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Surgery

Hearts and Hormones: Too Young to Bypass? A Case of Arterial Misconduct in PCOS

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Abstract | **Case Report**

Background: Premature coronary artery disease (CAD) in premenopausal women is rare and often underdiagnosed due to the assumed protective effects of estrogen. However, metabolic and endocrine disorders such as polycystic ovarian syndrome (PCOS) and early-onset type 2 diabetes mellitus (T2DM) significantly elevate cardiovascular risk through mechanisms including insulin resistance, dyslipidemia, endothelial dysfunction, and chronic inflammation. Despite this, PCOS is often overlooked in cardiovascular risk stratification and clinical decision-making. ***Case Presentation:*** A 36-year-old Malay woman with a history of poorly controlled T2DM (HbA1c 8.5%), PCOS, hypertension, and dyslipidemia presented with a one-month history of exertional chest discomfort and two episodes of severe angina. Her ECG showed T-wave inversion in lead III, and serial high-sensitivity troponin I levels were negative. Laboratory evaluation revealed hyperglycemia and an atherogenic lipid profile. Echocardiography showed preserved left ventricular systolic function (EF 60%) without regional wall motion abnormalities. Coronary angiography revealed severe triple vessel disease: 70% proximal stenosis of the left anterior descending (LAD) artery, two tandem high-grade lesions in the dominant left circumflex (LCx) artery, and a chronic total occlusion (CTO) of the small, non-dominant right coronary artery (RCA). After multidisciplinary heart team evaluation, coronary artery bypass grafting (CABG) was recommended due to anatomical complexity and her diabetic status. ***Discussion:*** This case illustrates the aggressive nature of coronary atherosclerosis in the setting of combined PCOS and T2DM, even in a relatively young woman. It also underscores the diagnostic challenges posed by non-classical presentations in females, where traditional tools such as ECG and biomarkers may be unremarkable despite significant coronary pathology. Evidence from trials such as SYNTAX and FREEDOM supports surgical revascularization in diabetic patients with multivessel disease, given superior long-term outcomes compared to percutaneous intervention. This case highlights the need for earlier cardiovascular risk screening in women with PCOS and for heightened clinical vigilance across specialties. This case also emphasizes the importance of long-term cardiometabolic management. The patient had been prescribed dapagliflozin, a sodium-glucose cotransporter-2 (SGLT2) inhibitor, which has demonstrated cardiovascular benefit in patients with diabetes and high cardiovascular risk. Early and sustained use of such agents may play a preventive role in attenuating progression of atherosclerotic disease and improving outcomes post-revascularization.
Conclusion: PCOS, when accompanied by diabetes and other metabolic risk factors, can result in premature and severe coronary artery disease. Early recognition, comprehensive evaluation, and appropriate referral for surgical intervention are critical to preventing adverse cardiovascular outcomes in this at-risk population. Multidisciplinary care and tailored long-term management strategies are essential.

INTRODUCTION

Coronary artery disease (CAD) remains a predominant cause of morbidity and mortality globally. While typically associated with older male populations, a growing body of evidence highlights its increasing prevalence among women, including those of reproductive age. The protective cardiovascular effects of estrogen have historically led to the underestimation of CAD risk in premenopausal women. However, the presence of coexisting metabolic and endocrine disorders may override these protective mechanisms, accelerating the development of atherosclerosis.

Polycystic ovarian syndrome (PCOS), a common endocrine disorder affecting approximately 6–12% of women of reproductive age, is characterized by hyperandrogenism, oligo/anovulation, and polycystic ovarian morphology. Beyond its reproductive implications, PCOS is associated with insulin resistance, dyslipidemia, central obesity, systemic inflammation, and endothelial dysfunction — all of which are established contributors to atherosclerotic cardiovascular disease. Despite these associations, PCOS remains under-recognized as a cardiovascular risk factor in routine clinical practice.

The interplay between PCOS and early-onset type 2 diabetes mellitus (T2DM) further compounds cardiovascular risk. Women with both conditions are significantly more likely to develop subclinical and overt CAD at a younger age. This risk is amplified when other traditional factors such as hypertension and dyslipidemia coexist. Unfortunately, due to the non-classical presentation of ischemic symptoms in women and underutilization of early cardiovascular screening tools in this population, diagnosis is frequently delayed until the disease is advanced.

