Case Study

An Interesting Case of Acute Ischemic Stroke in the Young

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Abstract:

Ischemic stroke in young adults (15-45 years) is relatively frequent, accounting for more than 10% of all first ischemic strokes. Unlike in the elderly, causes of ischemic stroke in young adults are diverse.Non-atherosclerotic arteriopathy– dissection of the extra cranial arteries, migraine, drug abuse, vasculitis, cardio embolic, hypercoagulable states and cerebral venous thrombosis are the most relevant. We present a 32 year male, non-diabetic, non-hypertensive who presented with acute onset left hemiplegia with facial palsy, who on evaluation found to have right MCA territory infarct with erythrocytosis, low serum erythropoietin level. Genetic analysis showed positive JAK2 mutation. We report this case, as stroke may be the initial presentation of Polycythemia Vera, and every stroke in the young must be investigated thoroughly.

Keywords: Polycythemia Vera, JAK 2, Erythropoietin, Phlebotomy

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Introduction

Strokes are frequently taken into consideration as a result of high blood pressure and atherosclerosis. Some uncommon reasons of stroke additionally consist of systemic hypo perfusion, sickle mobileular anemia, cerebral venous sinus thrombosis, arterial fibrillation, and cocaine abuse[1]. Approximately 15% of all ischemic strokes (IS) arise in teens and adolescents. Compared with stroke in older adults, stroke within side the younger has a disproportionately massive monetary effect through leaving sufferers disabled earlier than their maximum efficient years[2]. To date, best constrained earlier public fitness and studies efforts have in particular addressed stroke within side the younger. Early analysis stays tough due to the lack of expertise and the relative infrequency of stroke in comparison with stroke mimics[3]. Moreover, the reasons of IS within side the younger are heterogeneous and comparatively uncommon, ensuing in uncertainties approximately diagnostic assessment and cause-unique management.

Case Report:

32 years unmarried male, working as a manual laborer, residing in Chennai, presented with complaints of sudden onset weakness and inability to use left upper and lower limbs with deviation of angle of mouth to right side for 2 days. There was history of headache preceding the weakness. There was no history of head trauma, seizures, vomiting, altered sensorium, sensory loss, diplopia, double vision and nasal regurgitation. He was an alcoholic for 6 years, nonsmoker, non-hypertensive, non-diabetic, and denied illicit drug abuse. There was no

family history of any neurological or hematological disease.

On examination he was conscious, oriented and afebrile, with conjunctival suffusion and no rashes or purpuric spots. His pulse, blood pressure, respiration were normal with SpO2 of 98%. Neurological examination revealed decreased tone and exaggerated reflexes in left upper and lower limbs with a power of 5/5 in both right upper and lower limbs, 0/5 in left upper and lower limbs. Plantar was extensor in left side. There was Left facial nerve palsy while other cranial nerves were intact. There were no involuntary movements, sensory deficits, cerebellar signs or autonomic dysfunction. Cardiovascular, respiratory and abdominal system examinations were normal. A provisional diagnosis of acute cerebrovascular accident – stroke in young – with left hemiplegia and left facial nerve palsy was made and we proceeded with the investigations.

Laboratory investigations showed Total Count – 9200, DC – P 71%, L 20%, E 9%, and ESR – 6mm/hr, Hemoglobin – 19.8gm%, PCV – 55%, Platelets – 2.08 lakhs, RBC – 6.67 millions/cu.mm, Peripheral smear with normochromic, normocytic RBCs, neurophilia and adequate platelets. Liver function tests showed 3 fold rise in transaminases with normal bilirubin and albumin. Renal function test, fasting blood sugar, fasting lipid profile, ECG, Chest X-ray, USG abdomen were normal. Viral markers – HBs Ag, Anti HCV and HIV were negative.

CT brain plain showed a hypo dense lesion in right frontal and temporal regions suggestive of fronto-temporal infarct. MRI also revealed a large acute infarct in right MCA involving frontal & temporal regions and MRA showed occlusion of M1 segment of right MCA, with no aneurysm. Carotid vertebral Doppler showed acute thrombosis of right distal CCA, carotid bulb, ICA & ECA with near complete occlusion of right ICA.

PT, INR, APTT were normal. Anti-nuclear antibody (ANA), Anticardiolipin & Antiphospholipid antibodies, Antithrombin III, Protein C & S was negative. Serum and hemoglobin electrophoresis were normal. Homocysteine was 25mcmol/L (normal: 6 – 15 mcmol/L). Bone marrow study showed Trilineage hematopoiesis with decreased iron stores and mild lymphoplasmacytosis. Serum Erythropoietin was 1.88 mU/ml (normal: 3.7 – 31.5 mU/ml)

