Heart failure with reduced ejection fraction due to polycythemia vera

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Abstract

Polycythemia vera is a rare hematological disorder that can cause heart failure with reduced ejection fraction from chronic micro-vascular ischemia. Appropriately recognizing the underlying cause of cardiomyopathy is essential to decrease morbidity and mortality. Patients can present with elevated troponin level and have patent epicardial coronary arteries on coronary angiogram, hence presenting a diagnostic challenge for health care professionals. Furthermore, the presentation can mimic myocarditis. Herein, we report a case of a 61-year-old female who presented with heart failure due to microvascular thrombotic complication associated with polycythemia vera. Laboratory investigation and coronary angiogram were inconclusive. A high degree of clinical suspicion and utilizing non-invasive techniques, such as cardiac imaging, can describe myocardial pathology and aid with the diagnosis.

INTRODUCTION

The prevalence of heart failure in the United States continues to increase with 6.5 million cases reported in 2019 [1]. Patients with idiopathic cardiomyopathy have poorer outcomes as compared to those with a known cause. Therefore, a thorough workup of the underlying etiology of heart failure should be performed [2] to ensure appropriate therapy and a favorable outcome. Herein, we report a case of microvascular ischemia causing heart failure with reduced ejection fraction in a patient with polycythemia vera, a chronic myeloproliferative disorder that causes increased platelet, granulocyte and erythrocyte levels.

CASE REPORT

A 61-year-old female presented to the emergency room with intermittent chest pain and shortness of breath for the past one week. She described moderate-intensity, non-radiating chest pressure, that was associated with fatigue. Paramedics gave her aspirin 324 mg en-route to the emergency room, resulting in transient symptom relief. She did not relate any exacerbating factors. On arrival, her blood pressure was 107/57 mm Hg, pulse was 68 beats/minute. Cardiovascular exam revealed a regular rate and rhythm with no audible cardiac murmur. There was no jugular venous distention. Chest pain was not reproducible on palpation. No lower extremity edema present.

The patient had a history of polycythemia vera (JAK2-positive) treated with phlebotomy, hypertension and chronic kidney disease stage 3. She had a similar episode of chest pain eight months ago, diagnosed as myocarditis, wherein she was discharged on colchicine 0.6 mg daily. Since then, she presented to the emergency room twice for recurring intermittent chest pain episodes, diagnosed as recurrent myocarditis. She was a former smoker with 16 pack-years and had quit >10 years ago.
Figure 1: Electrocardiogram on presentation showing no acute ST-T wave elevation or depression.

Table 1: Laboratory investigation during hospitalization

| Measured             | Normal range |
|----------------------|--------------|
| Hb (gm/dl)           | 13.5         |
|                      | 11.7–15.5    |
| Hct (%)              | 47.8         |
|                      | 35–45        |
| Platelets (thousand/ul) | 583         |
|                      | 140–400      |
| BUN (mg/dl)          | 40           |
|                      | 9.8–20.1     |
| Creatinine (mg/dl)   | 1.7          |
|                      | 0.30–1.5     |
| GFR (ml/min/m²)      | 31           |
|                      | >60          |
| Troponin I (ng/ml)   | 11.06        |
|                      | 0–0.02       |
| BNP (pg/ml)          | 2456         |
|                      | <100         |
| CRP (mg/dl)          | 2.17         |
|                      | 0–0.50       |
| Ferritin (ng/ml)     | 10.24        |
|                      | 5–204        |
| ESR (mm/hr)          | 1            |
|                      | 0–20         |
| DS DNA (IU/ml)       | 21.8         |
|                      | 0–200        |
| ANCA                 | <1:20        |
|                      | <1:20        |
| C3 complement (mg/dl)| 104          |
|                      | 83–193       |
| C4 complement (mg/dl)| 24.5         |
|                      | 15–57        |
| IL-6 (pg/dl)         | <2           |
|                      | <2           |
| SPEP (g/dl)          | 5.7          |
|                      | 6.1–8.1      |
| Immunofixation urine | No monoclonal|
|                      | proteins detected |

ANCA, anti-neutrophil cytoplasmic antibody; GFR, glomerular filtration rate; SPEP, serum protein electrophoresis.

