Case
A 32-year-old woman with a 6-year medical history of perimenstrual chest pain and left ventricular systolic impairment after a presumed episode of idiopathic myocarditis presented to the emergency department with 2 hours of severe chest pain and an abnormal ECG with anterolateral ST-segment elevations (Figure 1A). During medical interview, the patient reported the use of cigarettes and cocaine in the past (not for the last 2 years) and very similar symptoms just 2 months earlier. At that time, troponin-I was elevated (12 ng/mL), and subsequent coronary angiogram revealed a dissection of the left circumflex artery, but percutaneous coronary intervention (PCI) could not be performed because of technical complexity, and the patient was commenced on aspirin and clopidogrel.

Cardiovascular examination was unremarkable. Laboratory testing revealed elevated creatinine-kinase muscle and brain and troponin-I (95.5 ng/mL and 12.6 ng/mL, respectively). Urine toxicology testing for the presence of cocaine and serum β-human chorionic gonadotropin was negative. Urgent coronary angiography showed a thrombotic subtotal occlusion of the mid-left anterior descending artery with probable vasospasm (Figure 1B). In addition, angiographically, the left circumflex artery had a moth-eaten appearance (Figure 1C). Successful PCI was performed with deployment of a drug-eluting stent. Thrombophilia testing was negative as was genetic interrogation for familial vasculopathies (TAAD1 [thoracic aortic aneurysm and dissection], TAAD2, and FAA [familial aortic aneurysm]), Marfan’s (FBNI), Loey-Dietz (TGFBRI and TGFBRII), and Ehlers-Danlos type 4 (COL3A1). Further surveillance of other vascular territories demonstrated an occluded left internal carotid artery from a previous dissection.

Figure 1. A, Presenting ECG demonstrating anterolateral ST-segment elevations. B, Angiogram of left anterior descending artery displaying a thrombotic occlusion within the middle third of the vessel. C, Angiogram of left circumflex artery displaying a moth-eaten appearance with an angiographically normal artery proximal to the coronary artery, consistent with epicardial coronary fibromuscular dysplasia. D, Confirmation of vasospasm of the left circumflex artery with 25 µg of intracoronary ergonovine, relieved with intracoronary nitroglycerin. Ergonovine, which stimulates both α-adrenergic and serotonergic receptors, has a vasoconstrictor effect on vascular smooth muscle.
Over the ensuing 3 months, the patient had 3 additional hospitalizations for non–ST-segment elevation myocardial infarcts, and she underwent 4 additional PCIs. Vasospasm of the left circumflex artery was confirmed with intracoronary ergonovine challenge, leading to transient left circumflex artery occlusion, which was relieved by intracoronary nitroglycerin (Figure 1D). As an attempt to medically manage refractory coronary vasospasm, the patient underwent consecutive trials of maximally tolerated doses of diltiazem, cyproheptadine, bosentan, and the combination of transdermal and short-acting nitrates. Unfortunately, none of these pharmacological approaches provided sustained anginal relief, and the patient continued to have recurrent myocardial injury. The patient ultimately developed cardiogenic shock necessitating emergent intubation. The subsequent angiography revealed focal thrombotic stenoses of the proximal left anterior descending artery and first diagonal, which were again treated by PCI with drug-eluting stents. An intra-aortic balloon pump was then required for hemodynamic support, and she underwent implantation of a left ventricular assist device 1 day thereafter. Within 7 months of implantation, the patient underwent successful orthotropic heart transplantation. Histological examination of the explanted heart demonstrated intimal fibromuscular dysplasia (FMD) within the epicardial coronary arteries with foci of cystic medial degeneration (Figure 2). At 6 months of follow-up, she has done well without recurrent angina.

Discussion
Our patient demonstrated recurrent coronary arterial vasospasm, superimposed thrombosis, and dissection, leading to refractory symptoms with extensive myocardial necrosis and left ventricular dysfunction. Multiple trials of medical therapy were attempted, along with multiple PCIs, mechanical circulatory support, and eventual heart transplantation.

On the basis of the histopathologic finding of FMD and cystic medial degeneration, we suspected a pathological process with abnormal connective tissue, rendering the vessel wall vulnerable to repetitive vasospasm. Coronary spastic angina has been demonstrated among patients with connective tissue diseases.1 FMD is a nonatherosclerotic noninflammatory vascular disease that disproportionately affects women. It most commonly affects the renal and carotid arteries, and epicardial coronary FMD is an uncommon entity.2 Data regarding epicardial coronary artery involvement in FMD are scarce. One case series describes 7 premenopausal or perimenopausal women with acute coronary syndromes and epicardial coronary artery FMD, in which all patients presented with mono or bilateral renal artery involvement as well.3 Recently, Olin et al4 presented the results of the United States registry for FMD. The registry included 447 cases of FMD, 88 of which presented with arterial dissections and aneurysms. Out of these, only 3 cases (3.4%) presented dissections on coronary arteries. The natural history, prognosis, and outcomes in FMD vary according to the vascular site that it involves. Disease progression is thought to take place in about one third of patients with renal FMD, whereas cerebrovascular disease is reported to progress infrequently.5 Data regarding outcomes on other arterial territories are scarce, and arterial dissection has been proposed as the most likely mechanism by which FMD causes acute coronary syndrome.6

This case highlights the devastating consequences of a vessel wall disrupted by FMD with coronary vasospasm refractory to traditional therapy. Unconventional, but hypothesis-driven medical and percutaneous treatments were unable to halt this unremitting disease process, with mortality averted only by aggressive surgical intervention and ultimate heart transplantation. To our knowledge, this is the first report of a patient affected by FMD in the epicardial coronary arteries requiring heart transplantation attributable to the aggressive nature of the vasospastic phenomenon despite all available medical and percutaneous management.

Disclosures
None.

References

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Coronary Vasospasm Attributable to Fibromuscular Dysplasia: The Long Bridge to Transplant
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