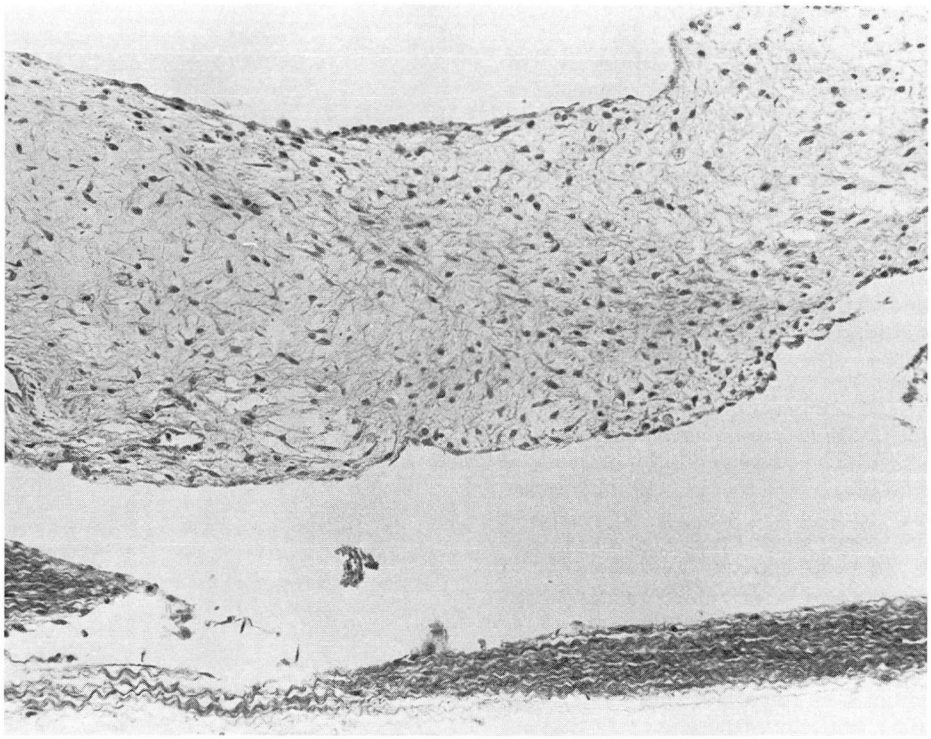

Fig. 4. Low-power view, Masson stain, of tricuspid valve tissue demonstrating valve tissue without mature collagen present. On the lower portion of the picture are seen the chordae, whose collagen has stained normally. The marked difference in the staining properties can be seen when comparing the tricuspid valve tissue with the mature collagen tissue in the chordae.

Discussion

Congenital tricuspid insufficiency of the newborn may have distinct etiologies, but we think our case is unique. Reports have described dysplastic tricuspid leaflets or chordal attachments without downward displacement.[2,3] The common pathology in these neonates has been tricuspid incompetence due to severe tethering of the tricuspid valve to the right ventricle by abnormally shortened chordae and papillary muscles without the downward displacement seen in Ebstein's anomaly.[2,3] However, marked myxomatous changes are not usually described in the valve tissue itself and the other cardiac valves in this condition tend to be normal.[2,5] Ebstein's anomaly[2,6] can also cause severe neonatal tricuspid regurgitation, but there was no evidence of downward displacement either clinically or at postmortem examination in our patient.

Mothers who have ingested a large amount of lithium carbonate during pregnancy have been described to have offspring with tricuspid regurgitation or Ebstein's anomaly,[6] but in this case there was no history of ingestion of any significant medications by the mother during her pregnancy.