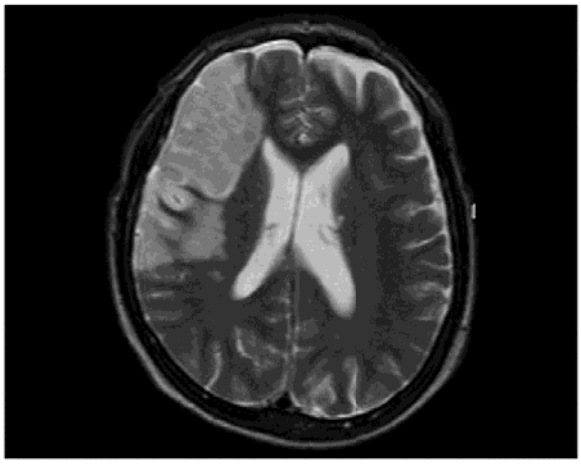

Figure.1*: T2 weighted MRI showing fronto-temporal infarct*

In view of erythrocytosis with trilineage hematopoiesis and low serum erythropoietin we proceeded with genetic analysis for JAK2-V617F mutation which was found to be positive. Patient was diagnosed as Polycythemia Vera, presenting as ischemic stroke and was treated with periodic phlebotomy, antiplatelet (aspirin) along with adequate hydration, physiotherapy and

supportive care. He gradually showed neurological improvement and his hemoglobin and hematocrit were reduced with above treatment.

Discussion:

Polycythaemia 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. It is classified under chronic myeloproliferative disorders[4].

Etiology of Polycythemia Vera is unknown. Mutation in auto inhibitory, pseudo kinase domain of tyrosine kinase JAK2 (Janase kinase 2), which replaces valine with phenylalanine (JAK2V617F) plays a central role in the pathogenesis of Polycythemia vera[5]. Incidence varies worldwide with slight male predominance.

Clinical features include non-specific symptoms like vertigo, headache, visual disturbance, transient ischemic attack (TIA) which occurs due to hyperviscosity of blood[6]. Patient may also present with aquagenic pruritus, erythromelalgia, abdominal pain, and splenomegaly. Arterial and venous thrombosis of the cerebral, cardiac and intrabdominal vessels can occur[7]. Due to thrombocytosis there may be digital ischemia, easy bruising, epistaxis, acid peptic disease or gastrointestinal bleeding.

Diagnosis:

Table 1 :*Revised WHO Criteria for diagnosis of Polycythemia Vera (2008)*[3]

Major criteria	Minor criteria
Hb> 18.5gm% (men) Hb> 16.5% (women), or Hct>52 in men and > 48 in women or other evidence of increased red cell volume.	Bone marrow biopsy showing hyper cellularity for age with trilinieage growth with prominent erythroid, granulocytic and megakaryocytic proliferation
Presence of JAK2V617F or other similar mutation	Serum erythropoietin level below the reference range for normal
	Endogenous erythroid colony formation in vitro.

Table 1 shows the diagnosis criteria of Polycythemia Vera given by WHO. This indicates,

- Both major criteria and one minor criteria
- First major criteria and 2 minor criteria

Treatment:

Phlebotomy

Phlebotomy is the removal of blood from a vein. It is the usual starting point of treatment for most patients. A volume of blood is drawn at regular intervals and the hematocrit concentration is brought down to normal values within a period of weeks to months. Levels of Haemoglobin - 14 g/dL (men) 12g/dL (women), and Haematocrit <45% (men) <42% (women) were maintained to prevent further complications.

Aspirin:

Low dose Aspirin is efficacious for preventing thrombosis and controlling microvascular painful symptoms (erythromelalgia) in patients with Polycythemia Vera without a bleeding diathesis[4]. (ECLAP –

European Collaboration on Low-dose Aspirin in Polycythemia Vera)

Hydroxyurea:

The most commonly used myelosuppressive chemotherapeutic agent for PV is hydroxyurea given through oral route. It helps to reduce both the hematocrit concentration and the platelet count. There is some controversial evidence that after long-term therapy hydroxyurea is associated with an increased risk for patients to develop acute leukemia[5] so this treatment method is frequently avoided as therapy for younger patients.

Anagrelide:

Anagrelide is a cyclic adenosine monophosphate phosphodiesterase inhibitor that prevents platelet aggregation and inhibits megakaryocyte maturation and thereby decreasing platelet counts.

JAK1/JAK2 inhibitor: (Ruxolitinib)

Ruxolitinib is the first US FDA approved drug for patients with intermediate or high-risk myelofibrosis, including primary myelofibrosis, post-polycythemiavera myelofibrosis, and post-essential thrombocythemia myelofibrosis.

Interferon alpha:

Results from non-randomized long-term studies suggest a possible advantage with IFN alpha 2a compared with phlebotomy or phlebotomy plus HU in terms of better control of splenomegaly, thrombocytosis, pruritus, and thrombohemorrhagic complications[6].

Imatinibmesylate:

Use of the tyrosine kinase inhibitor Imatinib mesylate has been reported in a number of patients with PV. In most of the reports response has been limited to a reduction in phlebotomy requirement and a reduction in the size of the spleen; it has been ineffective in controlling thrombocytosis[7].

Complications:

Polycythemia Vera may lead to Cerebrovascular accidents – stroke, Myocardial infarction, Budd Chiari syndrome, pulmonary embolism, and renal failure. It may sometimes transform in to acute leukemia.

Conclusion:

The main clinical challenge in management of a young adult with acute stroke is the identification of its cause. Current diagnostic investigations allow the identification of specific cardiac, vascular and coagulation abnormalities previously undetectable. Clinical manifestations and management are usually similar to, but prognosis is often better than, those in an older population. We should aware of the association of stroke and Polycythaemia Vera while evaluating a case of stroke.

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