The patient is a 48-year-old man with Treacher Collins syndrome (TCS) and a precordial murmur known since childhood. He was initially evaluated at 33 years of age for moderate aortic insufficiency and a noncoronary sinus of Valsalva aortic aneurysm. Over time, his aortic disease progressed. His ECG demonstrated sinus rhythm with borderline first-degree atrioventricular block, left ventricular hypertrophy with intraventricular conduction delay, and secondary repolarization abnormalities (Figure 1). His chest x-ray showed biapical pleural-parenchymal scarring with no acute cardiopulmonary abnormality (Figure 2). Transesophageal echocardiography demonstrated severe aortic insufficiency and a large noncoronary sinus of Valsalva (Movie I in the online-only Data Supplement). The aneurysm was also observed to protrude into the right atrium. Cardiac catheterization confirmed similar findings of the aortic root (Movies II and III in the online-only Data Supplement). The patient was treated surgically by an elective Tirone David operation with repair of the prolapsing aortic valve leaflets. This resulted in complete resolution of the aortic insufficiency and an uneventful postoperative recovery. Postoperative computed tomography angiography with 3-dimensional reconstruction is shown in Movie IV in the online-only Data Supplement.

TCS, also known as mandibulofacial dysostosis or Franceschetti-Zwahlen-Klein syndrome, is a hereditary condition associated with a mutation in the TCOFI gene. TCOFI is responsible for encoding treacle, a protein involved in mRNA formation in neural crest cells during embryogenesis. Abnormalities in this pathway are hypothesized to lead to early neuroepithelial apoptosis and neural crest cell depletion in pharyngeal arches 1 and 2. These events result in cartilage, bone, and connective tissue hypoplasia, which leads to the characteristic craniofacial abnormalities associated with TCS.1

The depletion of neural crest cells is also implicated in congenital heart disease. In normal embryological development, some neural crest cells migrate into the outflow tract and create aspects of the aortopulmonary and conotruncal complex. They participate in the formation of the outflow septum, become smooth muscle cells of the tunica media, and are involved in the creation of the semilunar valves.

Ablation of the neural crest cells in experimental models has led to truncus arteriosus, transposition of the great vessels, double-outlet right ventricle, tetralogy of Fallot, double-inlet left ventricle, tricuspid atresia, straddling tricuspid valve, and the absence of various combinations of aortic arch arteries.2 Neural crest cells deficiency in TCS could therefore have an association with several vascular and cardiac congenital anomalies.

There have been isolated reports of cardiac malformations in TCS, primarily atrial and ventricular septal defects, patent ductus arteriosus, coarctation of the aorta, and a similar case of a sinus of Valsalva aneurysm.3,4

The specific causes of sinus of Valsalva aneurysms have been difficult to determine, but studies have suggested both an acquired and congenital origin. Acquired sinus of Valsalva aneurysms are typically caused by parenchymal degeneration associated with syphilis, infection, atherosclerosis, or cystic medial necrosis. Congenital causes such as TCS involve abnormal development of the distal bulbar septum, which predisposes this structure to aneurysmal formation.

Various neural crest–derived congenital abnormalities are described in patients with TCS. Clinicians providing care to patients with this syndrome should be aware of its potential congenital heart disease associations. A better understanding of the pathogenesis of the syndrome could help identify cardiac manifestations. Although some TCS patients may exhibit congenital heart defects, such phenotypic expressions are surprisingly unusual or are widely underreported.

Disclosures

None.

References


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Figure 1. A 12-lead ECG showing sinus rhythm with borderline first-degree atrioventricular block, left ventricular hypertrophy with intraventricular conduction delay, and secondary repolarization abnormalities.

Figure 2. Chest x-ray showing biapical pleural-parenchymal scarring with no acute cardiopulmonary abnormality.
Treacher Collins Syndrome: Sinus of Valsalva Aneurysm
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Movie 1. Transesophageal echocardiography demonstrating severe aortic insufficiency and a large non-coronary sinus of Valsalva aneurysm. Best viewed with Windows Media Player.

Movies 2. Aortogram from a cranial left anterior oblique projection showing the large non-coronary sinus of Valsalva aneurysm. Best viewed with Windows Media Player.

Movie 3. Left ventriculogram from the right anterior oblique projection showing the large non-coronary sinus of Valsalva aneurysm. Best viewed with Windows Media Player.