POLYCYTHEMIA VERA PRESENTING AS SPLENIC INFARCT

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Abstract:
Polycythemia vera is most often recognized by the incidental discovery of a high hemoglobin or hematocrit. In about 20% of patients it presents with thrombotic complications. We are presenting one such case where polycythemia vera manifested itself as splenic infarct due to splenic vein thrombosis. A 49 year old female presented with left sided abdominal pain, mild fever and easy fatigability of 10 days duration. Imaging showed splenic vein thrombosis with splenic infarct. Hematological evaluation revealed increased hemoglobin, leucocytosis and thrombocytosis. Further investigations showed decreased erythropoietin and JAK2 mutation positivity. A diagnosis of polycythemia vera with splenic infarct due to splenic vein thrombosis was made and she was treated with phlebotomy.

Keyword: splenic infarct, splenic vein thrombosis, polycythemia vera

A 49 year old female presented with left sided abdominal pain, fever and easy fatigability of 10 days duration. The pain was over the left upper quadrant and unrelated to food intake. Fever was low grade, intermittent and not associated with chills or rigors. She denied dysuria, urinary urgency, or frequency. There was no history of diarrhea, constipation, rashes over the body or cough with expectoration. She was taking over the counter medications for fever. Her past history was significant for diabetes and hypertension of 3 years duration but she was not on treatment for the same. She had attained menopause 5 years back. Admission vital signs were as follows: blood pressure, 150/96 mm Hg; pulse, 102 beats/min; respirations 16/min; and temperature, 36.6°C. Examination was unremarkable except for a non-tender splenomegaly measuring about 7 cm below the left costal margin. There were no rashes, lymphadenopathy, hepatomegaly and bleeding tendencies. The levels of serum electrolytes, serum urea, creatinine, liver function test results were all within normal limits. Random blood sugar was 167 mg/dl. Urinalysis showed trace protein with no leukocytes, erythrocytes.
or casts. Chest X ray was normal, ECG showed left axis deviation with left ventricular hypertrophy. MP QBC, blood culture for salmonella, MSAT, HIV ELISA were negative. Echocardiogram showed moderate LV dysfunction with EF of 38%. Ultrasound abdomen showed splenomegaloy(18.8 cm) with hypoechoic areas suggestive of ?infarct/abscess. We proceeded with contrast enhanced CT abdomen which revealed splenic vein thrombosis with splenic infarct(Fig.1).

Her complete blood count was as follows :Total leucocyte count:(13,200/ mm³); Differential count-(Polymorphs 83 Lymphocyte 10 Monocyte 07); Packed cell volume-62% ;Total platelet count -5.47lakhs/mm³ ; Prothrombin time -25.55sec and INR (International normalized ratio)-2.04; Peripheral Smear-Normocytic hypochromic RBCs with increased platelets; Serum Uric acid-4.5 mg/dl. Since the patient had erythrocytosis in combination with leukocytosis and thrombocytosis a diagnosis of polycythemia vera was considered and further evaluation revealed decreased serum erythropoietin level 2.19 U/L(N=4-27U/L). Bone marrow aspiration showed platelet clumping with neutrophilia. JAK 2 mutation(Janus activated kinase) was positive. Taking all the above parameters into account and in consultation with a hematologist, the diagnosis of polycythemia vera with splenic infarct due to splenic vein thrombosis was made. The patient was treated initially with intravenous heparin, antibiotics, insulin, antihypertensives and analgesics. Therapeutic phlebotomy was done, each time removing 350 ml of blood and aspirin. Patient improved symptomatically and was discharged after two phlebotomies and advice to continue aspirin, and other drugs. Patient is on regular follow up for the past 1 year and is on regular aspirin and monthly phlebotomy with intermittent hydroxyurea as she could not tolerate phlebotomy. Her latest complete blood count was Total leucocyte count: 6000/ mm³, Differential count- Neutrophil 80 %, Lymphocyte 20 ; Hemoglobin- 14 gm%; Platelets-2.4 lakhs.

