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CASE REPORT

INTERMEDIATE

CLINICAL CASE

Eosinophilic Granulomatosis With Polyangiitis Presenting as an Acute Coronary Syndrome

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ABSTRACT

Eosinophilic granulomatosis with polyangiitis, formerly Churg-Strauss Syndrome, is an uncommon disorder that carries a high mortality when coronary artery disease develops. Early recognition and treatment is crucial. We highlight an unusual presentation of acute coronary syndrome not associated with atherosclerotic coronary disease. (**Level of Difficulty: Intermediate.**) (J Am Coll Cardiol Case Rep 2020;2:1062–5) © 2020 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

A 39-year-old Senegalese man presented with chest pain and dyspnea after an acute ST-segment elevation myocardial infarction (STEMI) 2 weeks earlier. Previous coronary angiography (CA) showed multivessel disease with a 99% proximal left anterior descending (LAD) artery lesion and high-grade stenosis of the left circumflex (LCx), obtuse marginal (OM1), posterior-descending artery (PDA), and right-posterior lateral branch (R-PLB). Coronary artery bypass grafting (CABG) was recommended, but the patient opted for a second opinion. In the interim, he was medically managed, including with subcutaneous injections of enoxaparin. On arrival, he complained of ongoing chest pain requiring a nitroglycerin infusion. Review of systems included orthopnea, dyspnea on exertion, and 1 year of unintentional weight loss. Physical examination revealed bibasilar rales and lower-extremity pitting edema.

LEARNING OBJECTIVES

- To consider the differential of eosinophilia.
- To appreciate that coronary vasculitis can present as an acute coronary syndrome much like atherosclerotic disease.
- To maintain a broad differential for premature coronary artery disease.

PAST MEDICAL HISTORY

The patient's medical history included hypertension, type 2 diabetes mellitus, hyperlipidemia, and childhood asthma.

INVESTIGATIONS

Admission electrocardiogram showed anterolateral ischemia (Figure 1). Echocardiography demonstrated

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a depressed ejection fraction (25% to 30%) with anteroapical hypokinesis. Serum troponin levels peaked at 1.34 ng/ml (normal <0.49 ng/ml), and a complete blood count (CBC) showed absolute eosinophilia of 1.6 10^3/μl (normal <0.7 10^3/μl). Erythrocyte sedimentation rate (ESR) was elevated to 75 mm/h (normal <15 mm/h) with a C-reactive protein (CRP) of 0.2 μg/ml (normal <0.3 μg/ml). Antineutrophilic cytoplasmic antibodies (ANCA) titers and results of antimyeloperoxidase and antiproteinase 3 antibodies were negative, with normal urinalysis test results. Chest computed tomography (CT) demonstrated perihilar and peri-bronchial consolidation. Cardiothoracic surgery was consulted for revascularization, but the patient was deemed a poor surgical candidate because of concerns regarding active pulmonary infection. The patient received salvage therapy with drug-eluting stenting (DES) to the proximal LAD, LCx, and OM1 (**Figure 1**). Because of the presence of pulmonary infiltrates and endemic infections in his home country of Senegal, a broad infectious work-up for tuberculosis, invasive fungal disease, HIV, opportunistic infection, and parasitic infections was completed, the results of which were negative.

Two months later, he presented with non-ST-segment elevation myocardial infarction (NSTEMI) and persistent eosinophilia of 1.6 10^3/μl. His pulmonary infiltrates had resolved (**Figure 2**). He was urgently taken for CA and received DES to the RCA and R-PLB. One month later, he had another NSTEMI, complicated by hemodynamic instability with engagement of the left main coronary artery (LMCA) during CA, requiring placement of an intra-aortic balloon pump (IABP). The possibility of eosinophilic granulomatosis with polyangiitis (EGPA) involving the coronary arteries was broached, given the patient's eosinophilia, negative infectious work-up, and repeated coronary events.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of coronary artery disease includes acute thrombotic plaque rupture, embolism, vasospasm, myocardial bridging, spontaneous coronary artery dissection, myocarditis, and vasculitis.

MANAGEMENT

The case was reviewed using a multidisciplinary team approach including cardiology, cardiac surgery, infectious disease, and rheumatology. Given the patient's ischemic burden and hemodynamic instability requiring IABP, the decision was made to revascularize with CABG. Because of a suspected uncontrolled systemic inflammatory disorder, evaluation for heart transplantation was not pursued. Intraoperative right upper-lobe and left internal mammary artery biopsies were obtained, which demonstrated prominent extravascular eosinophilic infiltrate consistent with EGPA (**Figure 2**). Because of concern for loss of graft patency, the patient received high-dose prednisone and guideline-directed cardiac medical therapy post-operatively. On discharge, he was prescribed mepolizumab.