Surgical revascularization, such as coronary artery bypass grafting (CABG), is uncommon in young women and is usually reserved for extensive or high-risk coronary pathology. Herein, we present a rare case of a 36-year-old woman with a constellation of metabolic risk factors, including PCOS and poorly controlled diabetes, who was found to have severe triple vessel coronary artery disease requiring surgical intervention. This case serves to emphasize the need for heightened cardiovascular surveillance and a multidisciplinary approach in managing young women with complex metabolic disorders.

Case Presentation

A 36-year-old Malay woman, employed as an accounting assistant, presented with a one-month history of intermittent exertional chest pain, progressively increasing in frequency and severity. She reported two episodes of central, pressure-like chest discomfort radiating to her left arm and neck, each lasting approximately 15–20 minutes and resolving with sublingual glyceryl trinitrate (GTN). There was no associated orthopnea, paroxysmal nocturnal dyspnea, palpitations, or syncope. She denied any history of smoking or recreational drug use. Her functional status had declined slightly over the past few weeks, with reduced tolerance for moderate physical activity.

Her past medical history included Type 2 diabetes mellitus (T2DM), diagnosed five years ago, with suboptimal glycemic control (HbA1c: 8.5%), hypertension, dyslipidemia, polycystic ovarian syndrome (PCOS) with longstanding primary subfertility and bronchial asthma (mild, triggered by cold air and upper respiratory infections).

She was not on regular follow-up and demonstrated inconsistent adherence to prescribed medications. There was no known family history of premature coronary artery disease (CAD) or sudden cardiac death. Her medications included metformin, dapagliflozin, perindopril, bisoprolol, rosuvastatin, and a salbutamol inhaler.

On examination, she appeared well, alert, and oriented. Vital signs were stable, cardiovascular and respiratory examinations were unremarkable, with no signs of heart failure or volume overload.

The initial investigations demonstrated a non-diagnostic ECG with sinus rhythm and T-wave inversion in lead III, without dynamic changes. High-sensitivity troponin I levels remained below 4 ng/L on two serial tests. Biochemically, she had marked hyperglycemia (fasting blood glucose: 14.48 mmol/L), and dyslipidemia characterized by elevated LDL-C (3.1 mmol/L), reduced HDL-C (0.9 mmol/L), and elevated triglycerides (2.8 mmol/L). Renal and liver function tests were within normal limits. Her hemoglobin level was mildly reduced at 10.3 g/dL.

A transthoracic echocardiogram showed preserved left ventricular systolic function with an estimated ejection fraction (EF) of 60%, and no regional wall motion abnormalities or valvular pathology.

Coronary angiography revealed severe triple vessel disease. The left main stem (LMS) was unobstructed. The left anterior descending (LAD) artery exhibited significant proximal stenosis of approximately 70%, with favorable distal segments for grafting. The dominant left circumflex (LCx) artery demonstrated two critical tandem lesions (70% proximal and 80% distal) with a large obtuse marginal branch, all providing suitable targets for revascularization. The right coronary artery (RCA) was chronically occluded at its origin, non-dominant, and supplied via bridging collaterals from the left system. (CTO) of a small, non-dominant vessel with bridging collaterals from the left system.

