



Ischemic Stroke as the Initial Presenting Manifestation of Polycythemia Rubra Vera- A Case Report

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Case Report

57 Year old Man who was previously healthy presented with sudden onset of slurring of speech with difficulty in walking with swaying to right since 3 days. There was mild holocranial headache along with it without vomiting. Past history of systemic hypertension since 5 years on medications with good control. No history of Smoking, Neck trauma, Cardiac illness or any other vascular risk factors. On General examination he had Conjunctival hyperemia. Neurological Examination showed gaze evoked nystagmus more towards right with dysarthria. There was intention tremor in right upper limb with dysmetria, wide based gait ataxia and swaying to right on walking with inability to perform the tandem walk test. Cardiovascular system examination was normal. There was no hepatosplenomegaly. In view of sudden onset Slurring of speech with right sided cerebellar signs a diagnosis of Cerebrovascular Accident involving the posterior circulation was considered. MRI scan of the Brain (1.5 Tesla) was done which showed Right cerebellar Acute Infarct without mass effect or hemorrhagic transformation. MR Angiogram with contrast was done which was normal. Blood investigations showed Hemoglobin of 21.8 gm/dl, Packed cell volume-66.6%, with

normal White cell and platelet count. ESR was 5mm in 1st hour. Serum Uric acid was 8.9mg/dl. Rest of routine investigations like Liver and Renal function tests, HBA1C, Fasting lipid profile and thyroid function tests and were normal. 12 Lead Electrocardiogram, Neck Vessel Doppler and 2DECHO was normal. Oxygen saturation was always above 96%, ruling out Hypoxic disorders. In view of True Polycythemia in absence of smoking and hypoxia possibility of Polycythemia Vera was considered. Bone Marrow biopsy was done which showed bony trabeculae with increased cellularity for age. Erythroid, Granulocytic and Megakaryocytic series were increased (Trilinear Hyperplasia). Serum Erythropoietin was level was 7.95mIU/ml (4.30-29). PCR for JAK2 V617 F genetic mutation was positive. PCR for JAK2 Exon 12 mutation was negative. Thus the WHO 2016 Diagnostic criteria for Polycythemia Vera (three major and one minor criteria) was satisfied. Patient was started on aspirin 75mg/day. Phlebotomy was done once in three days till the Hemoglobin decreased to less than 17gm/dl. The patient was also started on Hydroxyurea 500mg BD as cytoreductive therapy. Patient has improved Neurologically and haemoglobin is below 16 and is under regular follow up.



Figure 1-MRI Diffusion Weighted Image axial view showing diffusion restriction over the Right Cerebellum suggestive of Acute Infarct involving the superior cerebellar Artery Territory

Discussion

Polycythemia Vera (PV) is a clonal stem cell disease with trilineage myeloid involvement.^(1,2) Phenotypically normal red cells, granulocytes and platelets accumulate in absence of a recognisable physiologic stimulus.⁽³⁾ It is the most common type of myeloproliferative disorder. The Median age at diagnosis of PV is around 60 years with a (1.2:1) male preponderance.⁽⁴⁾

The Abnormally elevated hematocrit of PV is the main causative factor of increased blood viscosity. As the viscosity increases, cerebral blood flow decreases correspondingly^[5,6]. Platelet marginalize leading to increased contact to blood vessel walls, along with local effect of a high hematocrit on vessel walls^[5,6]. All of this factors contribute to the enhanced thrombogenicity seen in Polycythemia Vera^[5,6,7,8]. There are case reports which propose a microembolic mechanism from heart.⁽⁹⁾ 95 % of patients carry mutation of JAK2 V617 F. This gain of function mutation leads to excessive clonal proliferation in progenitor cells and also lead to the low erythropoietin levels. Rest of patients have mutations in exon12.

Haematological diseases such as Polycythemia rubra Vera can cause stroke though rare⁽¹⁰⁾. Though Major organ thrombotic events are the most important cause of mortality. Usually these disease conditions present with other symptoms and signs before development of stroke. Stroke

presenting as the initial manifestation is unusual. Strokes related to PV are both venous and arterial. Very rarely Hemorrhagic strokes can be associated. Mechanisms proposed for hemorrhagic strokes being dysfunctional platelets and acquired von Willebrand Disease.⁽¹¹⁾

Microvascular disturbances and hyperviscosity leads to transient inflammation based occlusive phenomenon due to interaction between clonal platelets and arteriolar endothelium. It manifests with headache, light-headedness, transient neurologic or ocular disturbances, tinnitus, atypical chest discomfort, paresthesias, and erythromelalgia.

Fluctuating dementia with reversibility, Confusional states and chorea in attributed to multiple small vessel occlusions in cortex and basal ganglia have also been recorded⁽¹²⁾

Evaluation of a polycythemic patient would be detailed history including that of smoking, high altitude stay, Chronic lung disorders, congenital heart diseases and use of anabolic steroids. This can be important in secondary causes of Polycythemia. Oxygen Saturation of more than 92% is highly unlikely in hypoxia being a cause of Polycythemia. Carboxy haemoglobin should be assessed in smokers. Serum erythropoietin levels are important levels are important in ruling out secondary causes. A low serum EPO level is highly suggestive but not diagnostic of PV (specificity of >90%)⁽¹³⁾. In contrast, the serum EPO level may lie within the reference range in patients with a definite diagnosis of PV. PV is highly unlikely to occur with an increased serum EPO level.⁽¹³⁾ Therefore, PV remains a diagnostic consideration in the presence of either a low or normal serum EPO level. Bone marrow biopsy is recommended in suspected cases of Polycythemia Vera which classically shows Trilinear hyperplasia.

In our patient there was absence of hepatosplenomegaly, which is well known in 20-30% of proven PV cases. The erythropoietin level was within the normal range which is again possible.⁽¹³⁾ Our patient responded well to

Repeated Phlebotomy ,Low dose Aspirin and Hydroxyurea.

Phlebotomy has been the mainstay of therapy for PV. Main aim is to remove excess cellular elements (red blood cells), to improve the circulation of blood by lowering the blood viscosity. Patients with very high hematocrit values (>65%) may undergo phlebotomy twice a week to reduce hematocrit to less than 45%.In order to avoid postural hypotension volume replacement with saline has to be in elderly patients with cardiovascular /Cerebrovascular issues. In patients with elevated platelet counts and previous thrombosis, phlebotomy may not be ideal as it may increase platelet counts and lead to thrombosis as noted in PSVG study^(14,15). Hydroxyurea (HU) is the agent of choice in such cases. In the PVSG trial, HU therapy reduced the risk of thrombosis compared with phlebotomy alone and should be the drug of choice for patients older than 40 years^(5,11). The ECLAP (The Italian study, European Collaboration on Low-dose Aspirin in PV) found aspirin efficacious for preventing thrombosis and also controlling erythromelalgia, which result from spontaneous platelet aggregation. Other studies have also shown that there is no increased risk of bleeding manifestations with use of low dose aspirin in Polycythemia Vera.

Conclusion

Stroke can be the initial manifestation of Polycythemia Vera. Proper and Appropriate investigations should be done in all cases of polycythemia with stroke. Early phlebotomy, Proper Hydration, low dose aspirin and Cytoreductive therapy (in selected cases) may give good outcome and can help in preventing recurrences of stroke.

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