J. Dhaka National Med. Coll. Hos. 2018; 24 (01): 48-51

Case Report

Polycythemia Vera initially presenting with Acute Ischemic Stroke: A Case Report

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Abstract

Polycythaemia Vera (PV) is an uncommon recognized cause of ischemic stroke. In the majority of cases of PV, thrombosis in cerebral artery is the main reason for ischemic stroke and if not treated, there is chance of recurrent stroke. Here, we present a case of PV who presented with acute ischemic stroke. Investigation revealed Hb% 19.4 gm/dl, hypercellular marrow without any evidence of malignancy in bone marrow and positive JAK2 mutation. We treated this case by hemodilution with venesection and later by cytoreductive drugs. The patient responded well. Early and effective treatment of PV can prevent the recurrence of stroke and other thromboembolic complications as well as increases the chance of survival.

Keywords: Polycythemia Vera; Acute Ischemic Stroke;

Introduction

Blood disorders are an uncommon primary cause of ischemic stroke.[1] Polycythemia is one of the blood disorders, which can present with arterial and venous thrombosis.[2] Ischemic stroke is the first presenting symptoms of Polycythemia Vera (PV) in 15% cases.[3] Thrombosis is the main perpetrator of the ischemic stroke secondary to polycythemia.[4] In Bangladesh, specialist physicians face this type of presentation seldom ever in their practical life and scarcity of related publication is seen.[5] Here, we discuss a case of PV, whose initial symptom was ischemic stroke and thrombosis is thought to be a core offender of that.

Case presentation:

A70-year-old right-handed lady, hypertensive, came from Dhaka presented with weakness of the left side of the body, slurred speech and vertigo for one day. Her left-sided weakness was suddenly developed and persistent. It involved both upper and lower limbs both proximally and distally. She had slurred speech and vertigo for the same duration. She described vertigo as the spinning of the surrounding objects around her. It had no specific relation to her posture. There was no hearing loss, tinnitus or any discharge through the ear. She had an occasional headache for the last 6 months. A headache was throbbing in nature, gradually developed, persisted 10-12 hours, relieved after taking paracetamol. It was not associated with vomiting and there was no blurring of vision.There was no history of convulsion, loss of consciousness, chest pain, shortness of breath, abdominal pain or discomfort. Her bladder and bowel habit were normal. She had been suffering from hypertension for the last 10 years and was taking tab losartan potassium 100 mg once daily. Family history was unremarkable for any neurological and haematological disorder. On examination, the patient was ill-looking and cachectic. Vital signs were stable (pulse78/min, BP 140/80mm Hg). There was no prominent injected conjunctive. She had had no pedal oedema, cyanosis, clubbing or lymphadenopathy. Skin, hair and nails were healthy and there was no other significant abnormality detected on general examination. Neurological examination revealed slurred speech with intact understanding, repetition and fluency. All cranial nerves were intact. There was an increased tone in both upper and lower limb of the left side. Muscle power was 3/5 of both distal and proximal group of the muscle of both upper and lower limb of the left side. Deep tendon reflexes were exaggerated over the left side and plantar responses were extensor on the left side. Sensory examination revealed an impairment of tactile sensations including light touch, pinprick, temperature and tactile localization of left side. There was also impairment of the sense of position on the left side of the body.Respiratory and cardiovascular system examination was normal. Laboratory investigations revealed hemoglobin of 19.40

gm/dl, total red blood cells (RBC) 8.02 ×1012/L, packed cell volume (PCV) 60.55%, white blood cells (WBC) 22.50 ×109/L, platelet - 450×109/L, mean corpuscular volume (MCV) 75.5fl, mean corpuscular hemoglobin (MCH) 24pgand red blood cells distribution width (RDW-CV)was 17.40%, random blood glucose 5.18 mmol/L, serum creatinine- 1.4 mg/dl. Ultrasonogram of the whole abdomen revealed mild splenomegaly. Chest X-ray and electrocardiography were normal, Color Doppler echocardiography was normal. Computed tomography scan of the brain revealed hypodense lesion in the right temporal lobe, involving cortex and subcortical white matter. Peripheral blood film showed normocytic and normochromic RBC with crowding. WBC was mature with neutrophilic leukocytosis and platelets were increased in number, features suggestive of polycythemia. Bone marrow examination was suggestive of hypercellular marrow with increased erythropoiesis, granulopoiesis was active and maturing into segmented form and megakaryocytes are increased in number. No evidence of malignancy or parasitic infestation is found. All these features consistent with the chronic myeloproliferative disorder. Later we checked JAK 2 mutation by polymerase chain reaction and found positive. A clonal and recurrent mutation in the JH2 pseudo-kinase domain of the Janus kinase 2 (JAK2) gene in most (> 80%) polycythaemia vera patients6. So, a diagnosis of acute ischemic stroke secondary to polycythemia was made. We treated her with intravenous fluids 1000 ml immediately and phlebotomy was done once at the time of hospital stay. Hydroxyurea as a cytoreductive agent was advised. Gradually patient's haemoglobin and PCV came to 15.50mg% and 49.20 % respectively. Later prophylactically allopurinol was started. The patient was gradually improved with resolving of sensory symptoms. She came to follow-up with motor power near normal.

