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Case Report

Double-Trouble Hyperhomocysteinemia and Lipoprotein(a)-Induced Myocardial Infarction in a Very Young Man: A Case Report

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ABSTRACT

Background: Acute coronary syndrome encompasses unstable angina, non–ST-elevation myocardial infarction, and ST-elevation myocardial infarction. Coronary artery disease stands as the leading cause of death worldwide. The condition is not typically suspected in young individuals, particularly those without a substantial family history. Hyperhomocysteinemia and elevated lipoprotein(a) levels are recognized as significant risk factors and can be integrated into screening tools for early identification and intervention.

Case Presentation: A 23-year-old man was diagnosed with an evolved anterior wall myocardial infarction, verified through ECG and echocardiography. Further investigation using coronary angiography revealed a single-vessel disease with the involvement of branch vessels, which was treated successfully via bifurcation stenting. Optical coherence tomography analysis of the lesion indicated a fibrous-atheromatous lesion accompanied by thrombosis. Upon evaluation, high lipoprotein(a) and hyperhomocysteinemia were identified as risk factors contributing to the patient's condition.

Conclusions: Lipoprotein(a) and familial hyperhomocysteinemia should not be exclusively linked to a family history of premature atherosclerotic cardiovascular disease (ASCVD). These factors should be considered important in screening due to their significant impact on ASCVD risk. Furthermore, intracoronary imaging should be employed extensively to gain insights into the pathophysiology of the disease and enhance interventional strategies in these situations. ***(Iranian Heart Journal 2025; 26(1): 113-121)***

KEYWORDS: CAD, OCT, IVUS, Lipoprotein (A), Homocysteine

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Coronary artery disease (CAD), an atherosclerotic cardiovascular disease (ASCVD), encompasses various clinical manifestations, including acute myocardial infarction (AMI), sudden cardiac death, stable angina, and unstable angina. Presently, CAD represents the leading cause of mortality worldwide. Over 80% of CVD cases are concentrated in low- and middle-income countries. The South Asian region comprises 8 countries classified as low- or lower-middle-income: Bangladesh, Bhutan, Sri Lanka, India, Nepal, Afghanistan, Pakistan, and the

Maldives, with a significant burden of CVD. South Asian ethnicity has been associated with an increased risk of developing CAD and other non-communicable diseases. [1] Apart from conventional risk factors such as smoking, sedentary lifestyle, hypertension, diabetes mellitus, and dyslipidemia, several non-traditional factors have also been identified as significant contributors to CAD in South Asian populations. These factors include psychosocial stress, educational attainment, and urbanization. Individuals with a healthy body mass index (BMI) may still fall under the "skinny fat" category, which predisposes them to metabolic syndrome and CAD. Research has shown that South Asians tend to develop CAD at a younger age compared with other populations. Furthermore, high C-reactive protein levels have been linked to an increased inflammatory predisposition and CAD development in this demographic. Studies have found that both hyperhomocysteinemia and elevated lipoprotein(a) levels are more common in South Asian populations, potentially contributing to the higher prevalence of CAD in this demographic. While young CAD is often associated with well-known risk factors such as smoking, hypertension, diabetes, dyslipidemia, obesity, and family history, less common risk factors like coagulation disorders, drug addiction, and vasculitis have also been implicated in its development. [2]

Case Presentation

Herein, we present the case of a 23-year-old male shopkeeper who experienced a sudden onset of severe compressive chest pain lasting for 5 hours, 10 days prior to seeking medical attention. The patient was initially treated at a local primary healthcare center, where he was prescribed aspirin, rosuvastatin, clopidogrel, and controlled-release nitroglycerin. Subsequently, he was referred to our center for further evaluation and management. The patient reported a reduction in pain following the initial treatment at the local hospital, although he continued to experience pain during periods of heavy exertion. Due to the alleviation of symptoms, he was not transferred to our center immediately. Additionally, he experienced dyspnea on mild exertion. A comprehensive evaluation of his family history did not reveal any significant risk factors, and there was no history of substance abuse, including cocaine or alcohol, or regular caffeine intake. The patient denied any personal history of smoking but mentioned exposure to smoke from cooking oil. Furthermore, the patient reported regular consumption of saturated fatty acids in the form of fried foods.

