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Serious Aortic Complications in a Patient with Turner Syndrome

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Abstract

An asymptomatic young woman was discovered to have life-threatening aneurysms and dissection of the thoracic aorta during routine evaluation in a Turner syndrome (TS) study. The presence of a heart murmur and hypertension had led to diagnosis and surgical repair of an atrial septal defect at age 5 and of aortic coarctation at age 12 years. The diagnosis of TS was made at age 16 year due to short stature and delayed pubertal development. She was treated with growth hormone from age 16–18 year, and with atenolol, thyroid hormone and estrogen. She discontinued her medications and was lost to medical follow-up at age 20 year. On presenting here at age 26 year, she reported a very active lifestyle, including vigorous exercise and an acting career, with no symptoms of chest or back pain or shortness of breath. Cardiovascular imaging revealed aortic regurgitation, an unsuspected dissection of a severely dilated ascending aorta, and a large descending aortic aneurysm. She required surgical replacement of her aortic valve and ascending aorta, followed by endovascular repair of the descending aortic aneurysm. Conclusion: This patient illustrates the importance of considering the diagnosis of TS in girls with congenital aortic defects and the absolute necessity for close, expert follow-up of these patients who are at high risk for complications after surgical repair due to an underlying aortopathy, hypertension and metabolic disorders. This patient also emphasizes the need to publicize and follow screening guidelines as an increasing number of patients with congenital defects transition to adult care.

Keywords

aortic dissection; X chromosome; hypoplastic aorta; congenital heart defect

Case Report

A 26-year-old woman was evaluated as part of a natural history protocol at the National Institutes of Health (NIH): Turner Syndrome Genotype & Phenotype (NCT00006334). She felt well, worked as a waitress and actress, and exercised 6 day/week with resistance training and running. She had surgical repair of an incomplete atrioventricular canal involving a cleft mitral valve and primum atrial septal defect (ASD) at 5 years of age. She had surgery for aortic coarctation at 12 years of age in 1994. The latter involved bypass of a hypoplastic arch with a 14 mm Dacron Hemashield graft implanted in the ascending aorta proximal to the innominate artery and in the descending aorta just distal to the origin of the left

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subclavian artery. She tolerated both surgeries well. Persistent arterial hypertension was treated with atenolol.

Turner syndrome (TS) was diagnosed at age 16 year due to short stature (138 cm; <1%) and absent pubertal development. Her karyotype was 45, X. She was treated with growth hormone from age 16–18 year (growing to 156 cm in height), and with estrogen to induce secondary sexual characteristics and menses. Transthoracic echocardiography (TTE) at age twenty year showed mild aortic regurgitation and normal left ventricular function. Shortly thereafter, due to loss of medical insurance, she discontinued estrogen and antihypertensive medications. She had no medical follow-up until she presented as a volunteer for the NIH study.

Physical examination upon admission to the NIH revealed a well developed woman without neck webbing or other features pathognomic of TS. Body weight was 56 kg, height 156 cm and BMI 23 kg/m2. Blood pressure was equal in the upper extremities at 138–140/80 mmHg, and similar in the lower extremities. Heart rate was 74 bpm; oxygen saturation was 100% on room air. She had a high-arched palate and multiple pigmented nevi. There was a well-healed mid-line sternotomy scar. There was a 3/6 systolic ejection murmur heard best at the left upper sternal border radiating to the neck and across the precordium, and a 2/6 moderately long, mid-frequency diastolic murmur heard best along the left mid-lower sternal border. Lungs were clear, abdomen normal and pulses intact, there was no peripheral edema.

A protocol related cardiac magnetic resonance (CMR) scan showed an unsuspected dissection of her dilated ascending aorta (maximal external dimensions 48 × 33 mm), which did not involve the origins of the coronary arteries (Fig. 1A). It also showed a hypoplastic native aortic arch supplying the innominate, left common carotid, and left subclavian arteries alongside the bypass graft (FIG. 1B and supplemental video). A large aortic aneurysm (54 × 38 mm) was located at the distal anastomosis of the ascending to descending aortic graft. The aortic valve was trileaflet. TTE the following day showed normal left ventricular size and function and confirmed the markedly dilated ascending aorta with a dissection flap extending from the aortic root to the arch. The aortic valve was not well seen, but the leaflets appeared thickened and there was moderate eccentric regurgitation.

