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Title

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Permalink

<https://escholarship.org/uc/item/2s0074pg>

Journal

Proceedings of UCLA Health, 23(1)

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Publication Date

2019-04-04

CLINICAL VIGNETTE

Thoracic Aortic Aneurysm: Diagnosis and Management

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Over the last 30 years there has been an increase in patients diagnosed with thoracic aortic aneurysms. This is a function of increased detection and potentially increased incidence. More patients with thoracic aortic aneurysm (TAA), increases the importance for Primary Care physicians and cardiologists to effectively care for this group. The goal of this vignette is to provide clinicians a clear framework for care of patients with aortic disease.

A Young Man with Chest Pains

A 23-year-old male presented for a general physical. He also noted recurrent chest pain, first on the right side, and then on the left side. For about one month prior to the visit the pain was moderate in intensity and sharp in quality, but not recurrent. He denied shortness of breath, cough, dyspnea on exertion, poor exercise tolerance, palpitations, dizziness, syncope, or edema.

His PMH was notable for Marfan's syndrome and remote history of spontaneous biapical pneumothorax, treated with pleurodesis and biapical wedge resection.

His blood pressure was 127/88 and his pulse was 90 and regular. He measured 1.88 meters in height and weighed 66.2 kg BMI 18.75 kg/m²), with a Marfanoid habitus. He had a high arched palate, moderate kyphoscoliosis, and arachnodactyly, positive wrist and thumb signs, slight bilateral cubitus valgus, and mild bilateral passive elbow hyperextension. Skin exam revealed diffuse striae distensae about the trunk and abdomen.

Heart auscultation revealed normal S1 and S2, with a regular rate and rhythm and a I/VI systolic murmur at the LLSB and apex, and a I/VI diastolic murmur at the LLSB. No gallop or rub was appreciated. Lungs revealed slightly harsh breath sounds at the right hemithorax during expiration but was otherwise unremarkable. The caliber of the abdominal aorta seemed slightly enlarged without definitive aneurysm, bruit, organomegaly, or tenderness. The exam was otherwise unremarkable.

Due to his history of Marfan's, his recent chest pain, and the exam findings, he was referred for echocardiogram, abdominal ultrasound, chest x-ray, and cardiology consultation.

Risk Factors

There are several risk factors for TAA. Well-described genetic conditions that lead to aortic medial weakness or destruction

include Loeys-Dietz syndrome (LDS), Marfan syndrome (MS) and Ehlers-Danlos syndrome (EDS). LDS is an autosomal dominant connective tissue disorder characterized by aortic aneurysms, generalized arterial tortuosity, hypertelorism, and bifid or broad uvula, or cleft palate. LDS is caused by mutations in TGBR1/2, SMAD2/3, or TGFB2/3, all coding for components of the TGF β -signaling pathway. Compared to MS, cardiovascular manifestations are more severe and aortic aneurysms tend to dissect or rupture at a smaller diameter and at a younger age.¹ MS typically has an autosomal dominant inheritance pattern and is caused by heterozygous mutations in FBN1 (coding for the extracellular matrix protein fibrillin-1). Patients are often identified due to non-aortic features, including skeletal, ophthalmological, or pulmonary abnormalities. The most common cardiovascular phenotype involves dilation of the aortic root at the sinus of Valsalva, which can evolve to aortic dissection and rupture. EDS is a group of clinically and genetically heterogeneous connective tissue disorders. EDS is caused by mutations in genes coding for collagen fibrils or for proteins involved in the processing of these collagens. Patients display joint hypermobility, skin hyperextensibility and tissue fragility. Up to one quarter of EDS patients show aortic aneurysmal disease.²

Additional risk factors for TAA include conditions that increase aortic wall stress, such as hypertension, cocaine abuse (implicated in 1.8% of patients with acute aortic dissection),³ extreme weightlifting (reported blood pressures near 300 mm Hg),⁴ trauma, and aortic coarctation. Patients who warrant screening include those with a family history of aortic aneurysm or dissection, a bicuspid aortic valve, and autoimmune disease such as Takayasu or giant cell arteritis.

Screening Tools

Common imaging for diagnosis of TAA include transthoracic echocardiography, cardiac-gated computed tomographic angiography (CTA), and MRI. Transthoracic echocardiography is widely available, and is often useful for screening low-risk patients. Alternatively, patients with connective tissue disease with a particularly severe vascular phenotype such as LDS should be screened with CTA, since it is critical to visualize the entire aorta and its branch vessels.

