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Severe multivessel coronary heart disease in a young woman with familial hypercholesterolemia and congenital heart disease: A case report

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ABSTRACT

The prevalence of premature atherosclerotic cardiovascular disease (ASCVD) ranges from 7% to 30%, but the incidence in young patients is increasing. Traditional risk factors, such as hypertension, hyperlipidemia, obesity, and diabetes, have an increasing prevalence in young patients and especially in young women. A 32-year-old woman presented with dyspnea and exertional chest pain. She had a history of familial hypercholesterolemia and unidentified aortic valve disease status after a pulmonary autograft at the age of 20. Due to insurance changes with the onset of the COVID-19 pandemic, she lost access to specialty care. She was not on any cholesterol-lowering agents prior to admission. An electrocardiogram demonstrated no ST changes with elevated high-sensitivity troponin-I concerning for non-ST elevation myocardial infarction. Laboratory data also revealed elevated LDL-C greater than 400. Due to concern for multivessel disease and complex anatomy, she underwent coronary computerized tomography angiography, which verified her multivessel coronary artery disease. An echocardiogram demonstrated a preserved ejection fraction and moderate aortic regurgitation. Her coronary artery bypass graft was deferred due to possible future valvular surgery. She underwent percutaneous coronary intervention with drug-eluting stents to left circumflex and left anterior descending arteries. Familial hypercholesterolemia is a prevalent but under-recognized and under-treated risk factor for premature ASCVD, which can be adequately identified through improved risk assessment and managed with aggressive combination anti-hyperlipidemia therapy.

1. Introduction

Premature coronary artery disease (PCAD) is a significant health concern as it affects men younger than 55 years and women younger than 65 years [1]. The burden of atherosclerotic cardiovascular events has declined in men but increased in young women [2]. Traditional risk factors, such as hypertension, hyperlipidemia, obesity, and diabetes, have an increasing prevalence in young patients and especially women. Disparate outcomes of coronary artery disease in women can be attributed to socioeconomic factors, absence of tailored secondary prevention, limited access to healthcare,and further prevention strategies [3]. We present a case of premature severe multivessel coronary artery disease in a 32-year-old woman.

2. Case Presentation

A 32-year-old premenopausal woman presented with subacute onset of exertional chest tightness with dyspnea and fatigue of one-month duration. She had a past medical history of unknown congenital aortic stenosis status after a pulmonary autograft at the age of 20, hypertension, familial hypercholesterolemia, and a family history of premature coronary artery disease. She was previously on standard therapy with statin and ezetimibe along with a PCSK9 inhibitor trial. However, prior to presentation, she had lost her health insurance during the COVID-19 pandemic. She denied previous pregnancies or contraceptive use.

On presentation to the emergency room, she was tachycardic (102 beats/min), normotensive (130/81 mmHg) and saturating well on room air. Her BMI was 33.86 kg/m^2. Her physical exam was unremarkable except for a well healed sternotomy scar. She reported she was menstruating. The only significant laboratory findings were elevated

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high-sensitivity troponin-I of 219 ng/L [reference range: 0–34 ng/L], which later peaked at 2151 ng/L, elevated total cholesterol of 509 mg/dL [reference range: 0–200 mg/dL] and low-density lipoprotein (LDL) of 443 mg/dL [reference range: 0–99 mg/dL]. A 12-lead electrocardiogram demonstrated sinus tachycardia, left-axis deviation with J-point elevation, Q wave in lead III, and anterolateral T-wave inversions (Fig. 1). A plain-film chest radiograph demonstrated no acute cardiopulmonary disease. She was admitted for management of non-ST elevation myocardial infarction.

Given her history of congenital heart disease, the decision was made to proceed with coronary computerized tomography (CT) angiography (CCTA) prior to left heart catheterization. CCTA was remarkable for moderate irregularity and mild degree of calcification of the left anterior descending coronary artery, consistent with premature atherosclerotic disease and atherosclerosis of proximal carotids bilaterally (Fig. 2). An echocardiogram showed ejection fraction of 50–55%, moderate aortic regurgitation, aortic and pulmonic valve repair (Fig. 3). Her left heart catheterization showed multivessel coronary artery disease with ostial left anterior descending coronary artery (LAD) with 70–80% narrowing, distal LAD with diffuse 50% narrowing, proximal left circumflex coronary artery (LCx) with 70% narrowing, and right coronary artery with ostium narrowing of 50–60% narrowing (Fig. 4).