Isolated severe tricuspid incompetence has also been seen in patients with pulmonary atresia with intact ventricular septum.[7] The differential diagnosis may be difficult between inherent tricuspid regurgitation and that secondary to severe right ventricular outflow tract obstruction.[7] Usually, however, left ventricular angiography, filling the patent ductus with subsequent filling of the pulmonary artery, will outline pulmonary valve tissue. Indeed, in our patient, one could see filling of the pulmonary artery and visualize the pulmonary valve following the left ventricular angiography, with flow from the aorta into the pulmonary artery *via* the patent ductus arteriosus. The pulmonary valve was mildly thickened (*Fig. 2B*). The ability to define pulmonary valve tissue accurately with a left-sided injection suggested the correct diagnosis was tricuspid insufficiency and not pulmonary atresia with an intact septum.

A syndrome of often severe but frequently

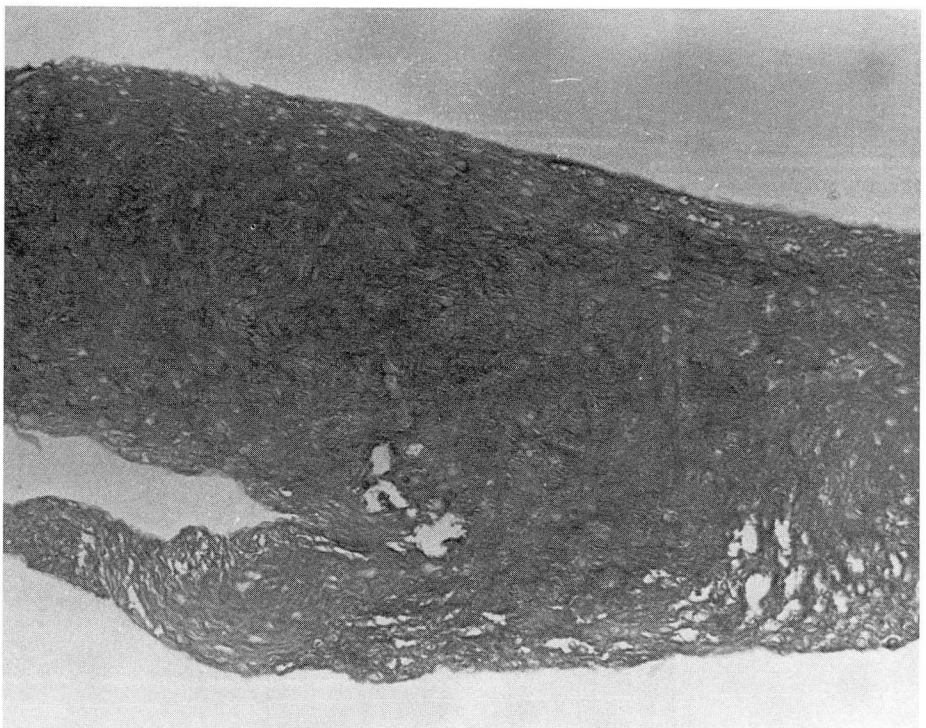

Fig. 5. Low-power view, colloidal iron stain, of the myxoid tissue of the tricuspid valve with little evidence of mature collagen. Colloidal iron stains the tissue for glycosaminoglycans. The valve is deeply stained, demonstrating the significant increase in glycosaminoglycans in the valve tissue.

transient tricuspid insufficiency of the newborn is a newly recognized clinical entity.[8] These newborn infants have been described as having severe tricuspid insufficiency associated with significant perinatal stress secondary to birth asphyxia with or without hypoglycemia. The tricuspid regurgitation in these infants has tended to resolve in one to two weeks. However, in two infants who died[8] the postmortem examination demonstrated an anatomically normal tricuspid valve, but the tricuspid valve had histopathologic evidence of necrosis of the distal portions of the anterior papillary muscle. All the papillary muscles of the mitral valve were normal. Thus, it was thought that the infants who died had hypoxic valvular damage of the papillary muscles of the tricuspid valve secondary to perinatal stress.[8,10,11] Premature closure of the patent ductus arteriosus may also be involved in this syndrome[9] and may also help produce a similar syndrome, but our patient's ductus was widely patent.

