

POLYCYTHEMIA VERA WITH ADVANCED ATHEROSCLEROSIS AND CEREBRAL ISCHEMIC STROKE- A CASE REPORT

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ABSTRACT

35 year old male presented with posterior fossa stroke with polycythemia vera. His right vertebral artery was occluded. There is significant stenosis of the left subclavian artery proximal to the left vertebral artery origin leading to posterior fossa ischemic lesions. The patient had bluish discoloration of the left hand fingers. Multiple phlebotomies were performed bring down the Packed cell volume in normal range. Patient started on cytoreductive drug (Hydroxyurea). Left subclavian artery stenotic lesion needs to be followed up to decide either conservative management or stent angioplasty.

Case Report

35 year old right handed male presented to our institution with complaints of occipital headache, gait disturbance, reduced vision in the left eye and tingling sensation and clumsiness in the left upper and lower limb. The onset was acute. There was no sensory dysfunction, any lapses of consciousness or seizures. Social history was unremarkable. He was occasional drinker, but denied any smoking or illicit drug use. Family history was unremarkable for any neurological or hematological disease. No risk factors like hyper-tension, diabetes or dyslipidemia.

Physical examination revealed a healthy appearing male who was afebrile, normotensive and in normal sinus rhythm. Neurological examination demonstrated slight dysmetria on left on finger to nose test. Gait disturbance noted on tandem walking. Reduced visual acuity in the left eye 6/18, otherwise other cranial nerves were all intact. Motor strength testing revealed intact strength throughout without any focal atrophy or abnormal involuntary movements.

Speech was fluent without aphasia or dysarthria, reflexes were 2/4 throughout. Mental status testing was completely intact. His hands and face were unremarkable for dermatological changes except for bluish discoloration of left hand fingers.

Laboratory investigation revealed high Haemoglobin of 22.5 gm%, Red Blood Cells 7.34 million/cmm, Hematocrit 63.8%, erythropoietin 6.61 mU/ml, White Blood Cells 12700/cmm, Platelets 1.95lakhs/cmm.

Imaging Findings

Non-contrast computed tomography (CT) of the brain showed multiple focal hypo-attenuation areas in the right cerebellum (Fig.1) and right occipital cortex (Fig. 2).

CT angiography of brain, neck, aortic arch and left upper limb shows focal concentric soft tissue at the origin of left subclavian artery for a length of about 1.1 cm causing focal moderate to severe stenosis (Fig.3) and complete occlusion of the distal right vertebral artery beyond proximal two third of its cervical segment (Fig.4).

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Color Doppler Imaging of left lower limb arteries show diffuse atherosclerotic changes more in the anterior tibial, posterior tibial (Fig.5) and peroneal arteries with dampened distal flow and mildly reduced distal run off without any significant stenosis. A trans-thoracic echocardiogram was unremarkable with ejection fraction of 55% and no vegetation.

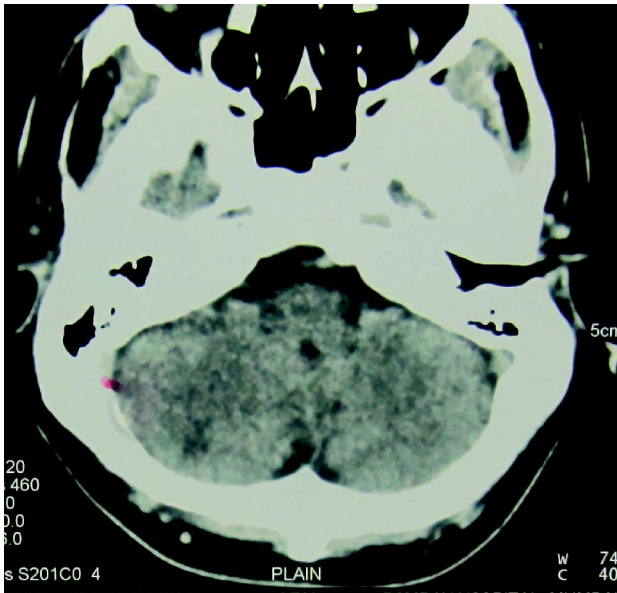


Figure 1: Plain C.T. scan of Brain showing acute focal infarct in right cerebellum (arrow).