Upon physical examination, the patient exhibited tachycardia and an upper limb sitting blood pressure of 90/60 mm Hg. Bilateral fine crackles were detected in the lower lung bases during auscultation, indicating Killip class II heart failure. The patient's BMI was 21.4 kg/m². Following admission from the outpatient department, an ECG demonstrated deep QS waves in leads V_1-V_4, accompanied by mild ST elevation, which was indicative of an evolved anterior wall MI (Fig. 1).

A comprehensive blood workup revealed several abnormalities, including an elevated homocysteine level of 28.52 µmol/L (reference range: 3.7–13.9 µmol/L), a vitamin B12 level of 996 pmol/L (reference range: 156–672 pmol/L), and an elevated lipoprotein(a) level of 105 mg/dL (reference range: < 20 mg/dL). Serum folate levels were within the normal range at 5 ng/mL (reference range: 2.5–20 ng/mL). The patient's lipid profile showed borderline abnormalities, with triglycerides at 131 mg/dL (reference range: < 150 mg/dL), low-density lipoprotein cholesterol at 101 mg/dL (reference range: < 100 mg/dL), high-

density lipoprotein cholesterol at 31 mg/dL (reference range: > 40 mg/dL), and total cholesterol at 158 mg/dL (reference range: < 200 mg/dL). High-sensitivity C-reactive protein was elevated at 5.47 mg/L (reference range: < 1 mg/L). Test results for syphilis, using the rapid plasma reagin (RPR) test, were negative. The patient subsequently underwent percutaneous angioplasty under optical coherence tomography (OCT) guidance. OCT imaging revealed a fibrous-atheromatous lesion in the proximal to mid-left anterior descending (LAD) artery, extending into the second diagonal branch (D2), with the presence of a red thrombus. A dense, lipid-rich plaque with underlying necrosis and calcification was observed at the ostium of the first diagonal branch (D1) (Fig. 2).

Under intravascular ultrasound (IVUS) guidance, a bifurcation stenting technique (V stenting) was performed at the proximal LAD and D1, while another drug-eluting stent was placed in the mid-LAD. Post-angioplasty, thrombolysis in myocardial infarction (TIMI) flow grade III was achieved, indicating successful revascularization (Fig. 3).

Following the procedure, the patient's ECG showed changes, with the evolution of deep QS complexes in the anterior leads and inverted T waves in leads V_3–V_4 (Fig. 4).

