Partial Status Epilepticus in Cerebral Venous Sinus Thrombosis, Initial Manifestation of Polycythemia Vera

Introduction

CVT Cerebral venous sinus thrombosis (CVT) is a heterogeneous disorder, with a wide spectrum of clinical presentation and marked risk factors mainly genetic or acquired prothrombotic disorders.[1] We present a case of polycythemia vera (PV) initially presenting with cerebral venous sinus thrombosis (CVT).

Case Report

A 63-year-old female patient was referred to and treated for partial tonic–clonic status epilepticus located on the right side of the body in the emergency room then in the intensive care unit. She had worsening headache and numbness on the right side that had been present for the past few days. The patient's history revealed no complaints other than occasional, nonspecific headache and no previously known chronic disease, medication, or smoking history. On physical examination, she was alert, conscious, had no nuchal rigidity and meningeal irritation symptoms and had hypoesthesia and decreased (3–4/5) motor muscle strength (Todd paralysis) on the right. The patient had leukocytosis and thrombocytosis with hematocrit 54.7%, hemoglobin 18 g/dl, platelet count 447×10^9/l, and leukocyte count as 20.85×10^9/l. Splenomegaly was detected in the ultrasound of the abdomen. Emergency diffusion-weighted magnetic resonance imaging (MRI) showed restriction in the left temporo-occipital region extending to the vertex level. Considering venous embolism, repeat brain MRI and MRI venography revealed a large left temporo-occipital region lesion extending to the vertex level that was iso-hypo dense in T1A series and hyperintense in T2A fluid-attenuated inversion recovery images. Superior sagittal sinus calibration was decreased and could not be followed clearly after posterior and inferior sagittal sinus levels. The right transverse sinus' current slowed down while no flow was observed in the left transverse sinus. Asymmetry was observed in ground activity, frequency, and amplitude between both hemispheres on electroencephalography. Further evaluation for blood abnormalities as a possible cause for thromboembolism yielded an erythropoietin level of 3.31 mIU/ml (2.59–18.5) and a hypercellular bone marrow representing a myeloproliferative disorder on aspiration biopsy. The patient was positive for Janus Kinase 2 (*JAK-2*) V617F mutation thus fulfilled the criteria for PV (hemoglobin >16 g/dl, hematocrit >48%, myeloproliferation in bone marrow, *JAK-2* V617F mutation).[2] Treatment course proceeded with low molecular weight heparin, acetylsalicylic acid, levetiracetam seizure prophylaxis for thrombosis, and phlebotomy and hydroxyurea therapy for PV including genetic counseling. During the follow-up, Todd paralysis disappeared and mild hypoesthesia remained. At the 5th month, she had normal complete blood count and MRI showed few scattered nonspecific ischemic-gliotic foci scattered in the white matter of both cerebral hemispheres. Control MRI venography retained the effects of the past dural venous sinus thrombosis as significantly decreased calibration of superior sagittal sinus and absence of signal void, especially in T2A axial sections as flow can be monitored in the superior sagittal sinus tracer.

Discussion

PV is a myeloproliferative neoplasm (MPN) characterized by clonal stem-cell proliferation caused by dysregulated *JAK-2* gene for transduction pathway in myelopoiesis. It is a chronic disorder with most common symptoms as fatigue, pruritus, abdominal pain, and constitutional complaints such as fever and weight loss.[3] Disease complications mainly (and more commonly arterial) thrombosis and bleeding could be more manifest than the disease itself and be the initial presentation. Advanced age and high hematocrit increase the risk of arterial and venous vascular events, particularly in the cerebral circulation. Proposed mechanisms are increased blood viscosity (increased number of clonal cells), easy activation of platelets, erythrocyte, and plate abnormalities that were found to be associated with *JAK-2* V617F mutation and endothelium impairment.[4] Accordingly, *JAK-2* V617F mutation is confirmed as an independent risk factor for thrombosis.[4] Dentali *et al*. investigated the frequency of PV in a series of 706 patients with cerebral vein thrombosis (CVT) and the frequency of CVT in a cohort of 2,143 MPNs (735 with PV) patients.[5] The incidence of MPN in CVT patients was 3.8%; however, among 735 PV patients, only 5 (0.7%) were documented to have CVT. Thus, the diagnosis of CVT is very uncommon in patients with an established MPN.[5] However, the prevalence of the JAK-2 V617F mutation in patients with the first episode of CVT was higher (6.6%) as 60% had the MPN diagnosis at the time of CVT while others were discovered during follow-up.[6]

