Tuberous Sclerosis Alliance

HEART MANIFESTATIONS IN TSC

The primary cardiac finding in patients with the tuberous sclerosis complex (TSC) is the presence of rhabdomyomas. These are non-malignant (or non-cancerous) tumors that can occur anywhere in the heart, but most commonly occur in the ventricular and septal walls. Approximately 50% of patients with TSC have cardiac rhabdomyomas, and 50% of patients with cardiac rhabdomyomas have TSC. The presence of multiple, rather than single, tumors is more consistent with a diagnosis of TSC. Sporadic vascular abnormalities can occur in TSC. Although rare, some patients have coarctation of the aorta, renal artery stenosis, or thoracic or abdominal aneurysms.

Diagnosis of Cardiac Tumors and Vascular Abnormalities

Echocardiography (ultrasound of the heart) is the modality of choice for the diagnosis of cardiac tumors and thoracic vascular abnormalities, including coarctation of the aorta. An abdominal ultrasound is the initial modality of choice to diagnose renal artery stenosis or abdominal aneurysms. Ultrasound is a non-invasive, safe, quick and painless test that allows the cardiologist to visualize the intra-cardiac anatomy and vascular structures.

With the advent of fetal echocardiography (ultrasound evaluation of the fetal heart) some fetuses may be diagnosed with TSC before they are born. In fact, some mothers have been diagnosed to have TSC only after their fetuses were found to have rhabdomyomas. Because the inheritance pattern of TSC is autosomal dominant (meaning the offspring of an affected person has a 50% chance of inheriting TSC) with variable expression (meaning that the manifestations may differ between affected persons), fetal echocardiography may be offered as a screening tool to these patients, as it may detect rhabdomyomas as early as 18 to 20 weeks of gestation. Some fetuses that initially present with arrhythmias may be found to have TSC and rhabdomyomas when the etiology for the abnormal heart rhythm is sought.

Magnetic Resonance Imaging (MRI) and Computerized Tomography (CT) scanning are other useful modalities to image both intracardiac tumors and vascular abnormalities.

Symptoms and Natural History

Rhabdomyomas are non-cancerous; they do not metastasize, or spread throughout the body. The symptoms associated with these tumors are largely dependent on their location, number and size. Most newborns and infants with rhabdomyomas do not have any symptoms at all (i.e. they are “asymptomatic”). However, some asymptomatic patients may have extensive cardiac involvement. Large tumors that nearly fill the ventricular cavity and obstruct forward blood flow may develop congestive heart failure (inability of the heart to pump enough blood to the body) or cyanosis (blue discoloration of the skin due to insufficient blood oxygenation).

Some rhabdomyomas are located in close proximity to the heart’s electrical conduction

system. In about 20% of cases, this may result in significant arrhythmias (abnormal heart rhythm) that could lead to an abnormally fast or slow heart rate. These patients may experience palpitations, chest pain, or fainting. Although these instances are rare, it would be advisable to monitor patients with rhabdomyomas near the conduction system for the presence of abnormal heart rhythms. Isolated reports of sudden death in pediatric and young adult patients have been attributed to ventricular tachycardia. In cases where ventricular tachycardia (fast heart rate) was attributed to a ventricular rhabdomyoma, surgical resection of the tumor resulted in resolution of the rhythm disturbance.

Rhabdomyositis is a rare form of cardiomyopathy (poor cardiac muscle function) in which the tumor nodules are not grossly apparent but are found microscopically within cardiac muscle fibers. Sudden death from intractable ventricular tachycardia or recurrent atrial tachycardia has been attributed to rhabdomyositis.

Fortunately, however, most rhabdomyomas do not grow over time; they either get smaller or remain stable in size. In fact, most tumors decrease in size over time and may no longer be visible by echocardiography. A notable exception is that some tumors were noted to increase in size in infants treated with ACTH for infantile spasms (a form of seizure). Therefore, it would be prudent to closely monitor infants treated with ACTH by serial echocardiograms for growth of the rhabdomyomas.

The vascular abnormalities in TSC include coarctation of the aorta, renal artery stenosis, and thoraco-abdominal aneurysms. With mild involvement, many patients may be asymptomatic or might have only hypertension (high blood pressure). Because some patients with TSC may have kidney involvement (angiomyolipomas and renal cysts), which may be a potential cause of hypertension, it would be prudent to obtain regular blood pressure measurements in all patients with TSC.

Children and adults with coarctation of the aorta will have a difference in systolic blood pressure between their upper and lower extremities. Obstruction to blood flow is responsible for the high blood pressure in the arms relative to the legs. Additionally, decreased blood flow to the kidneys may lead to enhanced renin secretion and subsequent volume expansion, which is also the mechanism for hypertension in renal artery stenosis.

An aneurysm is a localized dilation of the aorta greater than 50% of its normal diameter. It is associated with weakening of the aortic wall that occurs normally with aging. In young patients, it is most often due to genetic connective tissue disorders such as Marfan syndrome. Other risk factors for aneurysms include high blood pressure, high cholesterol, and smoking.

Management: Screening and Treatment

Cardiac evaluation and screening is recommended for all patients with TSC. Fetal echocardiography should be considered when rhabdomyomas are identified by prenatal ultrasound to detect individuals at high risk for heart failure after delivery. A baseline echocardiogram to image the heart and vascular structures is suggested for all patients, especially those younger than 3 years of age. In some older patients in whom ultrasound imaging may be inadequate, magnetic resonance imaging (MRI) of the heart may be necessary. For those diagnosed to have cardiac tumors, the frequency and necessity for follow-

up imaging will be done at the discretion of their cardiologists and will depend on many factors.

As pointed out earlier, arrhythmias may occur in patients with cardiac rhabdomyomas. A baseline electrocardiogram (EKG) is recommended for all patients, and 24-hour ambulatory monitoring may also be done to further diagnose any rhythm disturbances and aid in their follow-up during the course of treatment.

Because some rhabdomyomas result in clinical problems, monitoring by echocardiography every 1-3 years is recommended until regression of the tumors is documented. More frequent or advanced diagnostic assessment may be required for symptomatic patients. Because rhabdomyomas may cause arrhythmias and there is some evidence that older patients that no longer have heart tumors may develop arrhythmias, it is recommended that all asymptomatic patients obtain an electrocardiogram every 3-5 years to monitor for conduction defects. Patients who have significant arrhythmias may require treatment with medication or an electrophysiology study with radio- frequency ablation (a special cardiac catheterization procedure).

In the rare instances in which hemodynamic compromise is present (severe obstruction, congestive heart failure, or cyanosis as explained previously), prompt surgical excision of the tumors may be indicated. Even partial removal of the tumors may provide relief of the problem if complete excision would severely damage the remaining cardiac tissue. However, since even large tumors tend to regress in size or disappear completely, the presence of rhabdomyomas without severe obstruction or life-threatening arrhythmias is not necessarily an indication for surgical intervention. In most instances, rhabdomyomas do not require surgical intervention.

Because smoking and a high cholesterol level are independent risk factors for aneurysm formation, patients with TSC would be well advised to maintain a healthy lifestyle of diet, exercise, and smoking avoidance. Regular blood pressure monitoring is also prudent.

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Reviewed and updated by Robert B. Hinton, Jr., MD June 2014.