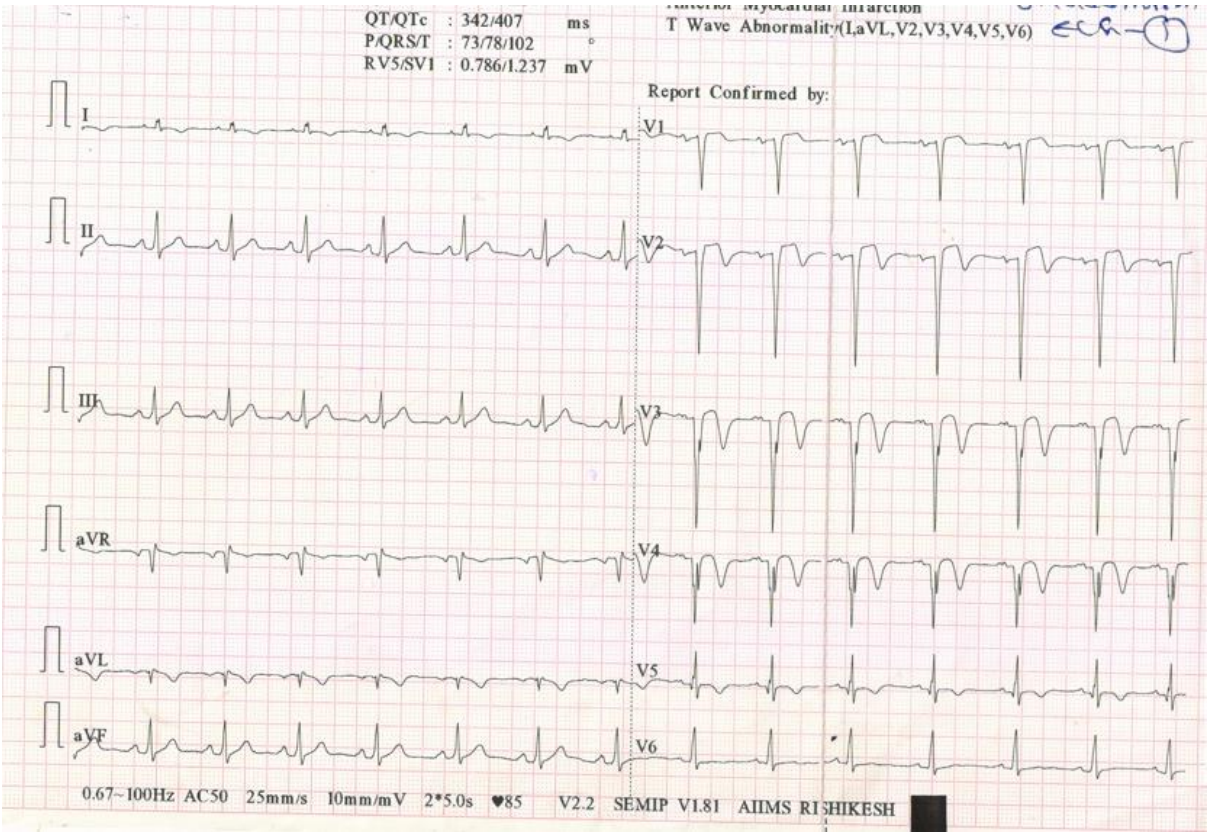
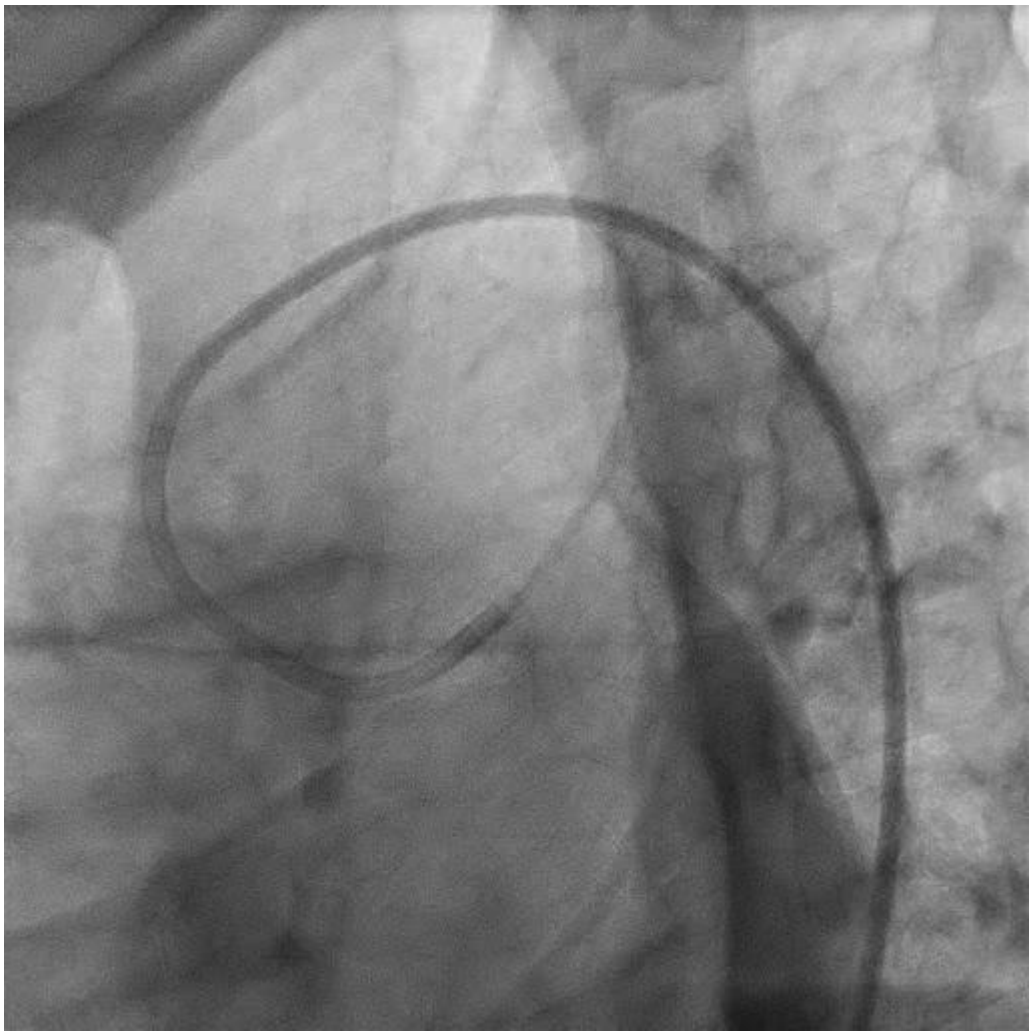


