A 28-year-old nonobese woman, with a history of hypertension, presented with fatigue and generalized weakness of 4-year duration. The physical examination was remarkable for bilateral pseudohypakia, hypertension, and a basal systolic murmur radiating to the right axilla and back. All peripheral pulses were symmetrical, and there were no bruit, either over the renal artery or elsewhere. Funduscropy was unremarkable. Basic laboratory tests, including sodium, potassium, and renal function tests, were normal, but there was persistent, mild transaminitis without hyperbilirubinemia or raised alkaline phosphatase. She did not have diabetes mellitus or dyslipidemia. She has 2 healthy children. Her electrocardiogram and chest radiograph were essentially normal (Figures 1 and 2).

Echocardiography showed mild bilateral peripheral pulmonary artery stenoses (PPS; ie, narrowing of the proximal left pulmonary artery [PA] and the upper lobe branch of the right PA), with a small patent ductus arteriosus (PDA) and normal biventricular function.

As part of her evaluation, she underwent a right heart catheterization 2 years previously that revealed a moderate increase in PA pressures (mean PA pressure = 43 mm Hg) with a systolic pressure gradient of 22 mm Hg between the right PA and the right upper lobe PA. Angiography of PA confirmed mild PPS at the level of the right upper lobe PA and mild stenosis in the left PA (Figure 3; see Movie I in the online-only Data Supplement). PDA was small, with a pulmonary:systemic blood flow ratio of 1.1:1. The renal arteries were normal. A provisional diagnosis of congenital rubella syndrome (CRS) with mild PPS, silent PDA, and hypertension was made. She was managed conservatively, and the blood pressure remained well controlled on multiple drugs. The fatigue was attributed to transaminitis and antihypertensive medications. However, it worsened progressively and was associated with atypical chest pain.

A repeat catheterization confirmed mild PPS. Despite multiple attempts using various catheters, the left coronary artery could not be engaged. Selective right coronary angiogram showed a normal right coronary artery (Figure 4), with retrograde filling of the left coronary system via collaterals from the right coronary artery (Figure 5; see Movie II in the online-only Data Supplement). There was no evidence of atherosclerosis and calcification. Aortic root angiogram revealed complete absence of antegrade flow in the left coronary artery (Figure 6; see Movie III in the online-only Data Supplement). A small PDA was also evident, and there was no supravalvular aortic stenosis, coarctation of aorta, or ostial involvement of arch vessels (Figure 7; see Movie III in the online-only Data Supplement). Descending aortogram did not show evidence of renal artery involvement (Figure 8; see Movie IV in the online-only Data Supplement).

Additional clinical history revealed that the patient’s mother had some viral exanthem while she was pregnant with the patient. However, she did not seek any medical advice for the same. The patient’s childhood and adolescence was relatively uneventful apart from bilateral intraocular lens implantation, for premature bilateral cataract, at aged 18 years. Her facies was normal, and screening radiographs did not reveal any typical skeletal anomaly that could suggest Alagille syndrome. Inflammatory markers, including erythrocyte sedimentation rate and C-reactive protein, were within normal limits. Serological testing for rubella was positive for immunoglobulin G antibodies, suggesting past exposure to rubella virus. She underwent coronary artery bypass grafting along with PDA ligation successfully and with significant improvement in fatigue at 2 months follow-up.