**DISCUSSION:**
Polycythemia vera is a clonal disorder involving a multipotent hematopoietic progenitor cell in which phenotypically normal red cells, granulocytes, and platelets accumulate in the absence of a recognizable physiologic stimulus. The most common of the chronic myeloproliferative disorders, polycythemia vera occurs in 2 per 100,000 persons, sparing no adult age group (1). Leukaemic conversion occurs in 1–3% and the median survival with treatment is 13 years (4). Untreated life expectancy is approximately 18 months from diagnosis (4, 5). A mutation in JAK2, that replaces valine with phenylalanine (V617F), causing constitutive activation of the kinase, appears to have a central role in the pathogenesis of polycythemia vera (2). Patients with polycythemia vera have an increased thrombotic tendency resulting from the expansion of the red cell mass which represents the main cause of mortality in these patients(3).
There is a direct relationship between the complications and age, being higher in patients over 65 years of age. Younger individuals are also at risk for thrombotic episodes, many of them life-threatening. The main rheological abnormality is elevated total blood viscosity(3). Thromboses at unusual sites are characteristic of polycythemia vera. They include occlusion of the splenic, portal, hepatic, and mesenteric veins. The prevalence of myeloproliferative neoplasms in patients with splanchic vein thrombosis was estimated to be as high as 49% for hepatic vein thrombosis and 23% for portal vein thrombosis. Splenic infarct in polycythemia vera can be asymptomatic (discovered incidentally on radiologic or postmortem studies, or at laparoscopy or laparotomy for another indication) to hemorrhagic shock (secondary to massive subcapsular hemorrhage with free rupture into the peritoneal cavity)(6). Approximately one third of splenic infarcts are clinically occult. The most common presenting symptom is left – upper quadrant abdominal pain (up to 70%) as seen in our case. Additional symptoms include fever and chills, nausea and vomiting, pleuritic chest pain, and left shoulder pain (Kehr sign). Intractable pain, splenic rupture, and abscess formation are clear indications for splenectomy in a case of splenic rupture. Otherwise patients can be managed conservatively as in our patient(6). Patients with polycythemia vera are also at an increased risk of developing life-threatening haemorrhagic complications. Abnormalities in platelet function and number have been implicated. Acquired von Willebrand syndromes have been described in patients who have very high platelet counts (>1000 x 10^6/l), in association with life-threatening bleeding episodes. Neurological abnormalities are also common and occur in up to 60 to 80 per cent of patients. They include transient ischaemic attacks, cerebral infarction, cerebral haemorrhage, confusional states, fluctuating dementia, and involuntary movement syndromes. Dizziness, paraesthesias, tinnitus, visual problems, and headaches are common symptoms attributed to the hyperviscosity state. With the exception of aquagenic pruritus, no symptoms distinguish polycythemia vera from other causes of erythrocytosis . (1) When polycythemia vera presents with erythrocytosis in combination with leukocytosis, thrombocytosis, or both, the diagnosis is apparent. However, when patients present with an elevated hemoglobin or hematocrit alone, or with thrombocytosis alone, the diagnostic evaluation is more complex because of the many diagnostic possibilities . Furthermore, unless the hemoglobin level is 20 g/dl (hematocrit 60%), it is not possible to distinguish true erythrocytosis from disorders causing plasma volume contraction (also known as stress or spurius erythrocytosis or Gaisböck’s syndrome ). This is true even with the finding of JAK2 V617F mutation, because not every patient with PV expresses this mutation, while patients without polycythemia vera do.(1) WHO diagnostic criteria: A1 Raised red cell mass or haemoglobin (Hb) > 18.5 (males), > 16.5 (females) A2 No secondary erythrocytosis A3 Splenomegaly A4 Abnormal karyotype (other than Ph chromosome or BCR/ABL fusion gene in marrow cells) A5 Endogenous erythroid colony (EEC) formation B1 Platelet count > 400 x 10^9/l B2 WBC > 12 x 10^9/l B3 Bone marrow biopsy (BMB) showing panmyelosis with erythroid and megakaryocytic proliferation B4 Low serum erythropoietin (EPO) Diagnosis A1 + A2 and any other category A establishes polycythemia vera A1 + A2 + two of category B establishes polycythemia vera
Our patient had trilineage cell hyperplasia with decreased erythropoietin and JAK2 mutation positivity, the diagnosis of polycythaemia vera was apparent. The main therapeutic objective is the reduction of the haematocrit to a safe level. This is usually accomplished by the implementation of repeated phlebotomies(3). It is often feasible to remove between 350 and 500 ml of blood every other day until the desired haematocrit level is attained. Haematocrit levels of less than 50 per cent and preferably below 45 per cent are desirable(3). Once the target haematocrit level is achieved, a maintenance regimen should be instituted. Venesection is preferred in those younger individuals without critical elevations in their platelet counts. Myelosuppressive therapy should be considered in elderly patients who are intolerant of phlebotomies, and in younger individuals with repeated thrombotic episodes and extremely high platelet counts (3). At present, hydroxyurea is the chemotherapeutic drug of choice in those patients who cannot be treated with phlebotomy alone (3). In younger patients, given their potential long-term survival, strong consideration should be given to the use of phlebotomy therapy in combination with low-dose aspirin (3). Our patient was given regular phlebotomy with aspirin, as she could not tolerate phlebotomy, she is now on hydroxyurea.

CONCLUSION:
Splenic infarction is a clinical entity that has received increasing clinical attention in recent years. Although it is seldom encountered, splenic infarction has many potential causes. The most frequent causes of splenic infarction include myelofibrosis and hematologic malignant neoplasms. Polycythaemia vera is one such cause and it should always be considered in the work up of splenic infarct.

REFERENCES:
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