Figure 1: The patient's ECG demonstrated deep QS waves in leads V_1-V_4, accompanied by mild ST elevation, indicative of an evolved anterior wall myocardial infarction.



Video 1: The spider view angiography (left anterior oblique caudal view) reveals near-total discrete occlusion of the mid-LAD, alongside complete occlusion of the first diagonal (D1) branch characterized by a grade V thrombus and diffuse plaque in the proximal-to-mid LAD.

LAD: left anterior descending

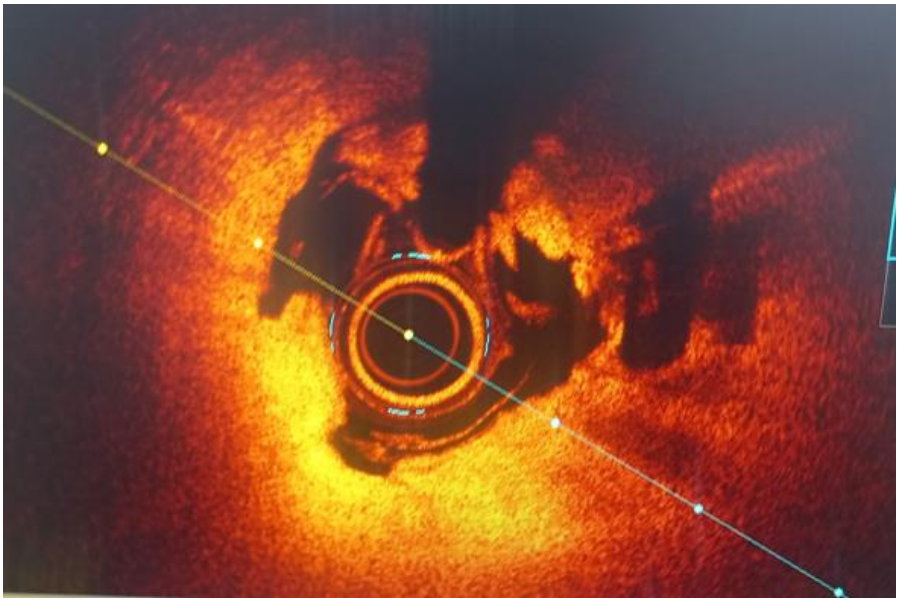
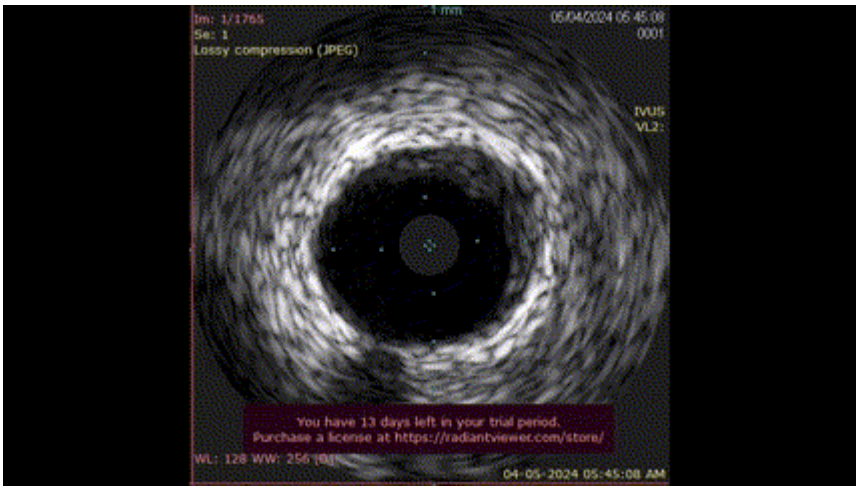