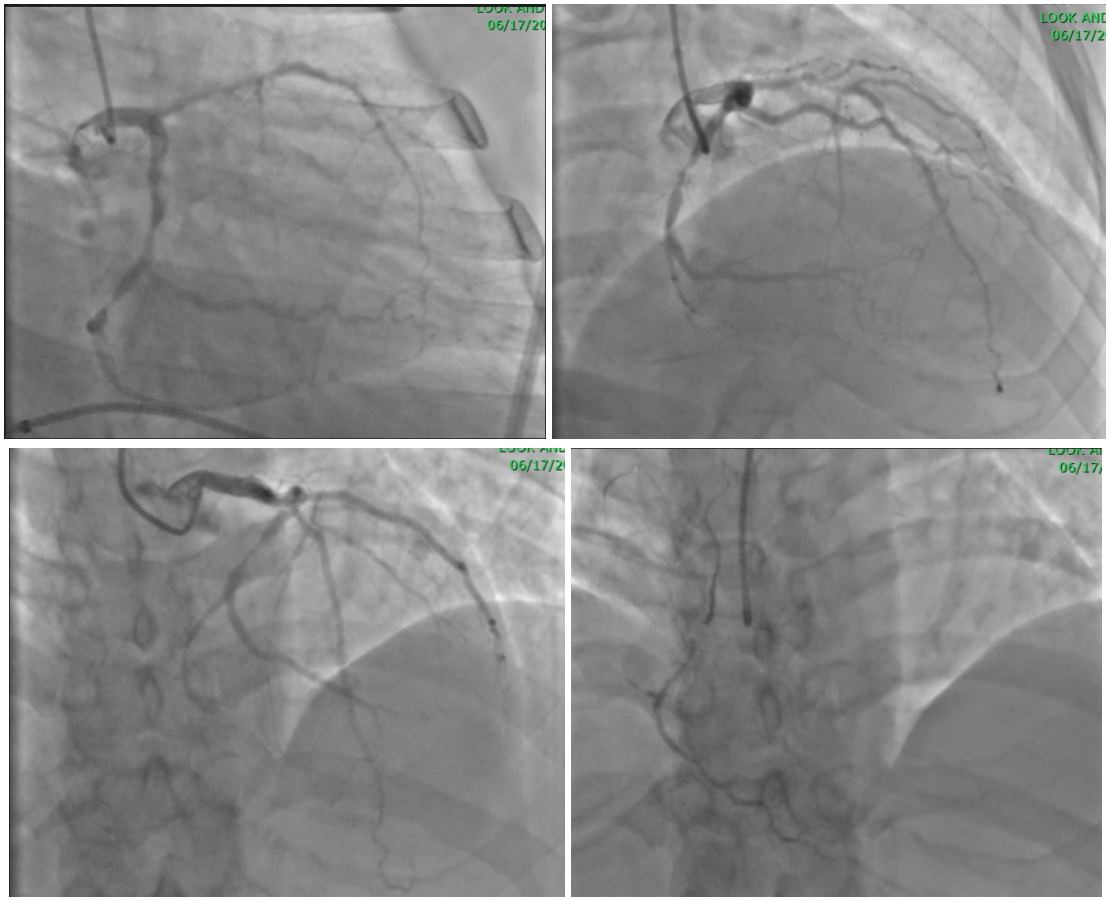

Figure 1: Coronary angiography revealed severe triple vessel disease. LAD: 70% proximal stenosis; good distal targets for grafting. LCx: Large and dominant with two tight lesions (proximal 70%, distal 80%); large OM branch. RCA: Chronic total occlusion; small, non-dominant vessel with bridging collaterals from the left system

The case was reviewed by the multidisciplinary heart team, including cardiology and cardiothoracic surgery. While initial considerations included percutaneous coronary intervention (PCI), the complexity of the anatomy and diffuse multivessel involvement in a diabetic patient favored surgical revascularization. The patient was stabilized medically, optimized on dual antiplatelet therapy and statins, and subsequently referred to the cardiothoracic surgery clinic for elective coronary artery bypass grafting (CABG).

DISCUSSION

This case underscores a critical intersection between reproductive endocrinology and cardiovascular medicine. Premenopausal women are traditionally considered to have a lower risk of coronary artery disease (CAD) due to the protective effects of estrogen, which has vasodilatory and anti-inflammatory properties. However, this hormonal protection can be nullified in the presence of significant metabolic disturbances. Polycystic ovarian syndrome (PCOS), a condition affecting 6–12% of reproductive-aged women, is one such condition known to dramatically increase cardiovascular risk.

PCOS is characterized by hyperandrogenism, insulin resistance, and chronic low-grade inflammation. These pathophysiological features promote endothelial dysfunction, oxidative stress, and adverse lipid profiles, all of which accelerate atherogenesis. Studies have shown that women with PCOS are more likely to develop coronary artery calcifications, have impaired flow-mediated dilation, and exhibit increased carotid intima-media thickness — all markers of early subclinical atherosclerosis [1,2]. Moreover, insulin resistance in PCOS promotes hyperinsulinemia, which enhances smooth muscle cell proliferation and contributes to plaque instability [3].

