(Figure 2A), and only slight residual mitral regurgitation. The QT interval returned to normal (Figure 2B). At the time of writing, the patient is asymptomatic and heart failure drugs have been discontinued.

Genetic study using massive, next-generation sequencing (NGS) detected the c.865C> T variant (p.Arg289*), a pathogenic truncation in the *SLC22A5* gene, present in simple heterozygosity. This variant was described previously in combination with a second pathogenic variant in another patient with PCD.[1] Analysis of a fibroblast sample showed a clear decrease in intracellular carnitine transport compared with controls, thereby confirming the suspected diagnosis of PCD.

Primary carnitine deficiency is a rare autosomal recessive genetic disease affecting 1:40 000-1:120 000 individuals.[2] It is caused by the presence of 2 mutated alleles (either in homozygosity or 2 mutations in compound heterozygosity) in *SLC22A5*, which codes for the *OCTN2* transporter, responsible for intracellular carnitine transport. Carnitine is an essential cofactor that enables long-chain fatty acids to pass through the inner mitochondrial membrane for beta-oxidation. Fatty acids that go unused accumulate in affected tissues. This disease has a wide spectrum of clinical manifestations, such as myopathy, hepatomegaly, hyperammonemia, recurrent episodes of hypoglycemia, and hypertrophic or dilated cardiomyopathy, which may be the only manifestation.[2,3] This condition is included in the neonatal screening programs of some autonomous regions of Spain.

In the case presented, although a second variant was not found, fibroblast study confirmed the suspected diagnosis of PCD. We do not know whether unusual genetic abnormalities undetectable by NGS might be present, which could affect the protein (deep intronic variants in promoter regions or variants that affect splicing); functional studies would be needed to confirm this hypothesis.

As to the electrocardiographic characteristics of the condition, abnormalities similar to those secondary to hyperpotassemia were described decades ago in PCD: abnormal, sharply peaked T waves in the middle precordial leads.[4] Other authors have reported cardiomyopathy and short QT interval in PCD patients.[3,5] In a murine animal model treated with Mildronate (which induces carnitine deficiency), Roussel et al.[5] reproduced the DPO phenotype, with the development of cardiomyopathy (hypertrophic) and short QT interval. Some authors have indicated that the predisposition to sudden cardiac death in patients with fatty acid beta-oxidation defects such as PCD results from arrhythmias caused by electrical repolarization abnormalities secondary to ion channel dysfunction. Ferro et al.[6] showed that high concentrations of long-chain acylcarnitines change the I_{kr} potassium current.

The case presented leads to 2 conclusions. First, it is essential to rule out potentially treatable etiologies in all patients with dilated cardiomyopathy, and particularly in children. In the case of a hereditary disease, other family members can be assessed. Second, DPC should be suspected in all patients with short QT and dilated cardiomyopathy. If the condition is diagnosed in time, it can be treated and the cardiac involvement completely reversed.

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Cardiac Involvement in a Patient With Behçet Disease. Diagnostic and Therapeutic Approach

Daño cardiaco en paciente con enfermedad de Behçet. Integración diagnóstica y terapéutica

To the Editor,

A 56-year-old man with no cardiovascular risk factors was admitted to our hospital for a 1-week history of exertional angina and asthenia. His medical history included Behçet disease with a previous hospitalization in the ICU for massive hemoptysis related to pulmonary aneurysms requiring a right lung lobectomy, and hepatitis B infection, likely transmitted by blood transfusion. The disease was currently in remission, and he was receiving immunosuppressive (interferon alfa-2a) and antiviral (entecavir) therapy.

On admission, the patient was asymptomatic. An electrocardiogram showed sinus rhythm with a 2:1 atrioventricular block and a wide QRS with right bundle branch block and left anterior hemiblock morphology. Transthoracic echocardiography showed no anomalies.

Coronary angiography (Figure A and B), depicted 2 calcified aneurysms in the proximal segment of the left anterior descending artery and the circumflex artery. The aneurysm in the circumflex was partially thrombosed, and distal flow was slowed. Computed tomography coronary angiography confirmed the presence of 2 saccular aneurysms (Figure C and D). The multiplanar reconstructions showed the true size of the aneurysm in the circumflex artery (30 × 24 mm) (Figure E and F, arrows), with a narrow neck (Figure E, thin arrow), calcified wall (“eggshell” appearance), thrombus, and irregular residual lumen. The aneurysm in the left anterior descending artery was smaller (15 × 14 mm; Figure 1E, arrowhead), and also showed a wall calcification.