Figure 2: Optical coherence tomography imaging shows a fibrous-atheromatous lesion in the proximal to mid-left anterior descending artery, extending into the second diagonal branch (D2), with the presence of a red thrombus. A dense, lipid-rich plaque with underlying necrosis and calcification is observed at the ostium of the first diagonal branch (D1).



Video 2: The intravascular ultrasound clip shows a maximum plaque burden in the mid-left anterior descending artery after the first diagonal (D1) branch and a completely occluded D1.

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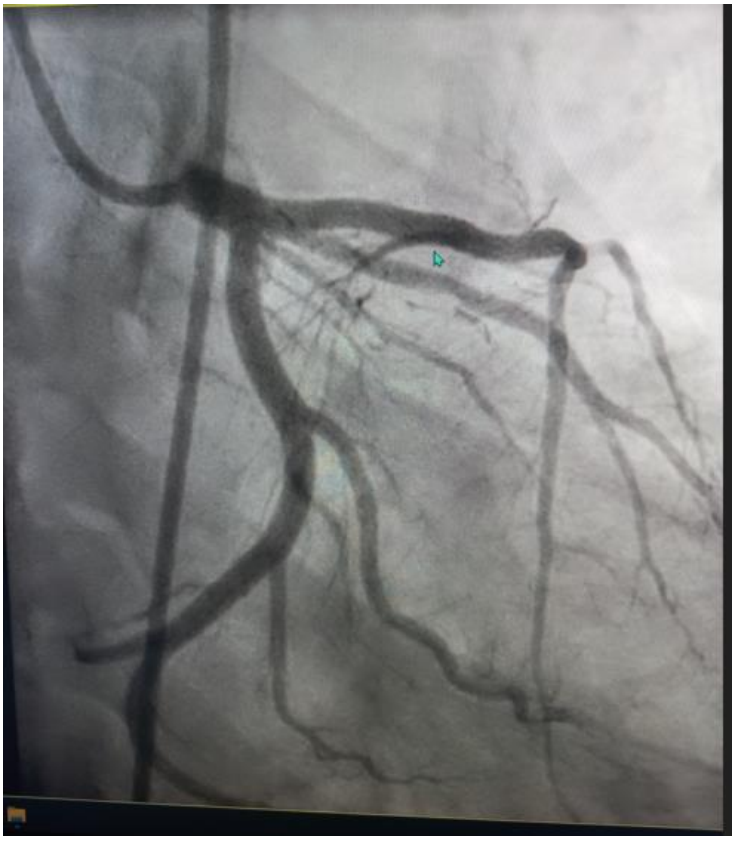

Figure 3: The image shows the patient's still angiogram in the right anterior oblique caudal view of a revascularized left anterior descending artery with a prominent first diagonal (D1) branch.

