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CASE STUDY

Supraventricular Tachycardia vs. Marfan's Syndrome

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Abstract: Marfan's syndrome is one of several genetic connective tissue disorders that manifest cardiovascular abnormalities. Paroxysmal supraventricular tachycardia is not one of these manifestations.

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Case Presentation

In October 1995, the mother of a male 14 year old high school student applied for a $50,000 whole life policy on her son. Three years prior to this application, a $50,000 policy was issued on him. His height and weight were listed at 6'0" and 162 lbs. The history admitted on the application was, "diagnosed with SVT, atrial flutter, under control with Lanoxin 0.25 mg. daily - gets a six-month checkup for this condition - under control. He is very active in sports, not limited or restricted." Because of the admitted history, an AP report was obtained.

Additional information from the AP report was quite extensive. He had been a normal, healthy nine year old when he presented to a cardiologist in April 1990 for a cardiac evaluation. Five months prior, the sudden death of his healthy 35 year old father occurred, and an autopsy showed some cardiac abnormalities. The coronary arteries were normal. All of the cardiac chambers were enlarged, and the valve tissue was considered dysplastic. A specific diagnosis was not given, but some type of connective tissue disease such as a forme fruste of Marfan syndrome was suggested as a possibility.

The proposed insured was asymptomatic at this time. The physical examination showed no cyanosis, clubbing, or edema. The blood pressure was 100/70, S1 and S2 were normal, at the cardiac apex a mid systolic click was audible in the erect position, there were no murmurs, and the liver and spleen were normal in size. An ECG showed a sinus rhythm of 82 per minute and was normal. The chest x-ray showed a normal heart. A 2-D echocardiogram was normal, showing no evidence of mitral valve prolapse. It was the cardiologist's opinion that the PI had a normal heart. No recommendations were made.

In May 1991, he fell off his bicycle, striking his

head with a loss of consciousness. A CT of the head was normal, and he was discharged from the emergency room. In April 1993, he again saw the pediatric cardiologist for a routine follow-up. It was noted that he had developed some mild exercise induced asthma for which he used an inhaled beta agonist on a prn basis. It was also noted that the PI's four grandparents were alive but all had "heart disease." At this time his pulse was regular, BP 108/70, and the rest of the exam was normal with no systolic click heard at this visit. The ECG continued to be normal. A 2-D echo was repeated and was still normal with no evidence of mitral valve prolapse or IHSS. He was again considered to have a normal heart.

However, beginning December 1994, the PI began complaining of spells of his heart beating fast, often accompanied by chest pain and headaches, lasting five to ten minutes in duration. They increased in both frequency and severity. The PI again presented to the cardiologist in May 1995 for evaluation of these apparent spells of tachycardia. He was still active in sports. A Holter Monitor revealed episodes of both narrow and wide QRS complex tachycardia with a rate of 200-205 per minute. The cardiologist recommended electrophysiological testing. These studies were carried out in August 1995. He was found to have easily inducible SVT, during which he would develop a transient RBBB, felt to mimic the findings of the Holter study. No other abnormalities were described. He was started on Digoxin 0.25 mg. daily. The cardiologist noted that if necessary, a radiofrequency ablation of the accessory pathway could be carried out sometime in the future. At follow-up one month later, he was described as doing well with no further spells or symptoms. This is the last notation in the AP report.

Case Discussion

This case brings up several points for discussion. The first has to do with the PI's father's death. The obvious assumption is that the father died of a cardiac arrhythmia, based upon the autopsy findings. Did the father suffer from some type of connective tissue disorder as suggested by the pathologist? If he did, could it be genetically passed on to his son?

In 85% of cases, Marfan's syndrome is inherited as an autosomal dominant with complete penetrance, but there is a wide variability of expressivity. Approximately 15% of the cases are sporadic and apparently represent a new mutation. The basic defect has been isolated to chromosome 15, FBN1 gene, and more than eighty specific mutations have been described.[1]

On a molecular level, this genetic defect leads to a defect in fibrillin, a glycoprotein that is one of the main structural components of microfibrils.[2] These microfibrils serve as a scaffolding for the deposition of elastin. The defective scaffolding results in defective elastic and collagen fibers causing biomechanical incompetence of tissue. The incompetence causes the eventual disruption of the tissue, leading to the pleomorphic manifestations of Marfan's syndrome.

Marfan's syndrome has three basic features.[3] Ectopia lentis, caused by elongated and broken ciliary zonular fibers is the first. Abnormally long limbs and loose jointedness is next, often with the arm span exceeding the person's height. The last are the cardiovascular manifestations, with aortic dilatation, aneurysms, and mitral valve abnormalities being dominate. The ectopia lentis is present in 80% of cases, often being present even at birth. Involvement of either the mitral valve or the aortic valve is present in 85% of the cases. The aortic dilatation can be found anywhere from one year of life onward. In the past, average life expectancy has been somewhere between 35-45 years of age. With prophylactic surgery and treatment with prophylactic beta-blockers, life expectancy has been increasing.

