Chronic Total Occlusion of the Left Main Coronary Artery in an HIV-Infected Patient

This article was published in the following Dove Press journal:
International Medical Case Reports Journal

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Abstract: Coronary artery disease (CAD) is amongst the leading causes of death in human immunodeficiency virus (HIV)-infected persons. Severe left main disease (LMD) occurs in approximately five percent of HIV-infected patients, with chronic total occlusion (CTO) of this vessel being an even rarer phenomenon. We describe a non-adherent HIV-infected patient with a left main coronary artery (LMCA) CTO that presented with heart failure with mildly reduced ejection fraction (HFrEF) and ventricular tachycardia (VT).

Keywords: left main coronary artery, LMCA, left main disease, LMD, chronic total occlusion, CTO, human immunodeficiency virus, HIV

Introduction

Coronary artery disease (CAD) is now amongst the leading causes of death in human immunodeficiency virus (HIV)-infected persons. This is principally ascribed to several factors such as increased longevity, antiretroviral therapy (ART)-induced dyslipidemias, and to the virion itself.^{1,2}

The pathophysiology of HIV-associated atherosclerosis includes endothelial dysfunction, thrombophilia, and conventional cardiovascular disease risk factors.³ It may also be accentuated by co-incident drug abuse, HIV-associated comorbidities, opportunistic infections, and renal dysfunction.⁴ In the HIV-infected subpopulation, the prevalence of severe left main disease (LMD) is approximately five percent as demonstrated in several studies with CTO being even less common.^{5,6}

We describe a non-adherent HIV-infected patient with a left main coronary artery (LMCA) CTO that presented with heart failure with mildly reduced ejection fraction (HFrEF) and ventricular tachycardia (VT).

Case Report

A forty-two-year-old South Asian male with HIV for approximately two years, presently non-adherent to his antiretroviral therapy (ART) of Atripla® (efavirenz, emtricitabine, and tenofovir) for the preceding month, presented to the emergency department with presyncope. His vital signs indicated systolic blood pressures of 94 mm Hg, heart rate of 163/min, respiratory rate of 32 breaths/min with an oxygen saturation of 94% on room air. His physical examination revealed an appropriate mental orientation with an elevated jugular venous pulse at 12 cm H₂O, grade three holosystolic apical murmur, bilateral mid-zone lung crackles, and generalized anasarca.

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Figure 1 The patient's electrocardiogram indicates a wide complex tachycardia (WCT) and atrioventricular dissociation suggestive of ventricular tachycardia. The black arrows indicated the prolonged QRS duration, intrinsicoid deflection, and the red lines underscore the regular WCT.

A 12-lead electrocardiogram (ECG) revealed ventricular tachycardia with atrioventricular dissociation and QRS concordance (see [Figure 1](#)). A chest radiograph revealed pulmonary edema with Kerley B lines, hilar congestion, and cephalization, while a bedside two-dimensional transthoracic echocardiogram demonstrated mild global hypokinesis with an estimated left ventricular ejection fraction of 45% and mild central mitral regurgitation. Pertinent diagnostic laboratory investigations included a d-dimer 121 ng/dL (normal ≤ 500 ng/mL), N-terminal-pro-brain natriuretic peptide 2257 pg/mL (normal ≤ 300 pg/mL), CK-MB 8 U/L (normal < 20 U/L), troponin I 0.88 ng/mL (normal < 0.15 ng/mL). Other routine investigations are indicated in [Table 1](#). The patient's arterial blood gas was consistent with mild hypoxia on 40% fractional inspiration of oxygen with an estimated alveolar-arterial gradient (A-a gradient) of 34 mm Hg.

He was initiated on amiodarone and furosemide infusion. His VT quickly reverted to normal sinus rhythm with an intraventricular conduction delay and secondary ST-T changes, and he was subsequently admitted to the cardiac care unit for further hospitalization. During the ensuing hospitalization, he was continued on an amiodarone infusion at one milligram per minute with hemodynamic improvement. He was commenced on an optimal guideline-directed,

cardiovascular regimen including dual antiplatelet therapy of aspirin and ticagrelor, neurohormonal inhibition of angiotensin-receptor neprilysin inhibitor, beta-blocker, mineralocorticoid receptor antagonist, moderate-intensity statin, and furosemide. He was also re-initiated with ART with Atripla® (efavirenz, emtricitabine, and tenofovir), for which he was intermittently adherent since his index diagnosis and non-compliant prior to this hospitalization. This single table regimen ART ("polypill") was selected as it was widely available in our limited resource setting.