The cardiothoracic surgery team were consulted for possible coronary artery bypass graft (CABG). However, the decision was made to proceed with high-risk staged percutaneous intervention (PCI) due to likelihood of needing aortic valve repair in the near future. She underwent successful PCI with 2 drug-eluting stents in the left anterior descending and left circumflex coronary arteries. Her left heart catheterization was complicated by flash pulmonary edema that required treatment with intravenous diuretics. She was discharged on aspirin, clopidogrel, empagliflozin and high-intensity statin. On outpatient follow-up, she was free of chest pain and referred to a lipid clinic at a tertiary referral center. Unfortunately, her insurance prevented her from starting PCSK9 inhibitor for optimal cholesterol control. She was not advised on contraceptive or pregnancy planning.

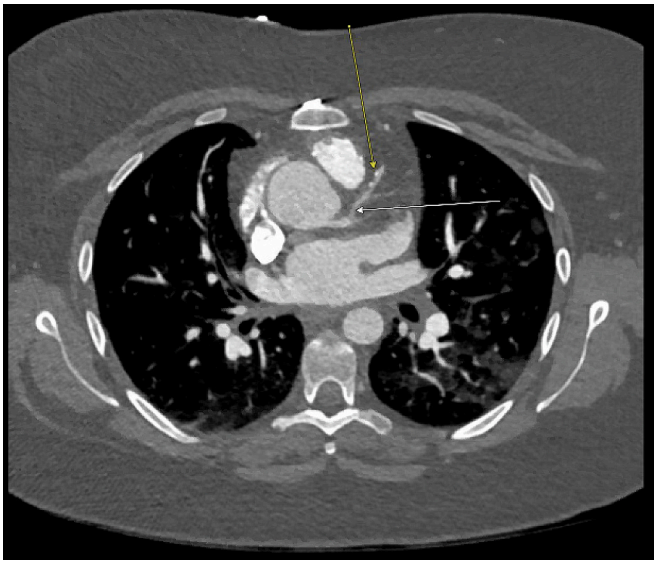

Fig. 2. Coronary CT angiogram demonstrating severe left anterior descending coronary artery disease (arrows).

3. Discussion

Premature coronary artery disease is a complex interaction between polygenic, environmental and lifestyle factors. Familial hypercholesterolemia is commonly recognized for its role in early plaque development. When familial hypercholesterolemia is left untreated, approximately 50% of men and 15% of women will succumb to their disease in their early years. Homozygous familial hypercholesterolemia often presents with coronary heart disease at much earlier ages [4]. Moreover, those with familial hypercholesterolemia experience an accelerated risk of coronary artery disease by 10–20 years in men and 20–30 years in women [5]. Premenopausal women are more likely to experience plaque erosion and coronary vasospasm as compared wtih

