Case Series

Primary polycythaemia: A neglected risk factor

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Abstract

In this case series, we report a 32-year-old male patient with myocardial infarction and 45-year-old female with portal vein thrombosis with splenic infarcts, which were the initial manifestations of polycythaemia vera. The awareness of myeloproliferative disorders as a possible underlying disease—especially in young patients presenting with myocardial infarction and portal venous thrombosis—is crucial for clinical management, as a missed diagnosis can worsen the patients' further prognosis.

Keywords: Hydroxyurea, myocardial infarction, phlebotomy, polycythaemia vera

Introduction

Myeloproliferative disorders, such as polycythaemia vera and essential thrombocytopenia, involve multipotent hematopoietic progenitor cell which causes in general an increased red cell, granulocytes, and platelets, most significantly erythrocytosis in polycythaemia vera. The occurrence of myocardial infarction and splenic infarcts in myeloproliferative disease is mostly attributed to thrombosis due to hyperviscosity and thrombocytosis. Although venous thromboembolism is common in polycythaemia vera patients, arterial ischaemic complication can also occur in 24 to 43% of these patients, particularly with those having cardiovascular risk factors (such as smoking).

Case Report 1

A 38-year-old male with no previous comorbidities and addictions presented to our Emergency Department with retrosternal chest pain for the last 24 h. The pain was squeezing in character, retrosternal, radiating to the left shoulder, associated with diaphoresis, and a feeling of impending doom. There was no history of cough with expectoration, fever, or palpitations. He had no prior comorbidities and addictions. He denied any history of recreational drugs prior to the episode and did not have any family history of cardiac disease.

On physical examination, he looked plethoric with conjunctival congestion. His temperature was 98.7 F, pulse 88/min (regular), blood pressure (BP) 140/80 mmHg, respiratory rate 18/min, and saturation in room air 99%. Systemic examination was unremarkable and all the peripheral pulses were equally palpable.

The ECG on admission [Figure 1] showed a biphasic T wave in leads V2 to V5, cardiac troponins, and creatine kinase—MB isoenzyme, however, was negative, so a provisional diagnosis of acute coronary syndrome—unstable angina was made. Two-dimensional (2D) echocardiography showed an ejection fraction (EF) of 55% with no regional wall abnormalities. CT Coronary angiography [Figure 2] showed 70% occlusion of left anterior descending (LAD). The patient was medically managed with antiplatelets, statins, and anticoagulation.

Laboratory investigations were as follows: total leucocyte count 18,300; neutrophils 80%; lymphocytes 17%; Hb **20.4 g/**L (118–148 g/L); haematocrit **70**% MCV 91 FL (82–98 FL); and platelets 8.5 lakhs. Her coagulation profile, renal function test, lipid profile, liver function test, and electrolytes were all within

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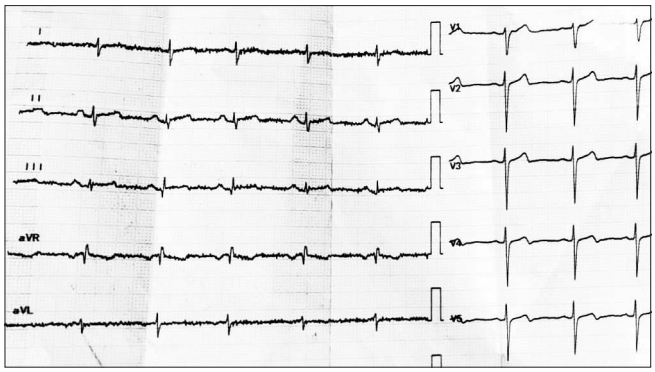

Figure 1: ECG on admission showed a biphasic T wave in leads V2 to V5

normal range. Blood culture and urine culture were sterile and serum procalcitonin was negative.

There were no risk factors present in our patient to develop ACS, only positive finding on CBC was polycythaemia. Serum erythropoietin levels were ordered which came out to be inappropriately normal, so JAK 2V617F mutation was done which came out to be POSITIVE [Figure 3]. Bone marrow aspiration and biopsy revealed trilineage hyperplasia. The final diagnosis of ACS—unstable angina secondary to polycythaemia vera was made based on clinical and laboratory investigations. The patient was started on hydroxyurea along with antiplatelet drugs, and anticoagulation received two phlebotomies during the hospital stay and was discharged to follow up with a repeat CBC.

