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Case Report

Cerebral venous thrombosis in polycythemia rubra vera: a rare case report

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ABSTRACT

Polycythemia rubra vera (PV) is a disease characterised by increased production of red blood cells due to genetic mutation which leads to increase in RBC mass and increased viscocity of blood. Myeloproliferative neoplasms have been implicated in the causation of cerebral venous thrombosis (CVT). Here we presented a 34 year old male who present with headache and diplopia. Fundus examination revealed bilateral papilledema. MRI brain with venogram was done which revealed right transverse and sigmoid sinus thrombosis. Blood investigations revealed polycythemia, elevated RBC counts and hematocrit levels. Peripheral smear showed increased RBC, WBC and platelets. Serum erythropoietin was low. Bone marrow aspiration study revealed hypercellular marrow. Patient tested positive for JAK2 V617F mutation. Patient was treated with anticoagulants, therapeutic phlebotomy and other supportive measures. Here we present a rare case of PV presenting with CVT.

Keywords: Polycythemia rubra vera, Cerebral venous thrombosis, Myeloproliferative disorder, Erythropoietin

INTRODUCTION

Polycythemia rubra vera (PV) is a disease characterised by increased production of red blood cells due to a genetic mutation which leads to increase in RBC mass and increased viscocity of blood. JAK kinase 2 is the gene that undergoes mutation in PV. 90% of cases of PV have a mutation in the intracellular signalling gene Janus kinase-2 (JAK2) (PV). Constitutively active cytokine receptors result from a valine to phenylalanine substitution at position 617 of the JAK2 gene, often known as JAK2V617F.

About 34% of individuals with PV have aberrant karyotypes in their hematopoietic progenitor cells, according to cytogenetic investigations.[1] 20% of patients had cytogenetic abnormalities at the time of diagnosis, and this number rises to more than 80% for those who have received follow-up care for more than 10 years. Patients with PV have normal stem cells in their bone marrow as well as aberrant clonal stem cells, which prevent healthy stem cells from developing and growing normally. Neoplastic growth that is not under control is the cause of panmyelosis. JAK2 kinase mutation is probably responsible for the signalling abnormalities that occur in PV. Over 90% of people with PV, 50% to 60% of those with primary myelofibrosis, and 50% of those with essential thrombocythemia have this mutation.[2] This process leads to increased production of red blood cells and platelets with associated thrombotic complications.[3]

Cerebral venous thrombosis (CVT) is disease caused by thrombosis of venous channels in the brain. Although superficial dural venous sinuses are commonly involved, deep venous system is involved in approximately 16% of the cases. Various etiologies have been implicated in causing CVT including dehydration, pregnancy and pueperium, oral contraceptive pill usage; antthrombin III, protein C and S deficiencies, APLA syndrome, cancer and so on.[4] Myeloproliferative neoplasms have been implicated in the causation of CVT as these conditions are associated with increased viscocity of blood leading to

formation of blood clots. Here we encountered a rare case of PV presenting as CVT.

CASE REPORT

A 34 year old male came to emergency department with complaints of holocranial headache which is worse in the early morning after waking up associated with diplopia for 1 week.

On general examination, patient had hyperemia of conjuctiva. Fundus examination revealed blurring of disc margins and disc hyperaemia in both eye suggestive of papilledema. Vitals were normal. Systemic examination was normal. Patient had features of raised intracranial pressure. Patient was then shift for MRI brain which showed partial empty sella with bilateral optic nerve tortuosities. Following that MR venogram was done which showed incomplete central filling of Right transverse sinus right sigmoid sinus suggestive of venous sinus thrombosis. Blood investigations revealed hemoglobin- 21 g/dl, RBC count- 8 million/mm^3 mean corpuscular volume- 86 fl, hematocrit- 56.3%, patelet count was 6 lakhs/mm^3. Peripheral smear revealed increased noemocytic normochromic RBCs and increased platelets. Patient was treated with injection enoxaparin 60 µg subcutaneously twice a day and bridged with acylcoumarin, therapeutic phlebotomy was done in view of high hematocrit values. Acetazolamide 250 mg was given twice a day in view of raised intracranial pressure. Serum erythropoietin levels were measured and was found to be 1 mu per ml (4.3 to 29 *mu per ml*). Bone marrow aspiration was done which revealed hypercellular marrow with erythroid and megakaryocytic hyperplasia. Patient tested positive for JAK2- V617F on EXON 14 mutation. Patient was started on hydroxyurea 500 mg twice a day. Patient improved symptomatically and was discharged.