Complete blood count showed hemoglobin (Hb) of 13.5 gm/dl, hematocrit (Hct) 45.1% and platelet count of 397 000/mcL. Blood urea nitrogen (BUN) was 40 mg/dl (range: 9.8–20.1 mg/dl) and creatinine 1.7 mg/dl (range: 0.30–1.50 mg/dl). Troponin significantly elevated at 11.06 ng/ml (range: 0.00–0.02 ng/ml) and B-type natriuretic peptide concentration (BNP) 2232 pg/ml (range: 0.00–100 pg/ml). Her c-reactive protein (CRP) was 2.17 mg/dl (range: 0.00–0.50 mg/dl). Electrocardiogram (Fig. 1) showed sinus rhythm with no acute ST-T wave elevation or depression. Chest x-ray findings were consistent with cardiomegaly with no hilar lymphadenopathy. Ejection fraction on transthoracic echocardiogram was 35% with apical-lateral hypokinesis and increased left ventricular cavity size. Her ejection fraction eight months ago was 55%.

Patient was started on low-weight molecular heparin. She underwent coronary angiography, which did not show any significant coronary artery disease or spontaneous coronary artery dissection. As she was previously presumed to have myocarditis, her respiratory viral panel was checked for adenovirus, SARS-COV-2, coxsackieviruses, which were all negative. Additional investigation was performed to identify the etiology of her cardiomyopathy. Urine protein electrophoresis did not show a monoclonal or polyclonal pattern. Serum iron and ferritin levels were normal. Autoimmune and inflammatory markers, antinuclear antibody, anti-neutrophil cytoplasmic autoantibody, complement level, erythrocyte sedimentation rate (ESR), and interleukin-6 (IL-6) level were all within normal range (Table 1). Her BUN was 40 mg/dl, not elevated enough to
Given her history of polycythemia vera with persistently elevated troponin level, and chest pain relieved with aspirin, there was suspicion for microvascular ischemia. Due to chronic kidney disease, she had cardiac magnetic resonance (CMR) imaging without contrast during the prior admission, which was inconclusive. The patient was hesitant to undergo invasive endomyocardial biopsy. Therefore, CMR with contrast was ordered after an informed decision was made with the patient and her nephrologist. Patient underwent CMR with contrast, which confirmed microvascular ischemia with areas of first-pass subendocardial perfusion defects and additional areas of <50% subendocardial late-gadolinium enhancement extending from the left ventricular base to apex (Fig. 2).

In addition to carvedilol, aspirin 81 mg daily and clopidogrel 75 mg were initiated on Day 3 for treatment of microvascular ischemia. Her chest pain had completely resolved. Troponin level and BNP rapidly decreased to 1.97 ng/ml and 309 pg/ml on discharge, respectively (Fig. 3). At 1-week follow-up, the patient reported no new episodes of chest pain. Troponin level was 0.07 ng/ml and CRP level was 0.31 mg/dl.

**DISCUSSION**

Polycythemia vera is associated with acute coronary syndromes [3]. However, polycythemia vera causing heart failure with reduced ejection fraction from chronic microvascular ischemia is rarely described. Previously, few cases of heart failure resulting from polycythemia-induced chronic coronary microvascular ischemia have been reported that were confirmed with CMR [4] and endomyocardial biopsy [5], and one case was diagnosed by causal association after other etiologies were excluded [6].

Patients with polycythemia vera are at high risk for arterial and venous thrombosis. This is due to hyperviscosity and slow blood flow from erythrocytosis and abnormal expression of platelet membrane glycoprotein. As a result, there is increased platelet-vascular interaction, especially in areas where there is excessive shear rate such as in arterioles and capillaries [3].
In addition to these risk factors, age >60 years, history of hypertension and smoking, JAK2-positive mutation, Hct of 45.1% and elevated CRP level are all risk factors for thrombosis [7–9] (Fig. 4). To prevent cardiovascular thrombotic complications associated with polycythemia vera, low-dose aspirin [10] and goal Hct of <45% has shown to decrease mortality and major thrombosis [7]. Since the patient had multiple risk factors for thrombosis associated with polycythemia vera, she was treated with dual antiplatelet therapy.

In conclusion, the utilization of non-invasive techniques, such as cardiac imaging, can be valuable in describing myocardial pathology and aiding with diagnosis. Patient’s comorbidities can influence diagnostic testing; nonetheless, establishing a multidisciplinary approach with shared decision-making can help correctly diagnose this rare condition.

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CONFLICT OF INTEREST STATEMENT
None to declare.

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ETHICAL APPROVAL
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CONSENT
Informed consent was obtained from the patient.

GUARANTOR
Bernard Kim, MD.

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