The patient subsequently underwent several testing modalities, which included a cardiac catheterization that indicated a chronic total occlusion of the LMCA and robust collaterals from the right coronary artery (RCA) to the left anterior descending (LAD) and left circumflex arteries (LCx) (see [Supplementary Video 1](#)). A cardiac computed tomography angiogram (CCTA) was performed to assess the occluded LMCA and also revealed mild luminal irregularities of the other coronary arteries and a calcium score of zero (see [Figure 2](#)). Cardiac magnetic resonance imaging (cMRI) affirmed the bedside transthoracic findings and suggested myocardial viability (see [Figure 3](#)). The remainder of his one-week hospital course was uneventful, and he was subsequently discharged against medical advice (patient

Table I Routine Investigations

Tests Performed	Result	Reference Range
Complete Blood Count		
Hemoglobin (Hb)	9.7 g/dL	14.0–17.5 g/dL
White cell count (WCC)	$6.3 \times 10^9/L$	$4.5–11.0 \times 10^9/L$
Platelet count	$153 \times 10^3/\mu L$	$156–373 \times 10^3/\mu L$
Comprehensive Metabolic Panel		
Serum sodium	134 mmol/L	135–145 mmol/L
Serum potassium	3.7 mmol/L	3.5–5.1 mmol/L
Serum bicarbonate	24 mmol/L	22–26 mmol/L
Serum creatinine (Cr)	0.6 mg/dL	0.5–1.2 mg/dL
Blood urea nitrogen (BUN)	12 mg/dL	3–20 mg/dL
Alanine aminotransferase (ALT)	43 IU/L	20–60 IU/L
Aspartate aminotransferase (AST)	89 IU/L	5–40 IU/L
Total bilirubin	1.2 mg/dL	0.2–1.2 mg/dL
Alkaline phosphatase (ALP)	143 IU/L	40–129 IU/L
Albumin	3.2 g/dL	3.5–5.5 g/dL
Albumin-corrected calcium	10.2 mg/dL	9.6–11.2 mg/dL
Magnesium	1.8 mg/dL	1.6–2.3 mg/dL
Phosphorous	3.3 mg/dL	2.5–6.5 mg/dL
Fasting blood sugar	94 mg/dL	60–120 mg/dL
Infectious Disease Panel		
Blood cultures	Negative	Positive or negative
Urine culture	Negative	Positive or negative
Cluster of differentiation 4 (CD4) count	623 cells/mm ³	500–1500 cells/mm ³
Human immunodeficiency virus ribonucleic acid (HIV RNA)	14 RNA copies/ μL	< 20 RNA copies/ μL
Cardiac Profile		
Glycosylated hemoglobin	5.7%	4.3–6.5%
Fasting lipid panel		
Cholesterol	142 mg/dL	170–200 mg/dL
Triglycerides	134 mg/dL	40–150 mg/dL
High-density lipoprotein	48 mg/dL	40–60 mg/dL
Low-density lipoprotein	68 mg/dL	60–130 mg/dL
Thyroid-stimulating hormone	2.87 mU/L	0.5–5.0 mU/L
Erythrocyte sedimentation rate (ESR)	34 mm/h	0–22 mm/h
High sensitivity C-reactive protein (hsCRP)	2.4 mg/dL	0.0–1.0 mg/dL
D-dimer	121 ng/mL	< 500 ng/mL
N-terminal-pro-brain natriuretic peptide (proBNP)	2257 pg/mL	≤ 300 pg/mL
Creatine kinase (CK)	167 U/L	30–170 U/L
Creatine kinase MB (CK-MB)	8 U/L	< 20 U/L
Lactate dehydrogenase (LDH)	533 U/L	313–618 U/L
High sensitivity troponin I (hsTnI)	0.88 ng/mL	0.0–0.15 ng/mL

preference) with a follow-up visit one week to discuss revascularization strategies, including coronary artery bypass grafting (CABG) and possible implantable cardioverter-defibrillator (ICD) device therapy. The patient defaulted for the following appointment and subsequently declined surgery and device therapy (invasive options) when contacted via telephone. A surveillance echocardiogram three months

later revealed near-normalization of his ejection fraction to 50%, and he reported complete cardiovascular medication and ART adherence.

Discussion

The prevalence of significant LMD in HIV-infected patients is approximately five percent, which is similar to

Figure 2 The patient's cardiac computed tomography angiography cross-sectional view illustrating the absence of the left main coronary artery (encircled in red) with the retrograde opacified left anterior descending (LAD), circumflex arteries (LCx) with their sub-branches, diagonal (D) and obtuse marginal (OM) (labeled).

Figure 3 The patient's cardiac magnetic resonance angiography short-axis view displaying spontaneous echo contrast (encircled in red) suggestive of the depressed left ventricular function.