Case Report 2

A 45-year-old female diagnosed hypertensive and hypothyroid for the last three years on medication presented to our emergency with complaints of pain abdomen for two months which was insidious in onset, localised to the left hypochondrium dull and aching in nature, nonradiating decreased on rest, associated with nonprogressive abdominal distention. There was a history of one episode of jaundice six months back, for which she took over-the-counter medications and it resolved in 10–15 days. No h/o blood transfusion, fever, vomiting, loose stool, hematemesis, bleeding from any site, melena, burning micturition, decreased urine output, shortness of breath, or cough was observed.

On the examination, she looked plethoric, with a temperature of 98°F, blood pressure of 130/70 mmHg with a pulse rate of 90/min (regular), and 99% oxygen saturation on room air. On systemic examination, per abdomen was distended with tenderness in the left hypochondrium with a palpable spleen 4cm below the left costal margin, shifting dullness was absent. The rest of the systemic examination was unremarkable. Ultrasonography of the abdomen showed splenomegaly with signs of portal hypertension with a 116cc heterogeneous area in the spleen (? evolving abscess? or infarct). The patient was initially managed with intravenous antibiotics considering a diagnosis of splenic abscess.

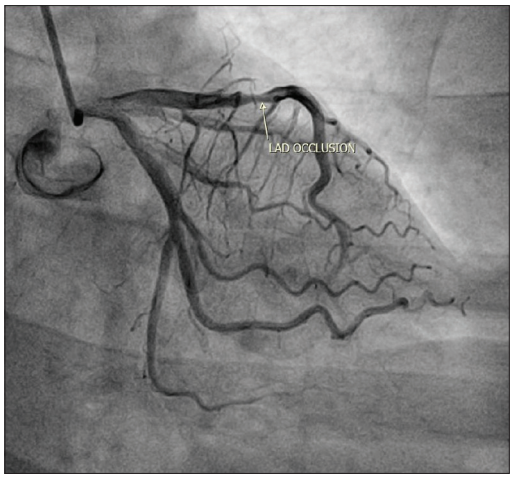

Figure 2: CT Coronary angiography showing 70% occlusion of the left anterior descending artery

On admission, investigation of the patient was as follows: total leucocyte counts 22,000; neutrophils 90%, 10% lymphocyte; Hb 16.1g/L (11.8–14.8g/l); platelets 5.4 lakhs, haematocrit −56% MCV-78.7 FL (82–98 FL). Peripheral smear did not show any atypical cells/blasts. Her coagulation profile, renal function, liver function test, liver function test, and electrolytes were within normal range. The patient's blood culture and urine culture were sterile with negative serum procalcitonin and normal CRP.

Contrast enhanced CT abdomen [Figure 4] showed splenomegaly with an irregular nonechoing area in the upper pole of the spleen and a smaller area of hypoattenuation without contrast enhancement in the lower pole of the spleen is suggestive of a splenic infarct. It also revealed portal venous thrombosis with multiple venous collaterals. As the complete blood count of the patient showed high TLC, HB, and platelets despite having portal hypertension, suspicion of myeloproliferative disorder being the underlying aetiology of portal vein thrombosis was considered. After ruling out relative polycythaemia by hydration and arterial blood gas, the analysis did not show that hypoxemia serum erythropoietin levels were ordered which came out to be inappropriately normal. Bone marrow aspiration and biopsy showed trilineage hyperplasia with no blasts, atypical cells, or granuloma. JAK 2V617F mutation also came POSITIVE.

The final diagnosis of portal vein thrombosis secondary to polycythaemia vera was made based on clinical and laboratory investigation. The patient was started on low-dose ecosprin and systemic anticoagulation and discharged to follow up in the outpatient department with CBC and INR reports.

Discussion

Polycythaemia vera is a chronic myeloproliferative disease associated with abnormal clonal proliferation of pluripotent stem cell, leading to increased red cell, haematocrit, leucocytosis, and thrombocytosis. Splenomegaly and bone marrow fibrosis are also observed in some stages of polycythaemia.[1] Patients