Medical treatment with metoprolol and losartan was initiated, and she underwent surgical repair of the ascending aorta dissection a few days later. The valve was excised and the root was replaced with a mechanical valve conduit in a Bentall fashion. Her vascular tissue was exceptionally friable, even distant from the aneurysm/dissection. Aortic valve pathology showed partial fusion of right and left non-coronary cusps, with severe myxoid degeneration of valve leaflets. Her post-operative course was uneventful and she returned for repair of the descending aortic aneurysm nine months later. Her descending aortic aneurysm was repaired by an endovascular approach.

She has been asymptomatic during 42 months follow-up. CT angiography showed a repaired ascending aortic diameter of 24 mm with significant reduction in the descending aortic aneurysm (area 20 cm^2 after fifteen months vs. 25 cm^2 postoperatively). CMR at 42 months follow-up confirmed progressive reduction of descending aortic aneurysm size, resolution of a small endovascular leak, and normal function of the prosthetic aortic valve. She has returned to full time work and has married.

Discussion

Our patient had major congenital cardiovascular issues associated with TS including ASD, aortic coarctation and ongoing hypertension after coarctation repair. Unfortunately, the

critical need for life-long follow-up was not recognized by her pediatric caregivers, and she developed life-threatening complications related to TS, including degeneration of her aortic valve associated with aortic regurgitation and dissection of the ascending aorta, and aneurysm formation at the site of graft insertion into the descending aorta

This patient's story illustrates critical issues related to congenital heart disease in TS. This disorder is due to complete or partial monosomy for the X-chromosome and occurs in ~1/2500 live female births [3]. TS is the most common cause of congenital heart defects in girls [2]. The most common cardiac anomalies include bicuspid aortic valve, coarctation, atrial and ventricular septal defects, partial anomalous venous connection, left superior vena cava and elongated transverse aortic arch. Of these, ascending aortic dilation is the most common and has been noted in 15–30% of TS patients. [2] This diagnosis was not considered by the cardiology teams at two centers involved in her care, perhaps because she lacks the neck webbing and facial dysmorphism emphasized in early reports [4]. However, these features are found in few TS patients diagnosed in the modern era. Short stature and primary ovarian failure are much more common, but usually not obvious until mid-late teens (as in our patient). Thus, we recommend that physicians consider karyotype testing for all girls with aortic coarctation or aortic valve abnormality.

