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Case Report

Acute Management of Stroke in Patients with Polycythemia Vera

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Abstract

Polycythemia vera is a rare, BCR-ABL negative, myeloproliferative neoplasm predominantly characterized by increased erythrocytes and elevated hematocrit. Although predominantly asymptomatic, potential symptoms may include headache, dizziness, and claudication as a result of a hyper viscous and hypercoagulable state. Despite the well-known risk between PV and thrombotic events, research describing this relationship and its treatment remains underreported. In this paper, we describe a PV patient with an acute presentation of cerebral ischemic stroke treated with phlebotomy and normal saline intravenous administration.

Keywords: Polycythemia Vera; Ischemic Stroke; Fluid Resuscitation; Phlebotomy; Thrombotic Complications in PV

Introduction

Polycythemia vera (PV) is a myeloproliferative neoplasm marked predominantly by an increase in erythrocytes resulting in elevated hematocrit [1]. It is associated with proto-oncogene mutations, of which the most common is the JAK2 V617F mutation [2]. This mutation is particularly represented in PV patients affected by cerebral infarction [3,4] due to its association with increased blood viscosity, impaired venous drainage, and altered platelet function, ultimately causing decreased cerebral blood flow (Figure 1) [5,6].

The acute treatment of patients who present with acute stroke associated with PV requires not just diagnostic evaluation and intervention of vascular thromboses, but also immediate reduction of viscosity by phlebotomy and the administration of intravenous fluids [8,9]. The acute management of the hyperviscous and rheologic implications of reduced microvascular flow within the area of the ischemic penumbra associated with PV strokes requires immediate therapy [10-12]. Hemorrhagic transformation after acute ischemic stroke caused by PV must also be considered [13-18]. There is a paucity of literature that describes the emergency treatment protocol for addressing stroke in this special population. We present a patient with an evolving brainstem stroke whose evolution was dependent on perfusion pressure, viscosity, and improvement of rheologic microvascular flow through the judicious maintenance of blood pressure with saline infusions in order to maintain pressure and reduce viscosity with simultaneous phlebotomy.

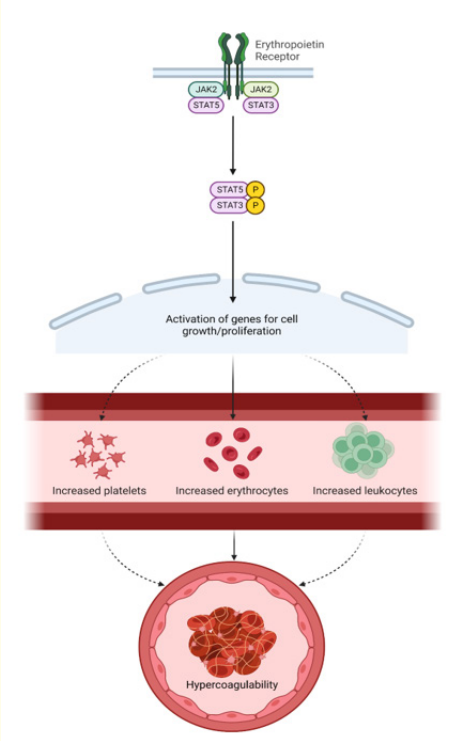

Figure 1: The JAK2 V617F mutation results in a constitutively active JAK2 protein in the absence of erythropoietin. This results in overactivation of STAT signaling (most notably STAT5 and STAT3), leading to increased proliferation of hematopoietic cells. Ultimately, the increase in erythrocytes, platelets, and leukocytes leads to an increase in blood viscosity and therefore, a hypercoagulable state. (Regimbeau, 2022;2 Adapted from How et al. 20237} (Created with Biorender.com).

Case Report

The patient is a 57-year-old gentleman with a past medical history of JAK2 V617F-positive PV for five years and was treated with 500mg of hydroxyurea and 81 mg of aspirin daily. His past medical history also includes hypertension, hyperlipidemia, myocardial infarction status post-stent placement, and a splenectomy following a motor vehicle accident at the age of 17. Between 2017-2018, he had been experiencing transitory diplopia associated with exertion. His longest episode of diplopia lasted 3 hours when he was visiting his sister in Denver, Colorado at 6000 feet elevation. He was on antihypertensive agents and cholesterol-lowering agents. The patient had a CT contrast allergy.

Six hours prior to admission, the patient awakened with double vision and slightly slurred speech. When the patient arrived in the emergency department, he was also unable to walk well because of ataxia, and his speech became more dysarthric. Vitals were remarkable for a pressure of 110/60, respirations 16/min, pulse 72 bpm, temperature 98.6 °F, oxygen saturation 100%. The patient received an immediate non-contrast CT scan of the head with subsequent CTA of the head and neck, which were both negative. Because of the IV contrast allergy, the patient was given 50 mg Benadryl and 200 mg IV Hydrocortisone succinate. The laboratory data revealed a hematocrit of 47% and a hemoglobin of 17 mg/dL. Other laboratory data were unremarkable.

While in the emergency department, physical exam revealed worsening dysarthria, complete paralysis of the right hand and right facial droop, and significant past-pointing of the right hand. At this point, the patient was quickly treated with 500cc phlebotomy with simultaneous administration of 2000cc of normal saline over the period of 1 hour.

