Early-onset atherosclerosis in a patient with Tangier disease: Not all that is gold glitters

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A 43-year-old woman with a previous history of smoking and hypertension was referred for cardiology consultation for recent-onset fatigue and dyspnea. She also reported upper limb joint pain and paresthesia. She denied a family history of cardiovascular disease.

Upon examination, the patient presented with periorbital xanthomas and significant blood pressure differential between the upper and lower limbs. A comprehensive neurologic examination showed motor deficits in the left hand and left facial paresis. Serum levels of total cholesterol and triglycerides were 99 and 105 mg/dl, respectively, and high-density lipoprotein (HDL) cholesterol was undetectable (<3 mg/dl). Other laboratory tests were unremarkable.

The initial transthoracic echocardiogram showed moderate aortic regurgitation with normal biventricular size and function. Computed tomography angiography showed complex atherosclerosis throughout the entire thoracic and abdominal aorta and their branches (Figure 1A; Supplementary material, *Figure S1*, *Video S1*).

Due to onset of exertional chest pain, invasive coronary angiography was performed which showed diffuse three-vessel coronary artery disease (CAD) (Figure 1B). Cardiac magnetic resonance demonstrated an unspecific focus of intramural fibrosis in the mid-segment of the anterior wall and extensive perfusion defect in all coronary territories, mainly in those irrigated by the left anterior descending artery (LAD) and right coronary artery.

The case was discussed by a multidisciplinary Heart Team, and a surgical approach was deemed impracticable due to porcelain aorta. Percutaneous coronary intervention on the LAD lesion was successfully performed. A conservative approach was adopted for other lesions.

Considering the cardiovascular and neurological findings, unmeasurable HDL cholesterol value, and extensive and diffuse accelerated atherosclerosis, the diagnosis of Tangier's disease was suspected, even without the hallmark sign of orange-colored tonsils. Genetic testing was performed and two heterozygous variants in the *ABCA1* gene — c.1834G>Tp(Glu612*) and c.4297G>Tp(Glu1433*) — were detected, confirming the diagnosis.

After a few months of clinical improvement, the patient showed symptomatic deterioration, with recurrent fatigue that significantly impacted her daily activities. A transesophageal echocardiogram was performed, which showed a tricuspid calcified aortic valve and worsened aortic regurgitation, now classified as severe (Figure 1C–E, Supplementary material, *Video S2*). Additionally, mild dilatation of the left ventricle was observed.

Percutaneous aortic valve implantation was deemed the only viable approach, and a 23 mm Edwards Sapien 3 Ultra valve was implanted, with no procedural complications (Figure 1F). During follow-up, the patient exhibited a significant clinical improvement.

Tangier disease is a rare genetic disorder characterized by extremely low levels of HDL cholesterol, with fewer than 150 cases reported worldwide. This results in cholesterol accumulation in various tissues, leading to an early onset of atherosclerosis and peripheral neuropathy [1, 2]. As no specific curative treatment is currently available, early identification of these patients and management of other risk factors such as low-density lipoprotein

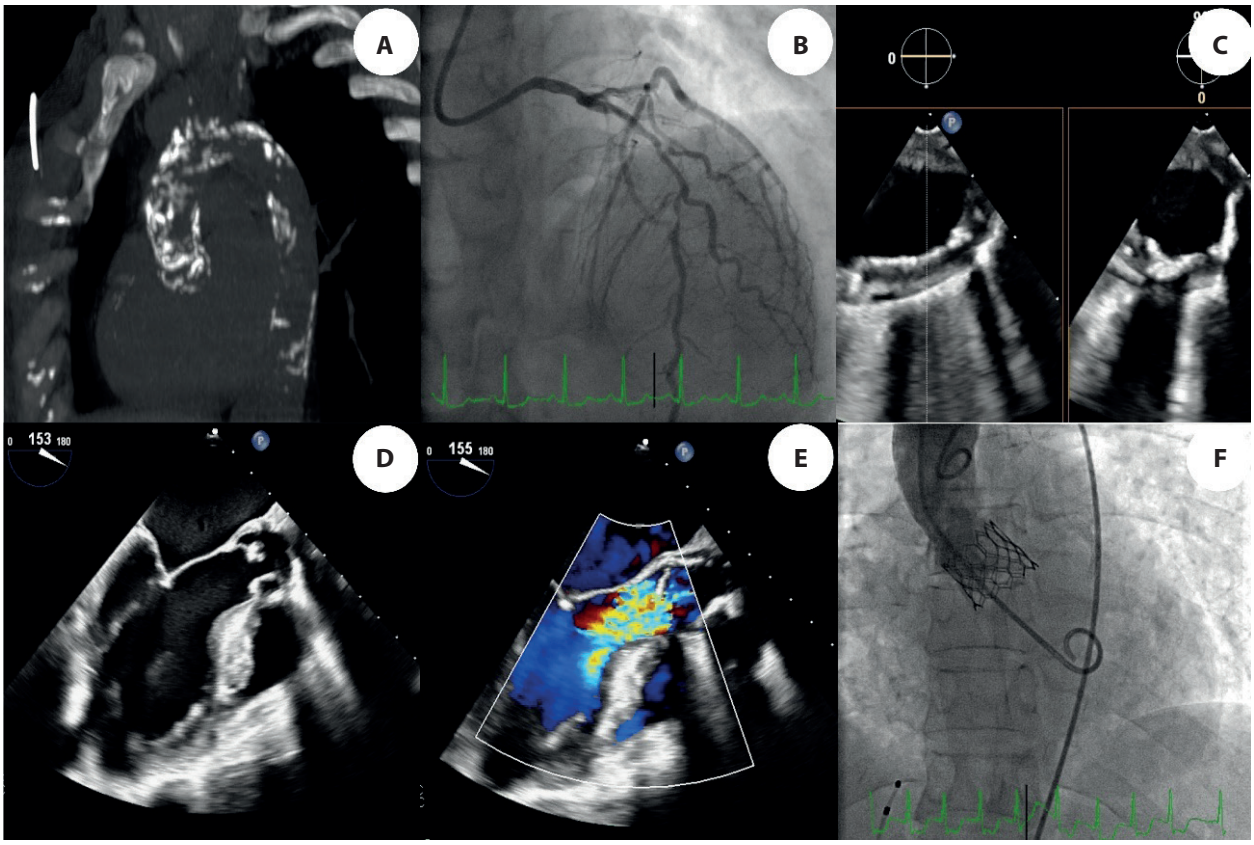

Figure 1. A. Computed tomography angiography showing massive calcification of the ascending thoracic aorta. **B.** Coronary angiography with diffuse and significant stenosis in the proximal/mid left anterior descending artery. **C–E.** Transesophageal echocardiogram showing calcified descending aorta (**C**) and aortic valve (**D**) and severe aortic regurgitation (**E**). **F.** Aortography showing TAVI in a patient with Tangier disease

Abbreviation: TAVI, transcatheter aortic valve implantation

cholesterol levels, hypertension, diabetes, and smoking are crucial. A lipid profile and molecular genetic testing are recommended in relatives.

We report a well-documented case of a young female diagnosed with Tangier disease, who presented with accelerated atherosclerosis in multiple arteries and required several challenging targeted interventions. In this case, an integrative and multidisciplinary approach was key to unveiling a rare diagnosis in a setting where some of the classic findings (such as the bright orange tonsils, hepatosplenomegaly, and corneal opacity) were missing — showing that not all that is gold glitters!

Supplementary material

Supplementary material is available at https://journals.viamedica.pl/kardiologia_polska.

Article information

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