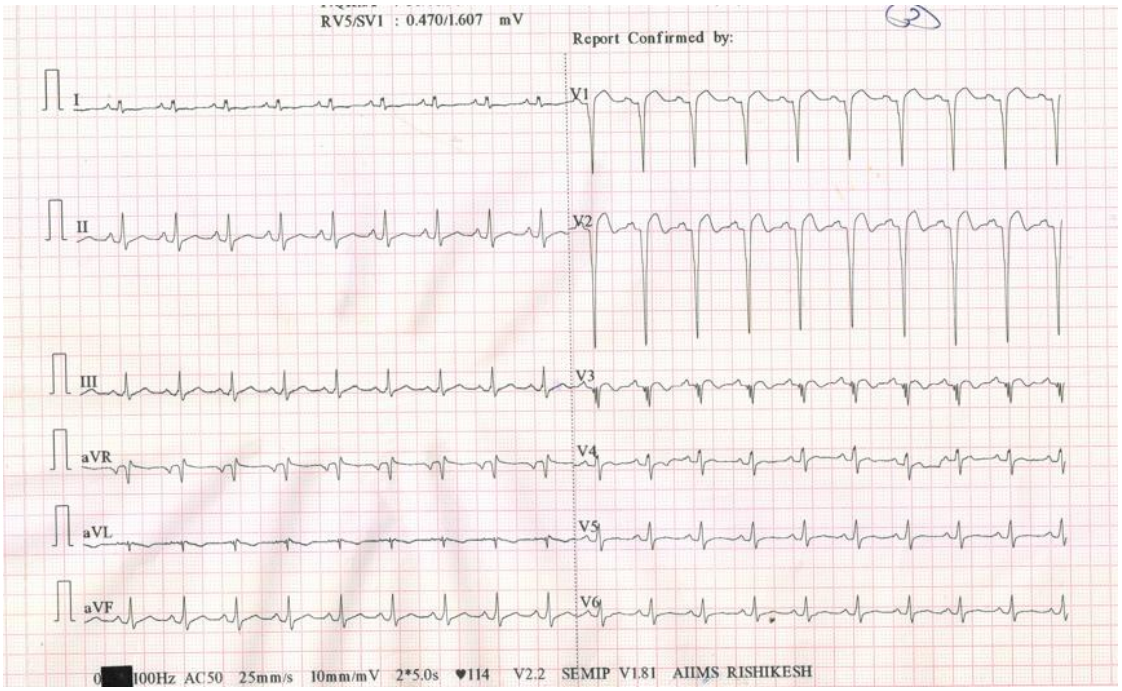

Figure 4: The patient's ECG shows changes, with the evolution of deep QS complexes in the anterior leads and inverted T waves in leads V_3–V_4.

The patient was initiated on dual antiplatelet therapy and prescribed a statin and ezetimibe for lipid management, as other lipid-lowering therapies were unaffordable. His financial constraints also precluded the performance of a genetic workup for hyperhomocysteinemia. Despite these limitations, he demonstrated symptomatic improvement following appropriate cardiovascular rehabilitation.

The patient was subsequently discharged and followed up after 2 weeks, showing further symptom relief and reduced dyspnea. The patient is scheduled for a re-evaluation of his lipid profile and lipoprotein(a) levels during future follow-up visits.

DISCUSSION

Elevated homocysteine levels and lipoprotein(a) have been recognized as risk factors associated with CAD. [3, 4] Lipoprotein(a) is considered the most prevalent monogenetic lipid disorder globally, with an estimated 1.4 billion individuals believed to have lipoprotein(a) levels exceeding 50 mg/dL. [5] Elevated lipoprotein(a) levels are associated with an increased risk of atherothrombosis, leading to a range of clinical presentations in patients. These manifestations may include stroke in younger individuals, ST–segment-elevation MI in young men, or calcific aortic valve disease in older adults. In the absence of conventional risk factors, Asian Indians have been shown to have extremely high prevalence rates of CAD. In migratory Asian Indians, elevated levels of lipoprotein (a) have been linked to premature CAD. [4] Still, there is a dearth of data on lipoprotein(a) in individuals with CAD from the Indian subcontinent.

Lipoprotein apheresis, PCSK inhibitors, and antisense oligonucleotides have demonstrated efficacy in managing elevated lipoprotein(a) levels. Nonetheless, these treatment options remain financially inaccessible for a majority of patients, necessitating the exploration of more affordable and accessible management strategies. Niacin presents a more cost-effective alternative for reducing lipoprotein(a) levels; however, its clinical efficacy in improving mortality outcomes remains inconclusive. Further, hormonal therapy in postmenopausal women has demonstrated the potential to decrease lipoprotein(a) levels and correct dyslipidemia, but further research is needed to establish its impact on cardiovascular outcomes and long-term benefits.