Following electrophysiological study, which confirmed the infra-Hisian location of the atrioventricular block, a definitive AAI-

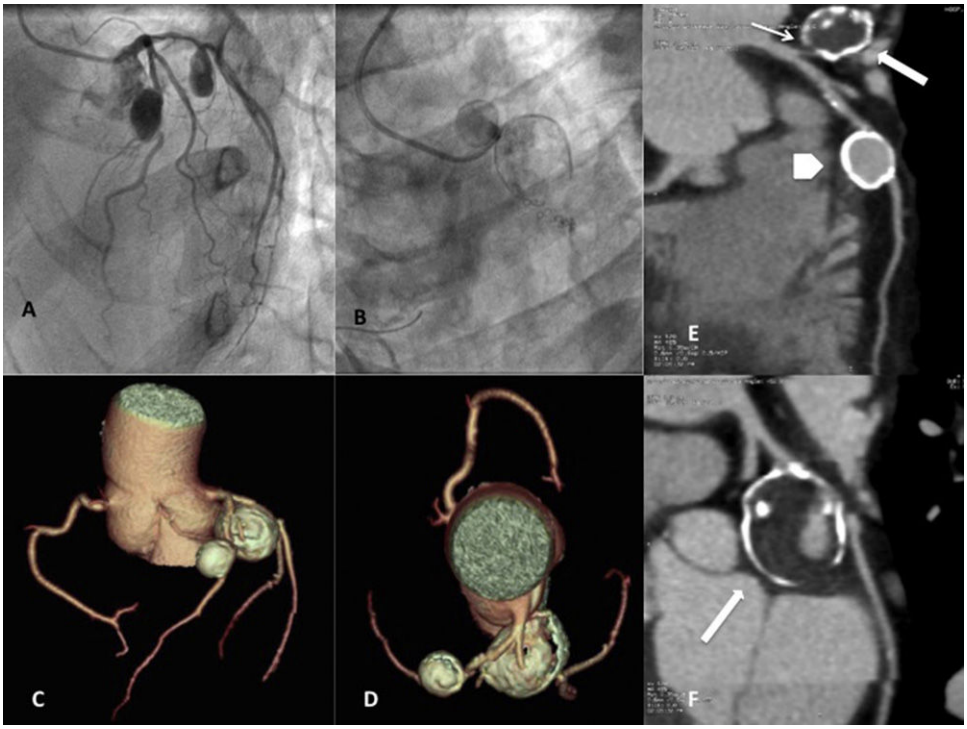

Figure. A and B, coronary angiography; aneurysmal dilatations in the proximal segment of the left anterior descending artery and the circumflex artery. C and D, computed tomography angiography showing 2 calcified, saccular, coronary artery aneurysms; the larger one is located in the circumflex artery. E and F, multiplanar reconstructions. Circumflex artery aneurysm, 30 × 24 mm in size (arrows), with a narrow neck (E, thin arrow), calcified wall ("eggshell" appearance), thrombus (interior, low-density area) and irregular residual lumen; 15 × 14 mm aneurysm in the left anterior descending artery (E, arrowhead), also showing a calcified wall.

DDDR dual chamber pacemaker was implanted. To control the aneurysms and revascularize, aortocoronary bypass surgery was then undertaken, with implantation of the left internal mammary artery to the left anterior descending artery and the right internal mammary artery in Y configuration to the obtuse marginal artery. Both aneurysms were ligated. The patient was discharged on the fifth day following surgery. At the 6-month follow-up visit, he was asymptomatic and free from angina.

Behçet disease is a chronic, multisystemic, inflammatory condition, whose main histopathological characteristic is vasculitis of the large, medium, and small vessels. The etiology of Behçet disease is unknown. Viral, bacterial, genetic, environmental, toxic, and immune factors have been implicated. The most widely recognized genetic factor is HLA-B51. The condition has a low prevalence in Spain (5-10/100 000 population), but it is more widespread in countries along the "Silk Road" (80-370/10 000 in Turkey and 3-20/10 000 in Asian countries). Age of presentation is usually the third or fourth decade of life. Cardiac involvement is estimated to occur in 6% of patients and implies a poor prognosis; hence, a prompt diagnosis is needed.[1] The cardiac manifestations include pericarditis, myocarditis, valve injury, endomyocardial fibrosis, acute myocardial infarction, intracardiac thrombosis, and conduction disturbances. Coronary aneurysm is one of the less common forms of presentation (0.5% of patients). Most are single lesions occurring in the right coronary vessels; coronary aneurysms are less common in the left coronary tree. The pathophysiologic mechanism includes obliterative endarteritis of the *vasa vasorum* and perivascular infiltration by mononuclear cells, with destruction of the media and weakening of the vessel wall.[2,3] The form of presentation is usually an acute coronary syndrome. Noninvasive imaging techniques (coronary computed tomography, transthoracic or transesophageal echocardiography or magnetic resonance imaging) are useful for diagnosis, and coronary angiography is the diagnostic technique of choice.[2,3] Intravascular ultrasound enables differentiation between the components of the coronary artery wall and is helpful to distinguish between a true aneurysm and pseudoaneurysm. However, it is less useful in large or thrombosed aneurysms.[4] The finding of cardiac involvement in a patient with Behçet disease should lead to a search for other affected vascular territories by computed tomography angiography, magnetic resonance angiography, or abdominal ultrasound. There are no treatment recommendations for this condition. The related literature contains 4 cases treated with surgery, which is reserved for huge (> 20 mm), rapidly growing aneurysms and those with a high risk of rupture.[2,5] Atrioventricular block is an uncommon manifestation of unknown etiology in Behçet disease that has been associated with inflammation of the atrioventricular node and surrounding conduction tissue. Definitive pacemaker implantation is usually required.[1] There is no specific treatment for the disease. The aim is to reverse the symptoms and prevent permanent injury. Complete remission of cardiac involvement has been associated with the use of immunosuppressive therapy, colchicine, and anticoagulants.[1,6]