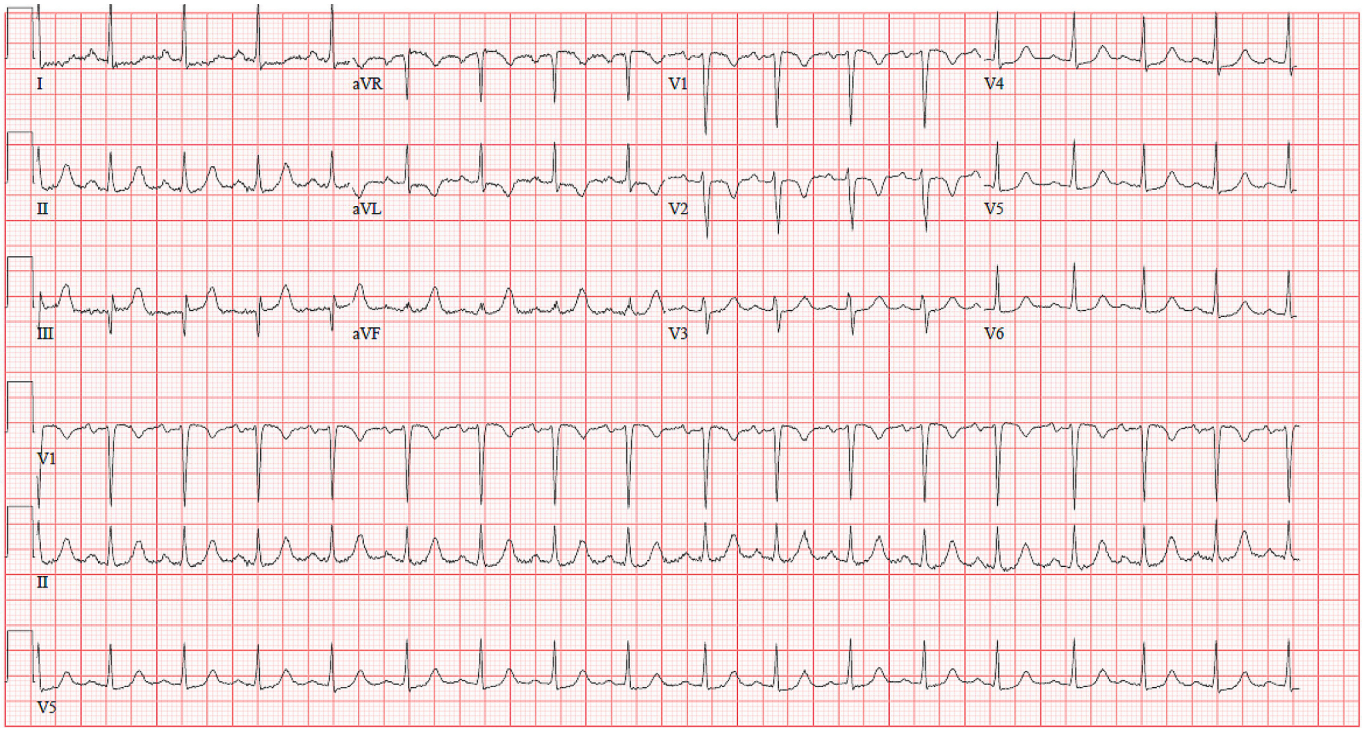

Fig. 1. A 12-lead EKG showing T-wave inversions in anterolateral leads.