This young woman did not have any symptoms related to hypertension, hypothyroidism or her aortic disease. She, her family, and her physicians were unaware of the importance of continued medical treatment and surveillance for potential aortic complications [5]. Making this diagnosis of Turner syndrome with cardiac involvement should alert the health care team, patient and family that life-long medical follow-up with cardiovascular imaging is essential to prevent potentially catastrophic complications related to the underlying aortopathy in TS [1]. Screening for aortic valve disfunction and/or aortic dilation should be initiated at six month after surgical correction and continued at annual or biennial intervals if the aortic size is stable. Cardiac magnetic resonance and transthoracic echocardiography are the primary screening tools to avoid radiation risks for patients and promote comprehensive care with early intervention as needed. It is important that pediatricians should transition care of these complex patients to adult congenital cardiology centers to provide expert continuing care. Often times, patients' families and care providers may underestimate the risk of future complications after surgical correction of congenital defects. Failure to investigate for long-term complications may lead to life threatening situations, as in our patient. This report illustrates the point that guidelines for management of adults with congenital heart disease should include imaging in asymptomatic patients and life-long follow-up.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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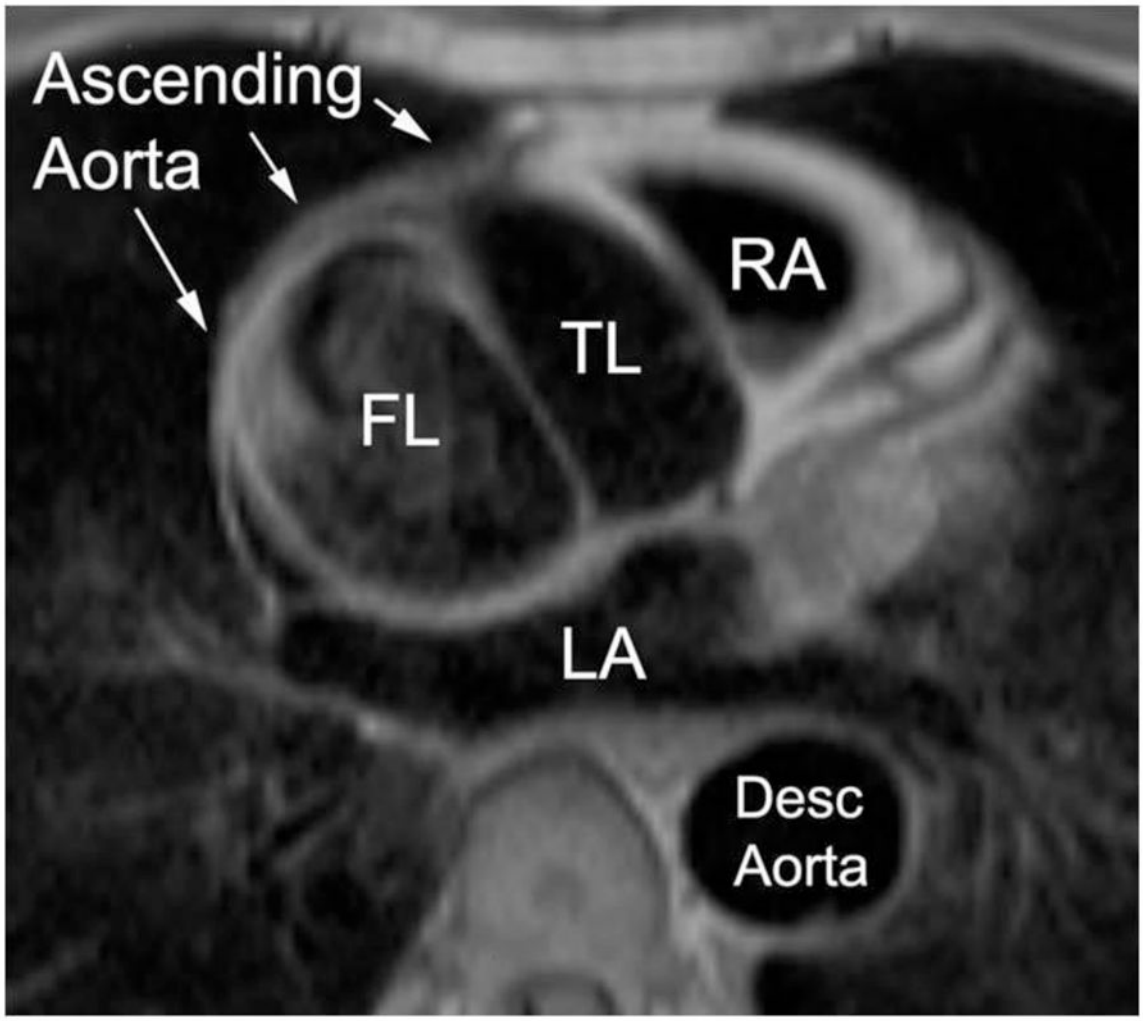

Fig. 1B

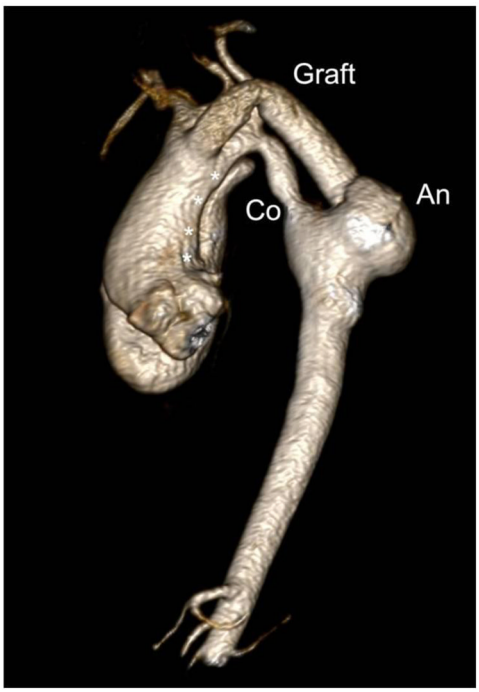

Fig. 1. Aortic pathology in an asymptomatic young woman with Turner syndrome

(A) Turbo spin echo axial CMR image of the severely dilated ascending aortic with dissection flap between the false lumen (FL) and true lumen (TL) of the ascending aorta (TE 3.9 ms, TR 1891 ms). Right atrium (RA), left atrium (LA) and descending aorta (Desc. Aorta).

(B) 3D surface rendering of contrast enhanced CMR. Note the dilated ascending aorta with dissection flap (asterisks), hypoplastic aortic arch with residual coarctation (Co) and extra-anatomic aortic arch bypass conduit (Graft) with aneurysm at the distal anastomosis site (An).