In the cardiovascular system, cystic and noncystic medial degeneration with intimal proliferation occurs in the aorta, and even in the

myocardium and conduction tissue of the heart.[4] This condition can cause dissection of the aorta. There are also fibromyxomatous changes causing defective valve cusps, leading to aortic insufficiency and mitral insufficiency. Conduction defects have also been noted. There can also be dilatation and dissection of the pulmonary artery. The most common abnormalities are dilatation and dissection of the aorta, along with prolapse of the mitral valve. The dilatation of the aorta can occur within the first few years of life, but usually manifests itself in the third and fourth decades. This condition accounts for the majority of the premature fatalities.

Annual echocardiograms are warranted in full-blown Marfan's patients and prophylactic beta-blocker therapy can be instituted when the aortic root diameter becomes increased. Prophylactic surgery can be performed if there is progressive diameter increase of greater than 6 cm. accompanied by significant aortic regurgitation. Progressive mitral regurgitation can also be seen and may require valve replacement. In pregnancy, there is an increased risk of aortic dissection with rupture.

If the father had some other type of unknown connective tissue disorder, could the son have it? The answer to this is unknown. It is possible the father had a garden variety dilated cardiomyopathy. If so, why did the pathologist describe a dysplastic tissue? The prevalence of idiopathic dilated cardiomyopathy is in the range of 2-8 per 100,000 individuals. Numerous occurrences of familial dilated cardiomyopathy have been reported, but there have not been adequate investigations into this area.[4] Therefore, it is unclear how many have a Mendelian disease, how many have new mutations, and how many have non-genetic causes. Many instances of familial occurrence do fit autosomal dominant inheritance. There is considerable clinical variability in the pedigrees. Histological examination of the myocardium shows non-specific hypertrophy and fibrosis, accompanied on electron-microscopy by abnormal mitochondria. This is a distinctly different abnormality than that seen in cardiomyopathy of other causes. It would be important in a patient with idiopathic dilated cardiomyopathy to have a detailed family history, since approximately 20% of the time it is discovered there is an affected relative. Identification of individuals with dilated cardiomyopathy may be life saving, if early detection can occur and treatment with antiarrhythmic agents instituted.

There are other connective tissue disorders associated with cardiovascular manifestations.[4] Cutis laxa has been associated with pulmonary stenosis and aortic dilatation. Ehlers-Danlos syndrome of various types can have mitral valve prolapse, and rupture of the great vessels. Osteogenesis imperfecta can be associated with mitral valve prolapse and mild aortic dilatation. Pseudoxanthoma elasticum can be associated with arterial occlusion, including the coronary arteries, and hypertension. Another entity is the MASS phenotype, which is an acronym standing for mitral valve in which mitral valve prolapse can be seen, aortic dilatation, skin manifestations, and skeletal abnormalities.

The MASS phenotype describes a group of patients who have mitral valve prolapse and who also have many features of either Marfan's or Ehlers-Danlos syndrome, but who do not meet specific diagnostic criteria. They often have mitral valve prolapse, mild aortic dilatation, various types of skin changes, and skeletal changes including joint hypermobility, scoliosis, excessive arm and leg span, and pectus excavatum. It is felt these individuals have some defect of extracellular matrix causing the cardiac and extracardiac features.

There are also two Mendelian inheritance disorders associated with dilated cardiomyopathy. One is the Familial Collagenoma syndrome, in which cardiomyopathy has been found. The other is Keratosis Palmoplantaris (Mal de Meleda syndrome), in which dilated cardiomyopathy and dysrhythmia have been described.

The next point of discussion has to do with the proposed insured's known accessory pathway tract that led to the episodes of the tachyarrhythmia. Paroxysmal supraventricular tachycardia (PSVT) describes a group of arrhythmias characterized by sudden onset and abrupt termination, and usually initiated by an atrial or ventricular premature beat. Electophysiological testing has shown four basic mechanisms: reentry in the AV node, reentry over a concealed extra nodal accessory bypass tract, reentry in the sinus node or atria, and an automatic mechanism. Our PI apparently has accessory bypass tract, in which functional bundle branch block is very common during the episodes. A very important aspect of the accessory bypass tract is that these tracts are usually only capable of retrograde impulse transmission, in contrast with the pre-excitation syndromes (example: WPW syndrome) in which the accessory bypass tracts normally conduct antegrade, causing the early ventricular activation. This antegrade conduction can result in atrial fibrillation or flutter progressing into ventricular fibrillation causing some cases of sudden cardiac death. Our PI has retrograde conduction and, therefore, should not be at any significant increase in mortality. The Medical Impairment Study of 1983 analyzed 8361 cases of PSVT, most of whom had mild infrequent attacks.[5] The mortality was not found to be increased, even in those who were issued substandard rates.

What if the patient should undergo a radiofrequency current transcatheter ablation? Presently, approximately 10,000 ablation procedures are performed annually. It is effective approximately 90% of the time in experienced hands. Major complications are unusual (AV block, cardiac perforation, valve injury, etc.) and procedure-related deaths should be considered rare. The long term effects of this procedure are unknown.

The last question that could be asked is what is the relationship between the PI's accessory pathway tract and his father's cardiac condition. In Marfan's, there is no known association with these types of cardiac abnormalities. It seems highly unlikely that the son's cardiac condition has any relationship to his father's autopsy findings.

In summary, one can only speculate on the relationship between the father's cardiac condition and the proposed insured. Mortality data would suggest that the proposed insured has a normal life expectancy based upon his own actual cardiac disease.

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