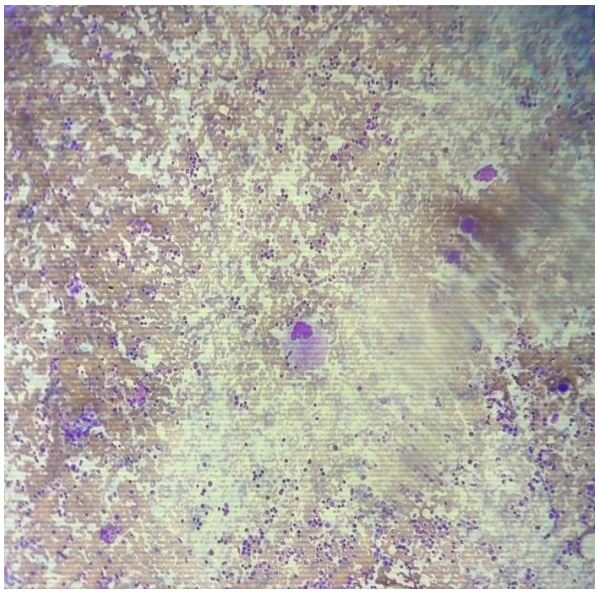

Figure 1: Bone marrow smear showing erythroid and megakaryocytic hyperplasia.

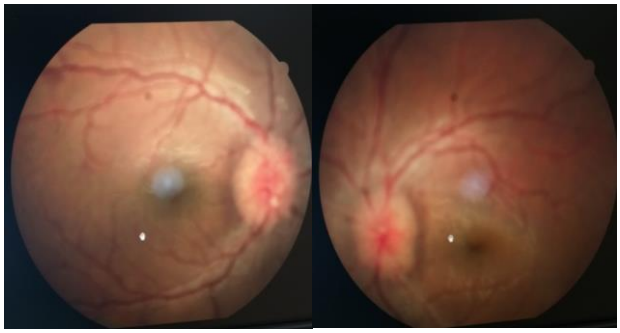

Figure 2: Fundoscopy revealing bilateral eye papilledema.

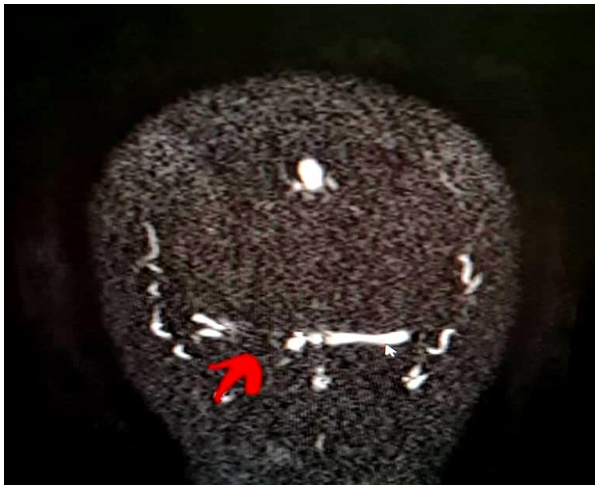

Figure 3: Magnetic resonance imaging with venogram revealing right transverse sinus and sigmoid sinus thrombosis.

DISCUSSION

PV can affect all ethnic groups with no sex predilection, although there are slightly more cases in men than women.[5] It can occur in all age groups, but the median age of diagnosis is 60.[6] PV affects 0.6 to 1.6 per million people in the United States whereas the prevalence of primary polycythemia is estimated to be 0.6 per 100,000 adults in India.[7] Dentali et al looked into the incidence of PV in a cohort of 2,143 MPN patients (735 with PV) and the frequency of CVT in a group of 706 individuals with cerebral vein thrombosis (CVT). In contrast to the 3.8% incidence of myeloproliferative disorder in CVT patients, only 5 (0.7%) had CVT reported. Thus, in patients with an established MPN, the diagnosis of CVT is quite rare.[8] Myeloproliferative disorders are more commonly associated with arterial thrombosis. Ischemic stroke may be the first presenting symptom of PV in 15%.[9] In a retrospective study of 100 patients by Bhat et al, 30 patients were found to have CVT and superior sagittal sinus was the most commonly affected (78%). Transverse and sigmoid sinus was affected in 22% of the patients with CVT. Among the patients with CVT, 10 patients had papilledema in which three patients had transverse sinus thrombosis, one had both transverse and sigmoid sinus

thrombosis, six had thrombosis of superior sagittal sinus. These patients also had a hematocrit of 56-60%.[10]

CONCLUSION

Headache is the most common presenting symptom of CVT and hence fundoscopy is an important tool to identify raised ICP which could aid in the diagnosis of CVT. Cerebral venous thrombosis usually occurs on the background of risk factors and etiologies that lead to hypercoagulability of blood and hence all etiologies that can cause CVT should be ruled out. Myeloproliferative neoplasms such as polycythemia rubra vera is an unusual cause of thrombosis and hence clinicians encountering CVT should evaluate for the same in patients with elevated blood cells.

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