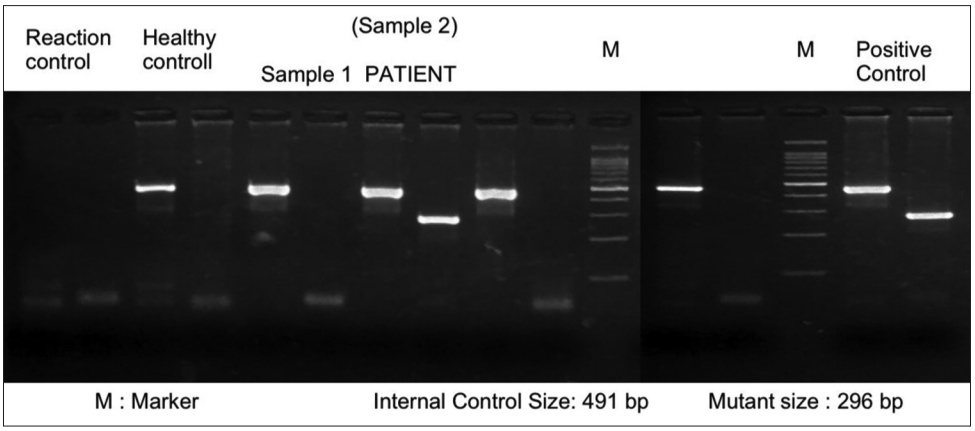

Figure 3: PCR showing JAK 2V617F mutation sequence (mutant: 296 bp) in the patient sample similar to positive control suggestive of positive mutation in the patient

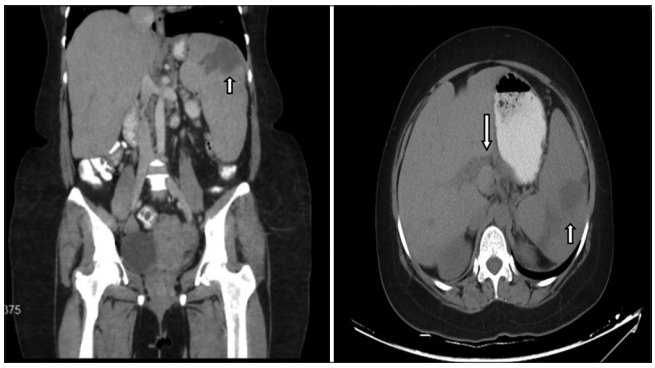

Figure 4: CECT Abdomen of the patient shown to have splenomegaly with irregular nonechoing area in the upper pole of the spleen (upright arrow). A smaller area of hypoattenuation without contrast enhancement in the lower pole of the spleen is suggestive of a splenic infarct, also portal venous thrombosis with multiple venous collaterals (downward arrow)

with the myeloproliferative disorder are very prone to venous and arterial thrombosis.[2] Thrombotic complications are more common with polycythaemia vera than essential thrombocytosis. It is believed that an increase in red cell mass and hyperviscosity are more important factors than an increased platelet count.[3,4]

Diagnosis of polycythaemia is made by using the World Health Organization (WHO) criteria Major criteria: (A) haemoglobin and gt; 16.5 g/dL in men or 16 g/dL in women or other evidence of increased red cell mass. (B) The presence of JAK2 V617F mutation or other functionally similar mutation (like JAK2 exon 12 mutation). (C) Bone marrow biopsy showing panmyelosis. Minor criteria: Serum erythropoietin level below the reference range for normal.[5]

Hyperviscosity and increased red cell mass can lead to the development of many complication like stroke, endothelial dysfunction, hypertension, and myocardial infarction. Thrombotic complications are more prevalent in polycythaemia vera affecting such that in 14% of cases thrombotic event precedes the diagnosis.[4] As in our study also both the patients presented to the hospital after a thrombotic complication. In this disease, arterial thrombosis is more common in comparison with venous thrombosis. Venous thrombosis is more prevalent in the brain and abdominal cavity and is more common in women[4,6] as seen in our second case. Bleeding may arise due to vascular stasis and thrombocytosis and is often the cause of mortality.

Splenic infarct occurs rarely due to thrombosis and lacks the signs such as abdominal pain, fever, and tachycardia. Radiologically splenic infarct in polycythaemia presents as a peripherally located, hypo-attenuated, and wedge-shaped lesion. In some cases, it can be seen as a massive lesion on a CT scan of the abdomen.[7]

However, our first patient is diagnosed with myocardial infarction due to primary polycythaemia at a very young age. A similar case was also reported by A. Nahler *et al.*[8] in which 22-year-old male patient found to have myocardial infarction as initial presentation polycythaemia. In a study by B.