Discussion:

Polycythemia Vera (PV) is a clonal disorder arising in a multipotent hematopoietic progenitor cell that causes the accumulation of morphologically normal red cells, white cells, platelets and their progenitors in the absence of a definable stimulus and in the exclusion of nonclonal hematopoiesis.[7,8] The hallmark of PV is trilineage hemopoietic cell hyperplasia.[9] In 1892, it was the first reported.[10] The incidence of this disease is 2 per 1,00,000.[11] Even if, it occurs in all populations, the median age at diagnosis is 71 years. [12] Arber and his colleague et. al.[13] revised the 2008 World Health Organization (WHO) criteria of PV. The revised criteria are

1) Major criteria:

a. i. Hemoglobin >16.5 gm/dl in men or hemoglobin >16.0 gm/dl in women or
ii. Haematocrit>49% in men or >48% in women or
iii. Increased red cell mass

b. Bone marrow biopsy showing hypercellularity for age with trilineage growth (panmyelosis) including prominent erythroid, granulocytic and megakaryocytic proliferation with pleomorphic mature megakaryocytes (different in size)

c. Presence of JAK2V617F or JAK2 exon 12 mutation

2) Minor criterion:

a. Subnormal serum erythropoietin level

According to the criteria, the diagnosis of PV requires either 3 major criteria or the first 2 major criteria and the minor criterion. They also stated that major criterion number 2 (bone marrow biopsy) may not be required in cases with sustained absolute erythrocytosis, hemoglobin level >18.5 gm/dl in men (hematocrit,55.5%) or >16.5 gm/dl in women (hematocrit, 49.5%) if major criterion 3 - presence of JAK2V617F or JAK2 exon 12 mutation and the minor criterion- subnormal serum erythropoietin level is present.

The patients of PV may be asymptomatic or commonly present with nonspecific symptoms like fatigue, headache, dizziness, vertigo, tinnitus, pruritus, dyspepsia or blurring of vision.[14] Venous and arterial thrombotic complications e.g. cerebrovascular event, myocardial infarction, superficial thrombophlebitis, deep vein thrombosis, pulmonary embolism is common and present in 15% patients.[14] Schwarcz et al. revealed that three-quarters of thrombotic presentation are arterial thrombosis and a quarter is a venous thrombosis.[15] Another study revealed ischemic stroke is the first presenting symptom of PV in 15% or more those affected mentioned earlier.[3] This occur due to the propagation of a local thrombus in the cerebral arteries which is formed due to increased blood viscosity secondary to increased hematocrit, decreased cerebral blood flow and thrombocytosis.[4] One study revealed that the incidence of recurrent thrombosis risk was 5% among the individuals under 65 years and 10.9% among those over 65 years of age.[16] In this case, we thought that thrombosis is the chief perpetrator of ischemic stroke. However, in 2013 Zoraster et al. postulated that polycythemia predisposes a patient to a prothrombotic state which resulted in an unseen cardiac thrombosis which in then embolized to the cerebrum.[17]

The management of acute ischemic stroke in PV consists of combining four elements: modification of risk factors (Hypercholesterolemia, Hypertension, Diabetes Mellitus, smoking and obesity), antiplatelet therapy, phlebotomy, and cytoreduction.[18] The most expedient acute treatment is hemodilution with venesection in a patient of PV with stroke, suggested by the American heart association stroke guideline.[19] The venesection has to run out at diagnosis by removing 250-400 ml of blood every other day until hematocrit reaches 40-45%, although lower quantity and frequency is suggested in older patients and in case of the cardiovascular disease. There is also a role of aspirin and cytoreductive agent hydroxyurea in the treatment of PV with ischemic stroke as the study revealed that aspirin and hydroxyurea reduce 67% and 30% recurrence rate respectively.[20]

Here, it is necessary to mention that median survival of patients with PV from the time of diagnosis is 6 to 18 months, whereas current median survival of treated patients for those <65 and ≥65 years at the time of diagnosis was17.5 years and 6.5 years respectively.[12] So, early and effective treatment of Polycythemia Vera prevents the recurrence of stroke and other thrombotic complications as well as increases the chance of survival.

Conclusions:

Though PV is an uncommon cause of stroke, it should be kept in mind at the bottom of the list of etiologies during the management of a stroke. Hence, a stroke patient should always go a thorough clinical, haematological and radiological workup. Early hemodilution, phlebotomy, low dose aspirin and cytoreductive therapy make an optimal outcome in a patient with PV with ischemic stroke.

Consent:

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal.

Abbreviations:

MCV = Mean corpuscular volume
MCH = Mean corpuscular haemoglobin
PCV =Packed cell volume
PV = Polycythemia Vera
RBC = Red blood cells
RDW = Red cell distribution width
WBC = White blood cells
WHO = World health organization

Conflict of Interest:

None of the authors has received any grant from any funding agency in the public, commercial, or not-for-profit sectors and no conflicts of interest or associations to disclose in regards to this case report.

Acknowledgments:

We acknowledge Professor Dr. Alamgir Kabir, MBBS, FCPS (Hematology), Head, Department of Haematology, Sir Salimullah Medical College & Mitford Hospital for the haematological work-up.

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