In addition, the co-existence of type 2 diabetes mellitus (T2DM) significantly amplifies cardiovascular risk. Diabetes is an independent predictor of multivessel coronary artery disease, and diabetic women tend to have more extensive and diffuse disease compared to men [4]. The combination of PCOS and T2DM (as seen in this case) exponentially increases the likelihood of early-onset, aggressive CAD. The patient's other risk factors, including hypertension and dyslipidemia, further compound this risk.

Despite her symptomatic presentation, this patient exhibited preserved left ventricular function and negative cardiac biomarkers, illustrating the well-

recognized phenomenon that women, particularly younger ones, often present with atypical or non-ST elevation myocardial infarction (NSTEMI)-equivalent symptoms and normal troponin levels [5]. This can delay diagnosis and appropriate management, emphasizing the importance of clinical vigilance in evaluating women with multiple cardiovascular risk factors.

Angiographically, this patient demonstrated severe triple vessel disease involving the LAD and dominant LCx, with a chronic total occlusion (CTO) of the RCA. In the presence of diabetes and multivessel disease, current guidelines favor surgical revascularization over PCI due to superior long-term outcomes, including reduced rates of repeat revascularization and myocardial infarction [6]. The SYNTAX and FREEDOM trials have both demonstrated improved survival and major adverse cardiac event (MACE) rates in diabetic patients undergoing CABG versus PCI, particularly in cases with complex or diffuse coronary lesions [7,8].

Beyond revascularization, long-term medical management is critical for reducing recurrent cardiovascular events in patients with diabetes and metabolic syndrome. Sodium-glucose cotransporter-2 (SGLT2) inhibitors, such as dapagliflozin, have gained prominence for their cardiorenal protective properties, independent of glucose lowering. Landmark trials such as DECLARE-TIMI 58 and DAPA-HF have shown that dapagliflozin significantly reduces the risk of heart failure hospitalization and cardiovascular mortality in high-risk patients, including those with preserved ejection fraction [9,10]. Although primarily used for glycemic control, early initiation of dapagliflozin in this patient may contribute to long-term cardioprotective effects post-CABG, particularly given her high atherosclerotic burden and diabetic status. Incorporating such agents into guideline-directed therapy is essential for comprehensive cardiovascular risk reduction in women with complex metabolic disease.

This case illustrates the importance of early identification and risk stratification of cardiovascular disease in women with PCOS. While guidelines such as those from the American College of Cardiology (ACC) and American Heart Association (AHA) recommend cardiovascular risk screening in women with diabetes and metabolic syndrome, there is still a lack of specific guidelines addressing women with PCOS. Given the emerging data, there is a compelling need to include PCOS as an independent risk-enhancing factor in cardiovascular risk assessment tools.

In clinical practice, this case highlights the need for a multidisciplinary approach involving cardiology, endocrinology, and cardiothoracic surgery in managing young women with complex metabolic syndromes. Beyond revascularization, long-term management should include aggressive lifestyle interventions, glycemic control, lipid management, and weight reduction — all tailored to the unique pathophysiological profile of PCOS.

Conclusion

This case highlights the complex interplay between endocrine, metabolic, and cardiovascular pathology in young women, particularly those with polycystic ovarian syndrome and early-onset type 2 diabetes mellitus. It demonstrates that despite a relatively young age and absence of traditional risk factors such as smoking or a family history of coronary artery disease, significant atherosclerosis can still develop in the presence of metabolic syndrome. The presence of multivessel disease, including chronic total occlusion and diffuse proximal lesions, underscores the importance of comprehensive cardiovascular assessment in this population.

From a surgical perspective, the decision to proceed with coronary artery bypass grafting (CABG) was guided by angiographic complexity, diabetic status, and long-term outcomes supported by evidence from landmark trials. This case reinforces the need for early risk identification, individualized treatment planning, and collaborative management involving cardiologists, endocrinologists, and cardiac surgeons. Further research and consensus are warranted to guide screening and management strategies for cardiovascular disease in women with PCOS, to ensure timely diagnosis and optimal intervention.

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