This case has distinct features: CVT usually affects younger patients and has a female preponderance due to risk factors as oral contraceptives, pregnancy, and puerperium. This patient was older and did not have known risk factors. The presence of leukocytosis, thrombocytosis, and a high hemoglobin level were alerting signs for a hematological disorder. Myeloproliferative disorders are more commonly associated with arterial thrombosis. Ischemic stroke may be the first presenting symptom of PV in 15%.[7] Rather than splanchnic venous thrombosis, CVT was the presenting sign of PV in our case. This patient was also a high-risk PV patient (leukocyte count >15 × 10^9/L, age 57–66, venous thrombosis)[4] demanding careful follow-up.

The clinical course in CVT is often subacute and the most common presentation is the syndrome of isolated intracranial hypertension with headache, visual disturbances, and papilledema.[1] However, similar to our patient, less frequent than arterial stroke, some patients can admit with focal syndrome with focal deficits such as paresis and/or seizures. Seizures are more specific and common in CVT compared to other types of stroke as 12%–31.9% of patients with CVT have seizures at presentation that associated with increased mortality.[8] The seizures are classified as acute-early (before or within first 2 weeks of diagnosis) or late/remote. Acute seizures in CVT can cause neurological and systemic deterioration, status epilepticus, and death, thus effective prevention of acute seizures is of utmost importance, especially in the high-risk population based on possible predictive factors. Mahale *et al*. reported the predictive factors for the acute seizures as altered mental status (Glasgow coma scale <8), focal deficits, hemorrhagic infarct, and involvement of frontal lobe and superior sagittal sinus with high D-dimer levels which somewhat fit to our patient. Thus, a new-onset seizure in the young- and middle-aged adult should alarm for CVT.[8] The more severe presentation syndrome with encephalopathy is more common in elderly.

PV represents a unique subset among stroke patients for pathophysiology and treatment. The reported association between PVR and CVT is low but may be underestimated as CVT may be an unrecognized disorder because of nonspecific and wide spectrum symptoms.[5] The search for a myeloproliferative disorder in unexplained CVT or a *JAK-2 mutation* is considerable, especially in high-risk patients such as elderly, unexplained, and with a fulminous clinical course.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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References

1. Ferro JM, Canhão P, Aguiar de Sousa D. Cerebral venous thrombosis. Presse Med 2016;45:e429-50.
2. Arber DA, Orazi A, Hasserjian R, Thiele J, Borowitz MJ, Le Beau MM, *et al.* The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood 2016;127:2391-405.
3. Artoni A, Bucciarelli P, Martinelli I. Cerebral thrombosis and myeloproliferative neoplasms. Curr Neurol Neurosci Rep 2014;14:496.
4. Radia D, Geyer HL. Management of symptoms in polycythemia Vera and essential thrombocythemia patients. Hematology Am Soc Hematol Educ Program 2015;2015:340-8.
5. Dentali F, Ageno W, Rumi E, Casetti I, Poli D, Scoditti U, *et al.* Cerebral venous thrombosis and myeloproliferative neoplasms: Results from two large databases. Thromb Res 2014;134:41-3.
6. Passamonti SM, Biguzzi E, Cazzola M, Franchi F, Gianniello F, Bucciarelli P, *et al.* The JAK2 V617F mutation in patients with cerebral venous thrombosis. J Thromb Haemost 2012;10:998-1003.
7. Zoraster RM, Rison RA. Acute embolic cerebral ischemia as an initial presentation of polycythemia Vera: A case report. J Med Case Rep 2013;7:131.
8. Mahale R, Mehta A, John AA, Buddaraju K, Shankar AK, Javali M, *et al.* Acute seizures in cerebral venous sinus thrombosis: What predicts it? Epilepsy Res 2016;123:1-5.

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