DISCUSSION

The American College of Rheumatology defines EGPA using 6 criteria: asthma, eosinophilia >10% on CBC, neuropathy, migratory pulmonary infiltrates, paranasal sinus abnormality, and extravascular eosinophils on biopsy (1,2). Using 4 of 6 criteria yields a sensitivity of 85% and specificity of 99.7% (1). Our patient presented with migratory pulmonary infiltrates, a history of asthma, peripheral eosinophilia, and biopsy-proven eosinophilic pleuritis and arteritis (**Figure 2**). Taken in context, his recurrent myocardial infarction was caused by coronary vasculitis secondary to EGPA. Patients with EGPA coronary involvement can present with vasospasm, diffuse multivessel disease, or without a definable acute lesion (3,4); however, this is the first case of hemodynamic instability requiring mechanical support.

The international incidence and prevalence of EGPA is rare, with approximately 0.5 to 4.2 and 11 to 14 cases per million, respectively (5). Epidemiologic data have not demonstrated a relationship between gender, ethnicity, or inheritance (5). Host immunogenetic factors and environmental exposures may play a role in triggering EGPA; there are reports linking leukotriene receptor antagonists, macrolide antibiotics, and silica particulates, although exact mechanisms remain poorly understood (5).

In a cross-sectional analysis of multicenter clinical trials in Europe, positive ANCA titers were found in 38% of patients and associated with a small-vessel vasculitis presentation, affecting the nerves and glomerulus (6). Our patient had normal renal function, no neuropathy, normal urinalysis, and negative ANCA titers, suggesting a separate subtype of EGPA. The ANCA-negative subtype of EGPA is driven by eosinophilic infiltration with cardiopulmonary predominance and accounts for 62% of all cases (6).

EGPA therapy is governed by the degree of organ involvement at presentation; the Five Factor Score (7)