With the completion of phlebotomy and the infusion of 2000cc to maintain blood pressure above 120, the patient's dysarthria, paralysis of the right arm, and right facial droop improved to the extent that he was able to use a cell phone with his right hand and speak with his wife. Two days later, MRI Head with and without IV contrast was done. T2/FLAIR showed hyperintensity with diffusion restriction in the left thalamus, which indicated acute ischemia of the left thalamus.

Discussion

The literature regarding the diagnosis and treatment of acute CVAs and TIAs in patients with PV describes, in general terms, the need to reduce viscosity through phlebotomy and the administration of fluid [19,20]. However, there are no specific protocols that guide the clinician during the tenuous time of the first moments after presentation [21,22]. Currently, a reduced percentage of patients with PV who present with CVA have macrovascular thrombosis amenable to fibrinolysis or thrombectomy [11,23,24]. In addition, the administration of thrombolytics with or without thrombectomy is fraught with the dangers of post-intervention hemorrhage, which has been reported in patients with PV [13-18].

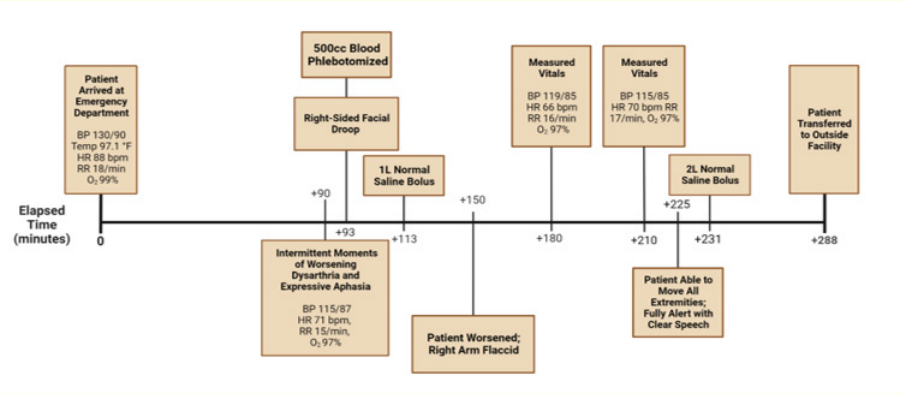

Figure 2: Schematic representation of clinical course timeline, with key clinical symptomatology and therapeutic actions detailed.

Therefore, the need to immediately reduce viscosity through phlebotomy and hydration is the most common initial therapy for patients with CVAs and evolution who have PV [19-21]. This case demonstrates the need to not only reduce blood volume through phlebotomy during which the patient began to deteriorate because of the presumed reduction of cerebral blood flow, but also the necessity to concomitantly maintain perfusion pressure with the administration of generous quantities of normal saline. Thrombotic complications occur rarely in patients with well-managed PV [1]. Naturally, it is imperative for the physician to obtain an accurate history to identify a patient with high-risk PV, [12,25] indicated in our case by our patient's prior history of MI as well as an age approaching 60.

Whether this patient's deterioration following phlebotomy was a function of reduced cerebral blood flow is not known, but the patient's positive response to a second liter of crystalloid within 15 minutes of that bolus reflects the delicate balance between cerebral blood flow and viscosity in these patients. The delicacy of this patient's cerebral blood flow was also evidenced by the patient's previous history of recurrent TIAs in high-altitude environments. These episodes seemed to be related to compensatory hyperviscosity secondary to the high altitude [26,27], since the CTAs and MRAs revealed patent cerebral blood vessels.

Typically, the clinician would otherwise not fluid resuscitate patients undergoing acute stroke to the extent that was done in this specific case [28]. Current thoughts on the amount of fluid resuscitation during acute stroke are mixed, with no clear consensus on either a liberal [29-31] or a restrictive [32,33] approach. This case represents, per the flowsheet in Figure 2, the delicate nature of the management of the rheologic complications of microvascular blood flow in this group of patients and suggests that simultaneous administration of higher volumes of fluid should accompany phlebotomy. Bolus quantities as little as 500cc have been shown to produce a measurable increase in cerebral blood flow [34]. This patient's outcome is suggestive of the need to maintain perfusion pressure as well as reduce viscosity. Recognition of this is highly dependent on eliciting the patient's history of PV on admission to the ED. For those patients whose blood pressure is low, especially in the instance of hypertension prior to phlebotomy, it may be wise to provide a buffer with 1L of normal saline while carefully monitoring the clinical situation.

Conclusion

In conclusion, management of acute ischemic stroke in PV patients may require a judicious balance of reduction of blood viscosity through phlebotomy while maintaining adequate cerebral perfusion via fluid resuscitation. In this particular case, phlebotomy accompanied by a liberal fluid resuscitation strategy was successful in preventing rheologic complications due to compromised cerebral microvascular blood flow and improving clinical symptoms of stroke. In this regard, phlebotomy with concomitant fluid administration and intensive clinical monitoring should be considered when managing stroke in PV patients.

Conflict of Interest

The authors declare that there are no competing interests, personal financial interests, funding, or employment to disclose.

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