Lifestyle modifications, such as diet alterations and physical exercise, have shown remarkable benefits in mitigating the risk of CAD. Nevertheless, their effectiveness in managing elevated lipoprotein(a) remains limited. Interestingly, research suggests that among the various dietary approaches to stop hypertension (DASH) diets, one rich in unsaturated fatty acids is associated with a relatively lower increase in lipoprotein(a) levels than high-protein or carbohydrate-focused diets. [6]

Hyperhomocysteinemia is commonly caused by a combination of genetic factors, certain medications, impaired renal function, and deficiencies in B vitamins, particularly folic acid, vitamin B(6), and vitamin B(12). Elevated homocysteine levels contribute to the development and progression of atherosclerosis through multiple mechanisms, including increased oxidative stress, impaired endothelial function, and the promotion of thrombosis. Prospective studies have demonstrated a twofold increase in the risk of CVD and a modest increase in the risk of cerebrovascular disease in individuals with elevated plasma homocysteine concentrations. [7] Given that our patient’s folate and vitamin B12 levels were within normal range, it is likely that inherited hyperhomocysteinemia could be the underlying cause of his elevated homocysteine levels.

Although hyperhomocysteinemia is recognized as a risk factor for CVD, several studies have shown that reducing homocysteine levels through vitamin B12 and folate supplementation does not consistently translate into a reduced risk of CAD. [8] It is important to note that many of these studies were conducted in developed countries where folate deficiency is uncommon. On the other hand, certain studies in South Asian countries have suggested the potential benefits of folate supplementation in preventing stroke. [9] In South Asian populations, the onset of acute MI often occurs at a younger age compared with individuals from other regions. While CAD is typically observed in adults over 60, our patient likely has a genetic predisposition to hyperhomocysteinemia and elevated lipoprotein(a) levels, which may explain the development of severe CAD at a relatively young age, despite the absence of a significant family history of early-onset CAD.

In young patients presenting with CAD, routine investigations should encompass assessments of protein C and S levels, antiphospholipid antibody levels, and antithrombin deficiency to identify potential contributing factors and guide appropriate management strategies. However, conducting these evaluations was not feasible in our resource-limited setting.

Study Points

1. Elevated lipoprotein(a) levels and familial hyperhomocysteinemia may contribute to the development of ASCVD in young individuals, even in the absence of a family history of premature ASCVD.
2. In the Indian population, screening for these parameters is recommended, particularly when traditional risk factors are not present.
3. Raising awareness of CAD and its potential severity among the young population is crucial to promoting early detection, prevention, and management strategies.
4. Intracoronary imaging techniques play a valuable role in elucidating the pathophysiology of CAD and should be employed in cases of suspected CAD, especially in atypical patient populations.

Patient Perspective

Our patient expressed surprise upon learning of his condition, given his healthy lifestyle and the absence of a significant family history. Following appropriate cardiac rehabilitation, he experienced noticeable improvements in his symptoms. He returned to his usual occupation 2 weeks post-discharge and has since adopted a healthier diet to reduce the risk of future complications.

CONCLUSIONS

This case demonstrates that familial hyperhomocysteinemia and elevated lipoprotein(a) levels can contribute to severe CAD in otherwise healthy individuals, even when they maintain a healthy lifestyle. The presence of these traits should be considered when evaluating patients, particularly those with few or no traditional risk factors.

Declarations

Ethical Statement

The project received approval from the Departmental Ethics Committee, ensuring adherence to all relevant guidelines and regulations throughout the study process. Informed consent was collected from all subjects involved. Data collection followed the fundamental principles of good clinical practice and the Declaration of Helsinki.

Informed Consent

The patient provided informed consent for the use of his information in this case presentation.

Consent for Publication

All named authors have read and approved the manuscript, and no additional individuals meeting the authorship criteria have been excluded. The listed authors have also approved the author order presented in the manuscript. Furthermore, there are no objections regarding intellectual property or the timing of publication.

Data Availability Statement

The data supporting the findings of this study are not openly available due to sensitivity concerns but can be obtained from the corresponding author upon reasonable request. The data are stored in a controlled-access facility at the Cardiology Department of AIIMS Rishikesh.

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