Estimating true aortic size is not simple. A transthoracic echocardiogram can only visualize the proximal several centimeters of the ascending aorta, to just above the sinotubular junction. Therefore, aneurysms of the mid-portion of the ascending aorta

may be missed. Even transesophageal echo is “blinded” to the upper portion of the ascending aorta. As the ascending aorta stretches, the aortic valve plane is forced into a more vertical orientation, rendering assessment of size on axial images difficult. Modern CT reconstructions are done in sagittal and coronal planes for this reason, however, the resolution in the nonaxial reconstructions is often insufficient to permit precise assessment of aortic diameter.⁵ In comparing measurements over time, it is important to compare the same longitudinal levels of the aorta. It is also critical to remember that in a given cross section, the aorta will not be a true circle. Thus asymmetric dilation may escape detection using transthoracic or transesophageal echocardiography.

Initial Management

Medical management for patients with TAA is aimed at reducing stress along the aortic wall by decreasing heart rate and blood pressure. Although beta-blockers have been traditionally used to achieve this goal, it must be remembered that their use is largely unproven and somewhat controversial. Studies in a mouse model of Marfan's syndrome showed that angiotensin II type 1-receptor blocker losartan attenuated TGF- β signaling, resulting in slower progression of aortic root growth among mice with Marfan's syndrome treated with losartan.⁶ This promised to be a targeted, disease-specific approach to treatment. Unfortunately, in a study involving 608 children and young adults with MS, no significant difference in the rate of aortic-root dilatation between was found between patients treated with losartan versus atenolol.⁷

Expert consensus is to target blood pressure of <130/80 mm Hg and a heart rate of < 70 beats per minute. Heavy lifting should be discouraged, due to brief, but potentially significant increases in blood pressure. Some experts also advise susceptible patients to seek attention when severely emotional personal situations arise, which may lead to elevations in blood pressure. In this setting, beta-blocker therapy, aimed at blunting pressure spikes may be reasonable.

Referral

After TAA is diagnosed, patients should be referred to a cardiologist for timely decisions about medical management, imaging, follow-up, and potential referral to surgery. Depending on the clinical circumstances, this may also be an appropriate time for genetics referral.

Research has identified critical points in aortic size progression. These are at 6 cm in the ascending aorta and 7 cm in the descending aorta. At these diameters, there is a near 30% risk of aortic dissection.⁸ Experts recommend intervention for the ascending aorta at 5.5 cm (or growth rate > 0.5 cm/year). For patients with MS, EDS, or family history of TAA, surgery is recommended when aortic diameter is 5.0 cm. Given the aggressive nature of LDS, surgery is recommended when aortic diameter reaches 4.4–4.6 cm.⁹

International Registry of Acute Aortic Dissection data suggest that nearly 40% of patients have aortic diameters <5 cm at presentation with type A aortic dissection. Masri et al.¹⁰ recently showed incremental prognostic utility of indexing aortic root/ascending aortic area to height, rather than using unindexed aortic diameter. During nearly years of follow-up, 78% of deaths in patients with aortic root diameters between 4.5 and 5.5 cm occurred in those with an abnormal aortic root area/height ratio (≥ 10 cm²/m). Similar findings have been reported in patients with bicuspid aortic valve and MS.

Screening of Family Members

Experts recommend routine screening of all first-degree relatives of patients diagnosed with TAA. Transthoracic echocardiogram is the preferred initial study but can be technically limited, as described above. It is to be accompanied by CT or MRI to ascertain aortic and branch vessel anatomy. The entire aorta should be imaged.

In patients with a strong family history of AAT, genetic screening and testing for known mutations are recommended for the patient as well as for the family members. Imaging in second-degree relatives may also be considered if one or more first-degree relatives are found to have aortic dilation. Screening of first degree family members of patients with bicuspid aortic valve is also recommended.

Case Conclusion

After referral to Cardiology, patient was started on low-dose losartan and low-dose metoprolol. Further titration was limited by low blood pressure. CT angiogram of the thoracic aorta with contrast showed a dilated aortic root measuring 4.6 x 4.1 x 4.3 cm in centerline at the sinuses of Valsalva. He was referred to Cardiothoracic Surgery and subsequently underwent a valve sparing aortic root replacement (David Procedure), replacement of ascending aorta and hemiarch, and mitral valve repair using a mitral annuloplasty ring (due to moderate mitral regurgitation noted intraoperatively). The post-operative course was complicated by complete heart block, treated with single-chamber leadless pacemaker placement), and moderate pericardial effusion treated with colchicine. Pacemaker check was arranged for 6 months and CT angiogram of the aorta was scheduled for one year from the date of surgery.

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Submitted March 3, 2019