Our case resembles cases of congenital polyvalvular disease described by Bharati and Lev.[12] However, their patients (1) were older (mean age two years), (2) had all the cardiac valves involved, (3) had a very high incidence of trisomy 13–15 and 17–18, (4) had other multiple congenital anomalies, (5) had a high incidence of coexistent congenital heart disease, particularly shunts and valvular obstruction, and (6) had valvular lesions that were primarily stenotic. Our patient had a normal mitral valve and no evidence of any chromosomal or coexistent congenital anomaly. In addition, there was no evidence of coexistent congenital heart disease.

We think our case is unique in that the tricuspid regurgitation was clearly caused by dysplasia of the tricuspid valve, with shortened chordae that prevented closure of the valve. The histologic studies clearly showed an increased amount of glycosaminoglycans and a decreased amount of mature collagen. What makes this case unique is the fact that both the pulmonary and aortic valve, although tricuspid in each case, clearly showed the same form of dysplastic changes but the mitral valve was normal. There was no evidence clinically or at postmortem examination that the infant had a generalized connective tis-

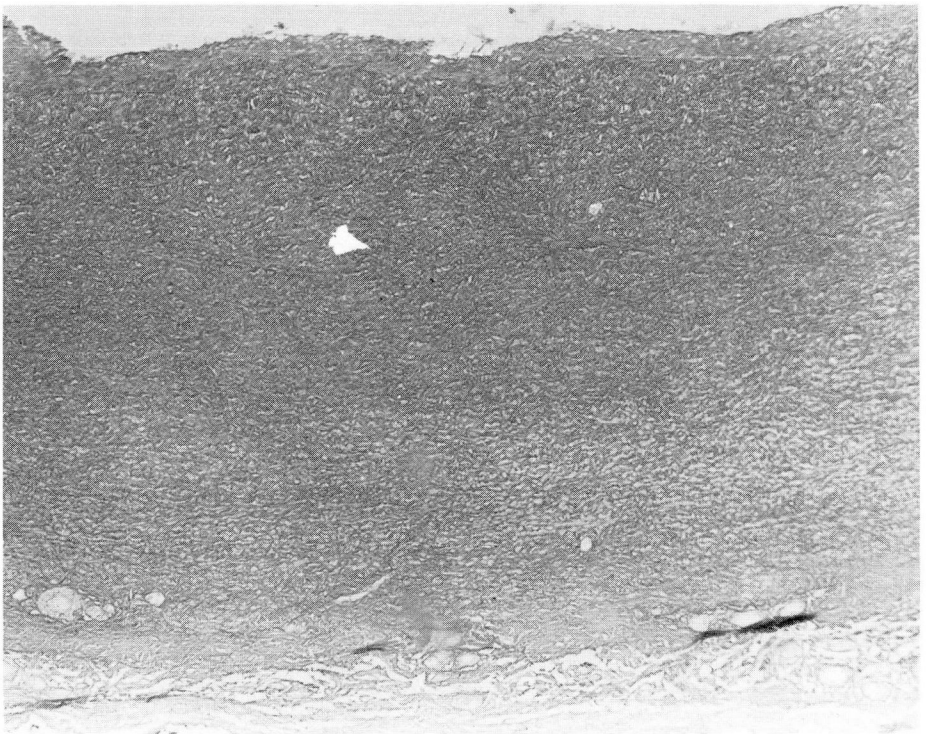

Fig. 6. Low-power view, colloidal iron stain, of the pulmonary valve demonstrating a similar appearance to the tricuspid valve noted in Figure 5, and showing the valve to be rich in glycosaminoglycans.

sue disorder, such as Marfan's syndrome or Ehlers-Danlos syndrome, or any chromosomal abnormality. We think that the list of causes for congenital tricuspid insufficiency of the newborn can be expanded to include failure of the valve leaflets to develop normally, a condition that is histologically similar to myxomatous degeneration in the adult. In addition, one may need to search carefully for clinical evidence of other valve involvement during the newborn period.

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