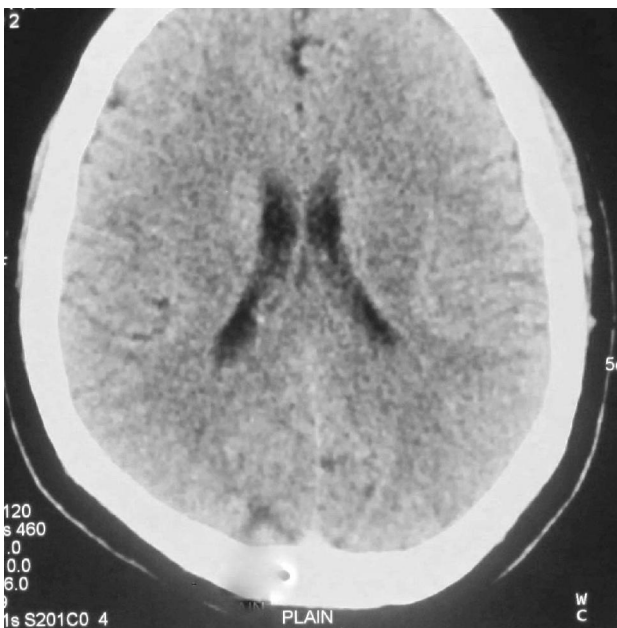


Figure 2: Plain C.T. scan of Brain showing acute focal infarct in right occipital cortex (arrow)

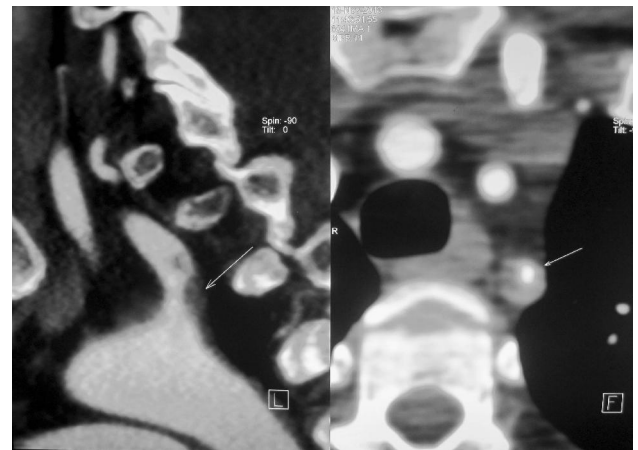


Figure 3: C.T.angiography of the neck in arterial phase showing severe narrowing of subclavian artery (arrow)

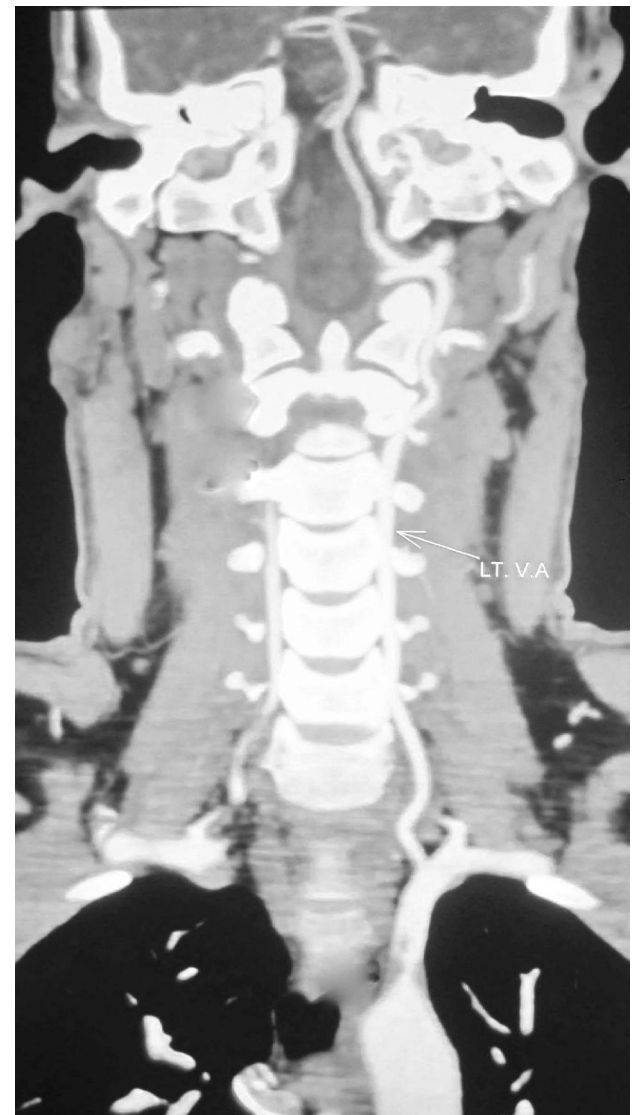


Figure 4: C.T.angiograph of neck in arterial phase neck showing complete occlusion of right vertebral artery (black arrows)

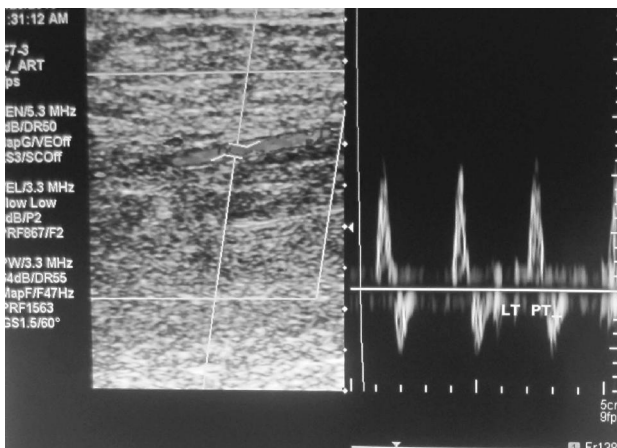


Figure 5: Colour Doppler imaging of lower limb showing atherosclerotic changes with dampened flow (arrow).