ABBREVIATIONS AND ACRONYMS

ANCA = antineutrophilic cytoplasmic antibody

CA = coronary angiograph

CABG = coronary artery bypass graft

CRP = C-reactive protein

DES = drug-eluting stent

EGPA = eosinophilic granulomatosis with polyangiitis

ESR = erythrocyte sedimentation rate

LAD = left anterior descending artery

LCx = left circumflex artery

LMCA = left main coronary artery

OM1 = obtuse marginal artery

RCA = right coronary artery

R-PLB = right posterior-lateral branch

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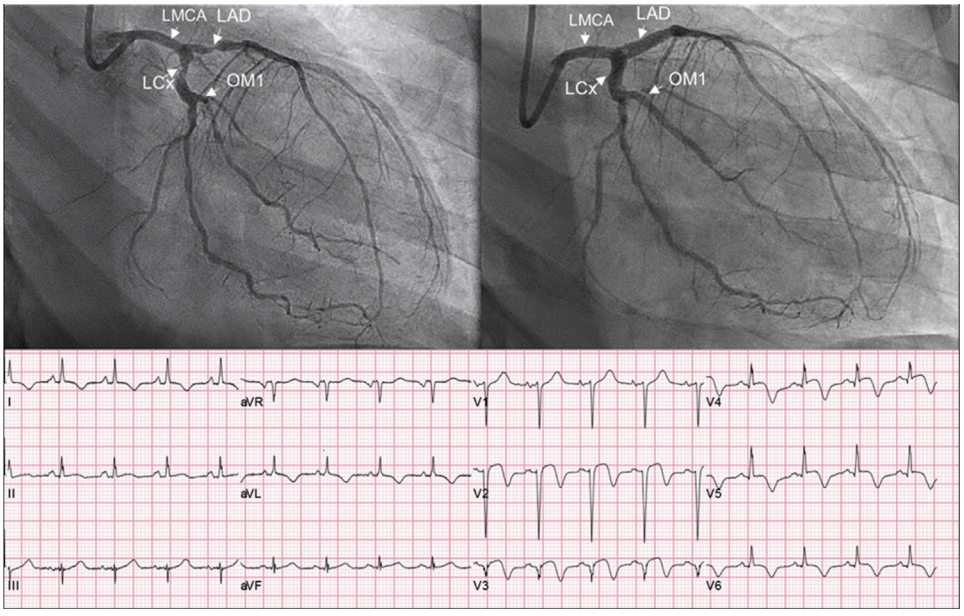
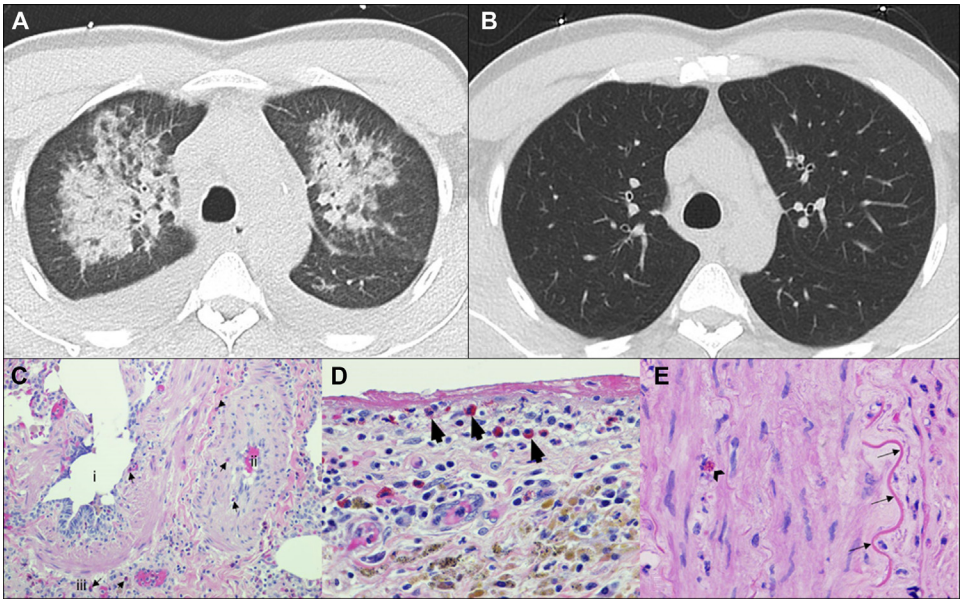
FIGURE 1 Coronary Angiography and Electrocardiogram on Admission



Significant stenosis of the proximal LAD, LCx, and OM1 were present. Electrocardiogram **(bottom)** shows anterolateral ST-segment elevations, lateral T-wave inversions, and Q waves through the anterior precordium. Angiography post-stenting **(top, right)** of the LAD, LCx, and OM1 with resolution of stenosis and flow. LAD = left anterior descending; LCx = left circumflex artery; OM1 = obtuse marginal artery.

FIGURE 2 Computed Tomography



CT image during first admission **(A)** demonstrating diffuse infiltrates, which are resolved on second admission **(B)**. Right upper lung wedge biopsy during second admission **(C)** showing eosinophilic infiltrate **(arrows)** with respiratory bronchiole **(i)**, pulmonary artery **(ii)**, and pulmonary parenchyma **(iii)**. Wedge biopsy showing abundant fibrinous eosinophilic pleuritis **(arrows) (D)**. Left internal mammary artery biopsy **(E)** with eosinophil **(chevron)** infiltrating the media. Lamina propria of the vessel intima on far right **(arrows)**.

is recommended for determining severity in each patient. Mild presentations can be treated with high-dose glucocorticoids, whereas more severe presentations may require steroids and an immunomodulator (8–10). Typical regimens include prednisone at 1 mg/kg with adjunctive therapy of either cyclophosphamide or rituximab (8–11). The use of immunomodulatory therapy has been reported to induce EGPA coronary vasculitis remission (3,4); however, as our patient had already suffered multiple ischemic insults with hemodynamic instability, a more urgent solution was required. Remission is maintained with steroids or steroid-sparing agents; mepolizumab, an anti-ILF immunomodulator, has recently gained FDA approval for relapsing EGPA (12).

FOLLOW-UP

The patient has been free of chest pain following surgery. Continued treatment with high-dose steroids and immunomodulators has induced clinical remission.

CONCLUSIONS

The presence of eosinophilia with the initial CT scan findings and endemic nature of parasitic infections in Senegal prompted an extensive infectious work-up that delayed diagnosis. At the time EGPA was considered, the patient was in cardiac extremis and required urgent surgical revascularization. Our case highlights the need to maintain a high index of clinical suspicion when laboratory values are incongruent with typical patient presentations.

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