their non-infected counterparts.^{5,6} Although coronary artery severity is variable with studies suggesting single-vessel involvement, while others display multivessel disease (MVD) when the LM is involved, the latter is more angiographically apparent.⁷ Our patient incurred a LMCA CTO, however, displayed mild, non-obstructive coronary artery disease in the other vessels, namely the RCA, LAD, and LCx. CTO of the LMCA is exceedingly rare (0.04%) and contingent on a right-dominant circulation with robust collateralization to the left coronary arteries.^{8,9} The

predominant etiology is usually atherosclerosis; however, radiation therapy, infectious, immunologic, and iatrogenic causes may precipitate the LM CTO. Most of these patients present with typical angina or heart failure symptomatology with a prior ACS, and only a minority are asymptomatic.¹⁰ The LM distal bifurcation is usually the most involved site, followed by the ostium and then mid-shaft. Ostial occlusion tends to occur more frequently in women, as well as younger patients with fewer traditional cardiovascular disease risk factors.¹¹ Our middle-aged male patient displayed an ostial occlusion, albeit with HIV and non-adherence, known risk factors for atherosclerosis. Patients with either a mildly depressed or preserved left ventricular function usually possess normal RCA and distal left vessels as displayed in our patient. Collaterals are integral in preserving systolic function; however, it may not preclude anginal symptoms that our patient did not exhibit.¹² The LMCA perfuses almost the entire myocardium in a left-dominant circulation. As a result, an abrupt index occlusion is usually associated with acute, fulminant infarction, with cardiogenic shock and possibly sudden cardiac death as the anticipated clinical trajectory.¹³ Our patient's index presentation was that of presyncope and ventricular tachycardia. He did not report any preexisting typical angina nor present with a prior acute coronary syndrome as aforementioned that

would be expected with this lesion. We postulate the lack of classical symptoms to a possible ART-induced neuropathy (non-adherence) with an oligosymptomatic presentation or the development of an acute, robust coronary collateral network which can confer an anti-ischemic myocardial effect.^{14–16}

With the advent of ART, there has been a transitional shift in mortality from opportunistic infections to HIV-associated vascular disease, now presiding as the leading cause of mortality amongst these patients.¹⁷ HIV infection, with its complex proinflammatory milieu, can impel atherogenesis. A pivotal mechanism involves intracellular oxidative and endoplasmic reticulum stress with the resultant formation of the inflammasome, and currently, there is a hotbed of research exploring other potential pathways. Additionally, specific pathological features of HIV-associated coronary artery disease include non-calcified, inflammatory plaques that are more susceptible to rupture and thrombus formation with sequelae of major adverse cardiovascular events.¹⁸ In patients with relatively controlled HIV infection, studies also allude to subclinical disease with a more significant plaque burden as compared to matched, non-infected patients.¹⁹ Our patient's CCTA alluded to a calcium score of 0, and paradoxically for his self-reported intermittent ART non-adherence, his HIV parameters were well regulated.

CABG is considered the treatment of choice for LMCA CTO.²⁰ Two studies in the HIV-infected population have alluded to near-equivalent short- and long-term prognosis with CABG as compared to non-infected patients.^{21,22} However, in an unprotected LMCA subgroup of a recent case series, technical and procedural success rates were approximating 80%.²³ After consultation with the heart team, CABG was considered the preferred revascularization strategy in this limited resource setting as the cardiac catheterization laboratory did not have an experienced CTO operator with the requisite imaging and interventional armamentarium to achieve successful recanalization confidently.

In the interim, the patient's HFrEF improved significantly to near-euvolemic state on his neurohormonal cardiovascular regimen. The cardiovascular team was cognizant of potential bleeding complications in an HIV-infected patient with anemia and borderline thrombocytopenia.³ Drug-drug interactions were also considered as several pharmacotherapies that share a central pathway of metabolism.³ Although HIV and ART are associated with elevated CVD risk, results from studies suggest that continuous HIV suppression attenuates this as opposed to drug interruption.²⁴ A high level of adherence

to ART is a principal predictor for the success of HIV treatment.²⁵ Studies indicate that high levels of adherence are necessary for viral suppression, prevention of resistance, and disease progression.²⁶ Patients' adherence to HIV medication is 5% higher than adherence to cardiovascular disease (CVD) medication.²⁷ As a result, we have attempted to minimize polypharmacy with both the patient's ART and CVD regimens.

In summary, there are several crucial issues to consider in our patient, namely the insidious clinical presentation and management of LMCA CTO in an HIV-infected patient. It is also essential to further define the clinical features and characteristics of LMCAD in such a high-risk subpopulation.

Conclusion

We describe a non-adherent HIV-infected patient with a left main coronary artery (LMCA) chronic total occlusion (CTO) that presented with heart failure with mildly reduced ejection fraction (HFrEF) and ventricular tachycardia (VT). The cardiovascular disease team should be aware of HIV implicating chronic coronary syndromes with a subtle index presentation with severe LMCAD.

Abbreviations

CAD, coronary artery disease; HIV, human immunodeficiency virus; LMD, left main disease; LMCA, left main coronary artery; CTO, chronic total occlusion; HFrEF, heart failure with mildly reduced ejection fraction; VT, ventricular tachycardia.

Data Sharing Statement

All available data can be obtained by contacting the corresponding author.

Compliance with Ethics Guidelines and Standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent

The patient has provided both verbal and written informed consent to have the details of his case published. Institutional approval was not required for publication.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

There is no funding to report.

Disclosure

The authors declare they have no competing interests, and there are no financial disclosures.

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