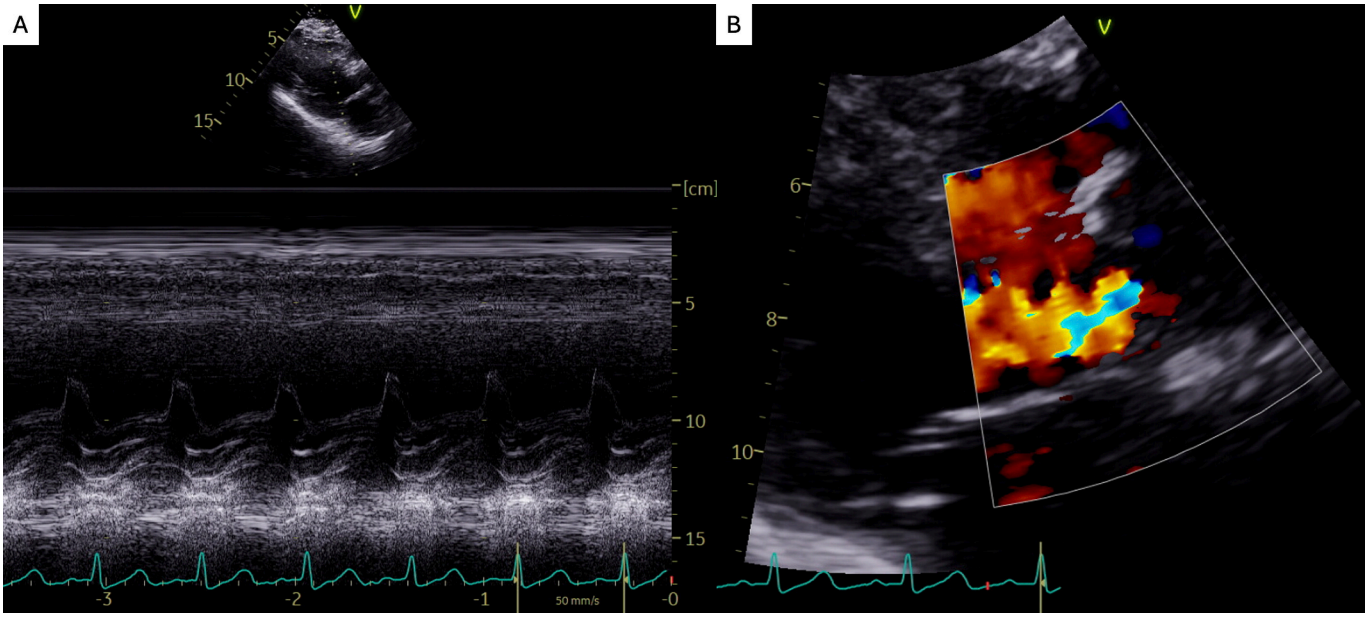

Fig. 3. Transthoracic echocardiogram. (A) Parasternal long-axis view revealing *E*-point septal separation suggestive of preserved ejection fraction. (B) Parasternal long-axis view revealing moderate aortic regurgitation.

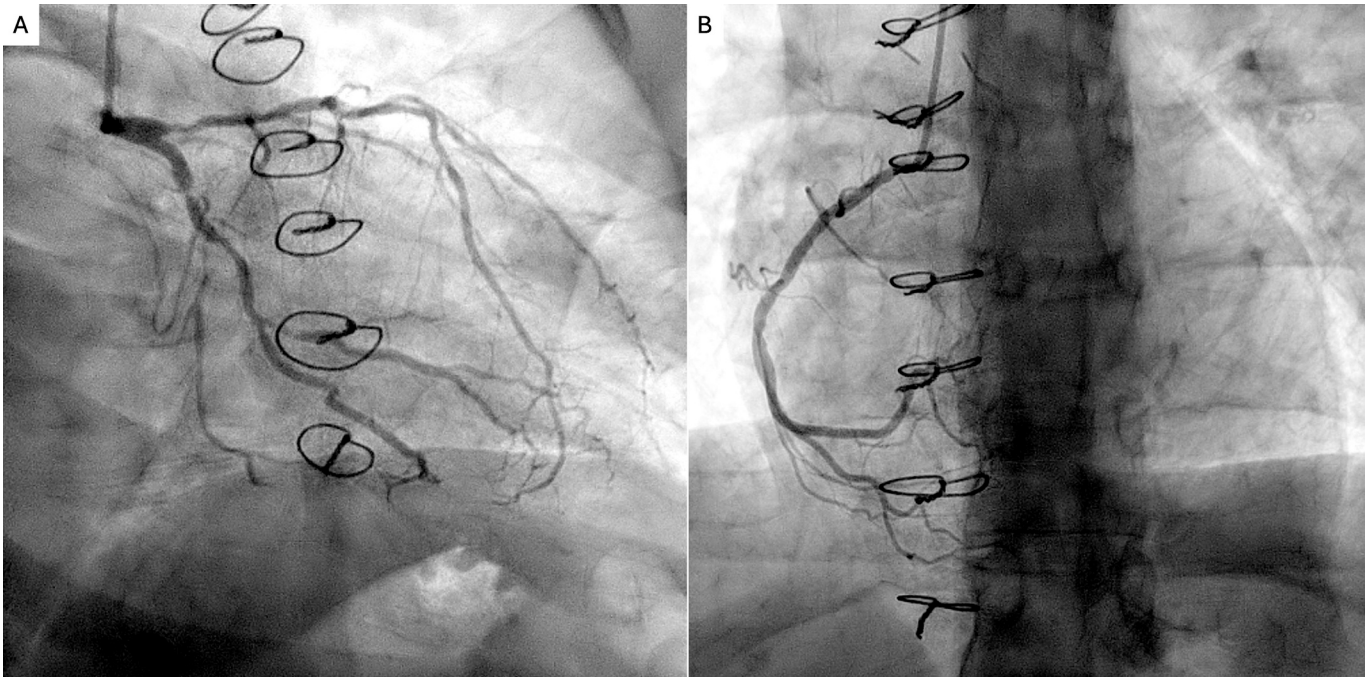

Fig. 4. Left heart catheterization showing multivessel coronary artery disease. (A) Ostial left anterior descending coronary artery (LAD) with 70–80% narrowing, distal LAD with diffuse 50% narrowing, and proximal left circumflex coronary artery with 70% narrowing. (B) Right coronary artery with ostium narrowing of 50–60% narrowing.

plaque rupture in men [6].