CRS can affect virtually any organ system and commonly presents as a multiorgan disease. The rubella virus exerts cytotoxic effects on developing fetal blood vessels, myocardium, the central nervous system, and epithelial cells of the inner ear, lens, and teeth. Although PDA and PPS are its predominant cardiovascular manifestations, congenital coronary stenosis presenting in adulthood has not been reported to our knowledge. In an autopsy study of 13 infants with CRS, 3 had coronary stenosis that involved the right coronary artery and left coronary artery in 2 and only right coronary artery in 1. The characteristic alteration responsible for vascular lesions, including coronary stenosis, is a striking intimal proliferation with a preserved media. The preservation of arterial structure and the absence of calcification and inflammation distinguish the lesions in CRS from other congenital vascular lesions. These arterial narrowings tend to progress with age. It is clearly challenging to rule out acquired causes, but absence of risk factors...
for atherosclerosis might help. Also, the presence of only a few full-diameter collaterals and a diminutive caliber of left-sided arteries, as in the present case, are suggestive of congenital origin ostial stenosis. Hypertension, diabetes mellitus, hepatitis, and premature cataracts can also manifest for the first time in adult CRS patients. The ability of the virus to establish persistent infection or an autoimmune response to the virus might be responsible for these delayed manifestations of CRS. Hence, it may add a new dimension to the pathogenesis of coronary artery disease either via direct coronary involvement or indirectly via predisposing to increased risk of hypertension, diabetes mellitus, and, thereby, accelerated atherosclerosis.

A high index of suspicion is required to diagnose this entity. Any patient with congenital cardiac defects, such as PDA and PPS with associated visual, hearing, or neuropsychiatric defects, should alert the presence of this very rare condition. Atypical and late presentation along with rarity of coronary involvement significantly delayed the diagnosis in our case. Because it leads to progressive multiorgan deterioration, the clinician should remain vigilant of the potential health problems, and affected patients should be kept under close follow-up. Last, prevention, by maintaining a vigorous campaign of rubella immunizations, remains the best strategy to eliminate all cases of CRS.

Disclosures

None.

References


Figure 1. Electrocardiogram with normal sinus rhythm, no chamber enlargement, or any ST-T changes.

Figure 2. Chest radiograph demonstrates normal heart size and pulmonary vascularity.

Figure 3. Pulmonary arterial angiogram reveals stenosis at the level of the right upper lobe pulmonary artery (left arrow) and left pulmonary artery (right arrow).
Figure 4. Selective right coronary angiogram showing a normal right coronary artery.

Figure 5. Selective right coronary angiogram demonstrates retrograde filling of the left coronary system via collaterals from the right coronary artery. The caliber of collaterals is smaller than that of the target left-sided vessels. The left anterior descending (extreme left arrow) and left circumflex (extreme right arrow) coronary arteries are connected as usual and proximally end blindly without any left coronary ostium or left main trunk (middle arrow). These findings suggest congenital-origin ostial stenosis.

Figure 6. Aortic angiogram reveals complete absence of antegrade flow in the left coronary artery.

Figure 7. Aortic root angiogram showing a patent ductus arteriosus (bottom arrow) and normal ostia of arch vessels (top arrow).
Figure 8. Renal arteries appear normal on this descending aortogram.
Congenital Rubella Syndrome Presenting in Adulthood With Fatigue
Varun Gupta, Sunil Verma, Sivasubramanian Ramakrishnan, Milind Hote, Sandeep Seth and Balram Bhargava

Circulation. 2013;128:2542-2545
doi: 10.1161/CIRCULATIONAHA.113.001955

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/128/23/2542

Data Supplement (unedited) at:
http://circ.ahajournals.org/content/suppl/2014/03/20/128.23.2542.DC1
Movie Legend

**Movie 1.** Pulmonary arterial angiogram reveals stenosis at the level of right upper lobe pulmonary artery and left pulmonary artery. Best viewed with Windows Media Player.

**Movie 2.** Selective right coronary angiogram demonstrates a normal right coronary artery (RCA) with retrograde filling of left coronary system via collaterals from RCA. The calibre of collaterals is smaller than that of the target left-sided vessels. The left anterior descending and left circumflex coronary arteries are connected as usual and proximally end blindly without any left coronary ostium or left main trunk. There is no evidence of atherosclerosis and calcification. Best viewed with Windows Media Player.

**Movie 3.** Aortic root angiogram depicts complete absence of antegrade flow in left coronary artery. A patent ductus arteriosus is also evident. There is no supravalvular AS, coarctation of aorta or any ostial involvement of arch vessels. Best viewed with Windows Media Player.

**Movie 4.** Descending aortogram without any evidence of renal artery stenosis. Best viewed with Windows Media Player.