Management

Hematological consultation was obtained and bone marrow biopsy showed the diagnosis of PV. Multiple phlebotomies were done on four consecutive days, each session of phlebotomy involves removal of 350 ml of whole blood (total of 1400 ml) along with replenishing the intravascular blood volume with normal saline. He was started on routine anti-stroke medicines which includes anti-platelets, statins along with low molecular weight heparin. The low molecular weight heparin was stopped after 5 days. He was started on Hydroxyurea (25 mg/kg/d).

During the hospital stay, neurological symptoms gradually improved and at the time of discharge his hemoglobin level was 17 gm%. We decided to manage him conservatively for time being. The stent angioplasty of the left subclavian artery was to be considered only if patient not responding to conservative management.

Discussion

Introduction:

Polycythemia vera (PV) patients are at high risk for vaso-occlusive disorders including cerebral ischemia. Acute ischemic stroke may be an initial presentation of PV in 15% or more of those affected.^{1,2} The cerebral ischemic events are due to increased blood viscosity and platelet activation within the arterial vessels causing advanced atherosclerosis in most patients but in few patients due to formation of emboli.^{3,4,5} The management of these patients includes treatment of acute stroke as published guidelines with antiplatelets, statins and in appropriate case thrombolysis along with con-

trolling the risk factors.⁶ Hydroxyurea, a cyto-reductive drug, remains the drug of choice to control PV.⁷ Hemodilution has been considered in multiple past studies, with conflicting results. A meta-analysis has concluded there is a lack of proven efficacy of hemodilution in acute ischemic stroke and did not specifically include patients with hematologic conditions.⁸

Etiology & demographics:

PV is a myeloproliferative disorder resulting in an elevated absolute red blood cell mass because of uncontrolled red blood cell production. This is typically associated with an increase in White Blood Cells and Platelet production. The increase in White Blood Cells and Platelets is secondary to an abnormal clone of hematopoietic stem cells with increased sensitivity to different maturation growth factors. PV is overall rare, occurring in 0.6-1.6 persons per million population. The peak incidence of PV is 50-70 years of age. However, PV may occur in persons of all age groups, including young adults as in our case and children, albeit rarely.⁹ One study followed 265 patients with PV for a mean of 3 years, with a 5% incidence of stroke.³

Clinical & imaging findings:

The increased hematocrit of PV is the main determinant of blood viscosity. As the viscosity increases, cerebral blood flow decrease. Platelet marginalization with increased contact to vessel walls occurs, along with local effect of a high hematocrit on vessel walls.^{4,5} This fulfils all three components of Virchow's triad,¹⁰ and this lead to early progression of the atherosclerosis. Strokes in polycythemic patients are due to propagation of a local thrombus.^{4,5,11,12}

Other mechanisms have been proposed. Four prior case reports in adult have documented scattered lesions in an embolic pattern without evidence of patent foramen ovale, cardiac vegetations, or plaque rupture.^{13,14,15} In two of these cases, transesophageal echocardiography demonstrated left atrial "micro-thrombi".^{13,14} While these were not seen in our case report. We therefore postulate that the patients with polycythemia vera predisposed to a prothrombotic state which resulted in an advanced atherosclerotic and thrombotic changes in most vessels which in turn embolised.

Treatment & Prognosis:

Management of acute ischemic stroke in PV is also unique; it is the only situation where the American Heart Association stroke guidelines suggest a possible value of hemodilution.⁶ Additionally, although a meta-analysis of publications did not show a convincing benefit of hemodilution in clinical outcomes of stroke patients in general, the conclusion was that it might be beneficial in polycythemic patients with acute ischemic stroke. If the etiology is the formation of microemboli in the atria due to hyperviscosity, then hemodilution with venisection is likely the most expedient and safest acute treatment.

We feel that this is unique case in view of PV patient presenting with acute ischemic embolic stroke resulting from ruptured atherosclerotic plaque unusual for the age of the patient. We hope that this case report denotes the early onset of advanced atherosclerosis due to PV.

Differential Diagnosis:

Atherosclerosis disease- age related with multiple risk factors like Diabetes, hypertension, dyslipidemia, smoking. But no risk factors found in our case.

Conclusion / Teaching Point

Although uncommon, acute cerebral ischemia may be an initial presentation of PV. All clinicians involved in the care of stroke patients should be aware of the association of PV and early onset advanced atherosclerosis presenting with ischemic stroke.

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