Cengiz *et al.*[9] on 11 consecutive patients with the diagnosis of myeloproliferative syndrome who had acute coronary syndrome at a very young age, most of them were found positive for JAK2mutation. Ten patients were found to have anterior MI and one had inferior MI. Treatment involved low-dose aspirin and phlebotomy. In the first case with left anterior descending artery occlusion, hydroxyurea was administered. The European collaboration on low-dose aspirin in polycythaemia vera (ECLAP) has been reported to be highly effective in preventing thrombosis as it results in a 60% reduction of nonfatal myocardial ischemia, nonfatal stroke, and death from cardiovascular complications.[10,11] Also in a retrospective analysis by Posfai *et al.*,[12] 14 MI events were seen in 263 patients of myeloproliferative disease. 71.4% of MI complication was found to occur within 12 months of diagnosis of myeloproliferative disease.

Abdalla *et al.*[13] and Qusay Abdoh *et al.*[14] reported splenic infarct secondary to polycythaemia vera similar to our case of portal vein thrombosis with splenic infarct secondary to polycythaemia vera.

Polycythaemia vera is a neglected risk factor and should be suspected in young patients and patients with thrombosis of unusual sites. What mind does not know eyes can't see!

Conclusion

1. Polycythaemia vera is a common neglected risk factor that can present thrombotic complications and treating the underlying disorder can lead to decrease complications.
2. Hypercoagulable states should be ruled in young patients who present with ACS and thrombosis at unusual sites in the absence of other risk factors.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

References

1. Barbui T, Finazzi G, De Gaetano G, Marchioli R, Tognoni G, Patrono C, *et al.* Polycythemia vera: The natural history of 1213 patients followed for 20 years. Ann Intern Med 1995;123:656-64.
2. Hoffman R, Silverstein MN. Polycythemia vera. In: Hoffman R, editor. Hematology: Basic Principles and Practice. New York: Churchill Livingstone; 1991. p. 834-54.
3. Schafer AI. Bleeding and thrombosis in the myeloproliferative disorders. Blood 1984;64:1-12.
4. Cortellazzo S, Viero P, Finazzi G, D'Emilio A, Rodeghiero F, Barbui T. Incidence and risk factors for thrombotic complications in a historical cohort of 100 patients with thrombocythemia. J Clin Oncol 1990;8:556-62.
5. Barbui T, Thiele J, Gisslinger H, Kvasnicka HM, Vannucchi AM, Guglielmelli P, *et al.* The 2016 WHO classification and diagnostic criteria for myeloproliferative neoplasms: Document summary and in-depth discussion. Blood Cancer J 2018;8:15. doi: 10.1038/s41408-018-0054-y.
6. Gumina RJ, Foley DA, Tefferi A, Rooke TW, Shields RC. Polycythemia vera -- A case report and discussion on pathogenic mechanisms of increased thrombosis: A case report and discussion on pathogenic mechanisms of increased thrombosis. Angiology 2002;53:587-91.
7. Balcan I, Seltzer SE, Davis S, Gellen S. CT patterns of splenic infarction: A clinical and experimental study. Radiology 1984;151:723-9.
8. Nahler A, Fuchs D, Reiter C, Kiblböck D, Steinwender C, Lambert T. Myocardial infarction with proximal occlusion of the left anterior descending coronary artery in a 22-year-old patient with polycythemia vera. Clin Med 2017;17:46-7.
9. Cengiz B, Aytekin V, Bildirici U, Sahin ST, Yurdakul S, Aytekin S, *et al.* A rare cause of acute coronary syndromes in young adults-myeloproliferative neoplasms: A case series. Rev Port Cardiol 2019;38:613-7.
10. Landolfi R, Marchioli R, Kutti J, Gisslinger H, Tognoni G, Patrono C, *et al.* Efficacy and safety of low-dose aspirin in polycythemia vera. N Engl J Med 2004;350:114-24.
11. Barbui T, Finazzi G, Falanga A. Myeloproliferative neoplasms and thrombosis. Blood 2013;122:2176-84.
12. Posfai E. Myocardial infarction as a thrombotic complication of essential thrombocythemia and polycythemia vera. Anatol J Cardiol 2016;16:397-402.
13. Abdalla E, Musa M, Musa M, Hatem A, Fadul A, Ahmed AO. Splenic infarctions in polycythaemia vera are not always a catastrophe. Eur J Case Rep Intern Med 2022;9:003370. doi: 10.12890/2022_003370.
14. Abdoh Q, Alnees M, Rajab I, Zayed A, Salim H, Barqawi A, *et al.* Splenic infarction secondary to polycythemia Vera: Case report and literature review. Radiol Case Rep 2023;18:3636-41. doi: 10.1016/j.radcr.2023.07.049.