Acute myocardial infarction commonly presents with chest pain typically described as pressure, tightness or squeezing. However, sex differences in presentation are evident with atypical, angina-equivalent presentations. Notably, women are more likely to have high-risk presentations and less likely to have central chest pain. Women more often report unusual fatigue, dyspnea, indigestion, nausea, vomiting, palpitations, and a sense of dread [6]. Interestingly, shoulder and arm pain were more predictive of acute coronary syndrome in women than in men, with an odds ratio twice as high [7]. The present patient was noted to have fatigue, chest pain and dyspnea for one month. The US Variations in Recovery: Role of Gender on Outcomes of Young AMI Patients (VIRGO) study was an observational cohort study examining 1465 patients with a 2:1 ratio of women to men. Younger women were more likely to present to the hospital with symptoms lasting more than 6 h compared with young men [8]. In their case series of 22 patients, van der Bijl et al. observed a higher propensity of acute coronary syndrome (ACS) events during menstruation, when estrogen levels are their lowest [9].

Familial hypercholesterolemia is a diagnosis based on physical

findings of xanthomas, personal or family history, early-onset of ASCVD, and LDL-cholesterol (LDL-C) concentration. Most commonly due to genetic variants of LDL receptor, and less commonly mutations in apolipoprotein B (ApoB) and gain of function mutation in proprotein convertase subtilisin/kexin 9 (PCSK9) [10]. Homozygous familial hypercholesterolemia criteria is untreated LDL-C greater than 500 mg/dL or treated LDL-C greater than 300 mg/dL and cutaneous or tendon xanthomas or elevated LDL-C levels in family members with heterozygous variant. Given the high risk for premature coronary artery disease, patients are recommended annual echocardiogram evaluation for structural heart disease and CCTA every 5 years. Stress testing and invasive coronary angiography is reserved for symptoms suggestive of ischemia or impaired valve function [11].

Approximately 2.7 million US adults aged 18 to 64 years faced uninsurance during the COVID-19 pandemic [12]. Our patient had recently moved between states and lost insurance due to unemployment during the pandemic. She was previously on targeted lipid-lowering therapy with high-dose statin, ezetimibe and a PCSK9 inhibitor trial. Medical management of familial hypercholesterolemia focuses on reducing atherosclerotic cardiovascular disease risk by lowering LDL to less than 70 mg/dL in adults and 100 mg/dL in children. This is primarily achieved through multidrug treatment with statins, niacin, ezetimibe, bile acid sequestrants, and PCKS9 inhibitors. Lipoprotein apheresis once weekly can be considered in patients with persistent LDL-C greater than 100 mg/dL. Lifestyle modifications with tobacco abstinence, weight loss, exercise and a healthy diet low in fats are recommended. Modifiable risk factors such as diabetes mellitus and hypertension should also be treated [10].

Given the present patient's unknown congenital aortic valve degeneration and history of familial hypercholesterolemia, she underwent CCTA to evaluate her epicardial coronary arteries for disease. She underwent high-risk percutaneous coronary intervention as opposed to coronary artery bypass graft since she was at high risk for early aortic valve repair.

This case is remarkable for the atypical presentation of acute coronary syndrome in a woman with familial hypercholesterolemia and socioeconomic disadvantages. The case focuses on the importance of early recognition of modifiable risk factors in highly susceptible individuals and of tailoring strategies for them. It also highlights the need for anticipating future complications and interventions in those with multiple comorbidities and individualizing treatment options.

Contributors

Shaikh B. Iqbal contributed to patient care, conception of the case report, acquiring and interpreting the data, drafting the manuscript, undertaking the literature review and revising the article critically for important intellectual content.

Shraddha Poudel contributed to acquiring and interpreting the data and drafting the manuscript.

Nicholas Huerta contributed to patient care and drafting the manuscript.

Ajay Kumar contributed to patient care and drafting the manuscript.

Sean Shieh contributed to revising the article critically for important intellectual content.

Shiavax J. Rao contributed to revising the article critically for important intellectual content.

All authors approved the final submitted manuscript and agree to be accountable for all aspects of the work to ensure that the questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Patient consent

Obtained.

Provenance and peer review

This article was not commissioned and was peer reviewed.

Conflict of interest statement

The authors declare that they have no conflict of interest regarding the publication of this case report.

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