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Cardiac Involvement in a Patient Cohort With Val30Met Mutation Transthyretin Amyloidosis

Daño cardiaco en una cohorte de pacientes con amiloidosis por transtiretina por la mutación Val30Met

To the Editor,

Hereditary transthyretin amyloidosis is an autosomal dominant disease caused by mutations in the transthyretin gene. Of the more than 100 such mutations reported, Val30Met is the most common; the condition is called familial amyloidotic polyneuropathy (FAP) or Corino de Andrade disease in patients with predominant neurological damage.[1] Identification of patients whose amyloidosis is due to a genetic defect is vital because such information affects the treatment strategy and is of great importance for relatives.[2] Although its worldwide prevalence is low, various endemic foci have been described. The island of Mallorca currently has the fifth highest number of affected individuals, behind Portugal, Sweden, Japan, and Brazil. In addition, Spain has another endemic focus, albeit smaller, in Valverde del Camino (Huelva).[3] Individuals with the Val30Met mutation generally present with peripheral neuropathy and progress to autonomic and motor neuropathy, with late onset of cardiac conduction disorders and without cardiac hypertrophy.[4] Currently approved treatments for FAP include liver transplant and tafamidis, a drug that stabilizes transthyretin. The other drugs under study show promising initial results. Current recommendations are to begin drug therapy or consider liver transplant at the first appearance of neurological signs and symptoms. Cardiac amyloidosis is one of the main causes of death in FAP but many of these patients with cardiac involvement are underdiagnosed.[5]

Our objective was to evaluate cardiac involvement in a large series of patients with FAP because this aspect of the disease is poorly characterized in the literature due to its low prevalence, particularly in Spain, for which there are no published data. We reviewed the medical records of patients with FAP (positive genetic study findings for the Val30Met mutation in the transthyretin gene in all patients and the presence of amyloid in subcutaneous fat, rectal, and salivary gland biopsy in all symptomatic patients). Demographic, clinical, electrocardiographic, echocardiographic, and Holter monitoring data were collected, as well as cardiac magnetic resonance imaging and diphosphonate scintigraphy data if they had been performed. Cardiac involvement was defined as the presence of specific signs or symptoms, arrhythmias, atrioventricular (AV) conduction disorders, left ventricular hypertrophy on electrocardiography (ECG) or echocardiography, or late enhancement on cardiac magnetic resonance imaging. Data from 132 patients were analyzed (Table): 104 symptomatic carriers (78.8%) and 28 asymptomatic carriers (21.2%). The mean ages were

Table
Clinical Data of the Patients Included in the Study

Variables	Total	Without cardiac involvement	With cardiac involvement	*P*
Sex (n = 132)				
Men	69 (52.2)	38 (50)	31 (55.4)	.2
Women	63 (47.8)	38 (50)	25 (44.6)	.1
Phenotype (n = 132)				
Asymptomatic carriers	28 (21.2)			
Symptomatic carriers	104 (78.8)	48 (46.2)	56 (53.8)	.05
Age at diagnosis, y	47.4 ± 17	42.9 ± 16	53.6 ± 17	0.03
Age at follow-up, y	57.2 ± 16.4	51.3 ± 15	65.3 ± 15	.01
Polyneuropathy (n = 104)	83 (79.8)	37 (50.7)	46 (85.2)	< .001
Nephropathy (n = 104)	22 (21.2)	5 (7.8)	17 (31.0)	< .001
Palpitations			19 (15.0)	
Dyspnea			13 (10.4)	
Syncope			5 (4.0)	
Heart failure			13 (9.8)	
Dysautonomia symptoms			26 (20.6)	
Pathologic ECG			39 (36.0)	
Conduction changes				
Sinus node dysfunction or atrial fibrillation			13 (9.8)	
AV block			17 (12.9)	