

## Psychiatric Manifestations in Polycythemia Vera: A Case of Refractory Delirium and Psychosis Responding to Hematological Treatment

Polisitemia Verada Psikiyatrik Belirtiler: Hematolojik Tedaviye Yanıt Veren Dirençli Deliryum ve Psikoz Olgusu

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### To the Editor,

Neuropsychiatric symptoms are among the less common manifestations of polycythemia vera (PV), a myeloproliferative neoplasm characterized by increased red blood cell mass and associated complications. While depression, delirium, and psychosis have been reported in PV, our understanding of their pathophysiology and optimal management remains limited [1,2,3,4,5]. The hypothesized mechanisms for psychiatric symptoms in PV include cerebral hypoperfusion due to hyperviscosity, reduced brain metabolism, and the development of microischemic areas [6]. Previous reports suggest that these symptoms are often resistant to conventional psychiatric treatments and are better managed by addressing the underlying hematological condition [5]. In this letter, we present a 68-year-old man with PV who developed refractory neuropsychiatric symptoms, emphasizing the need for multidisciplinary collaboration.

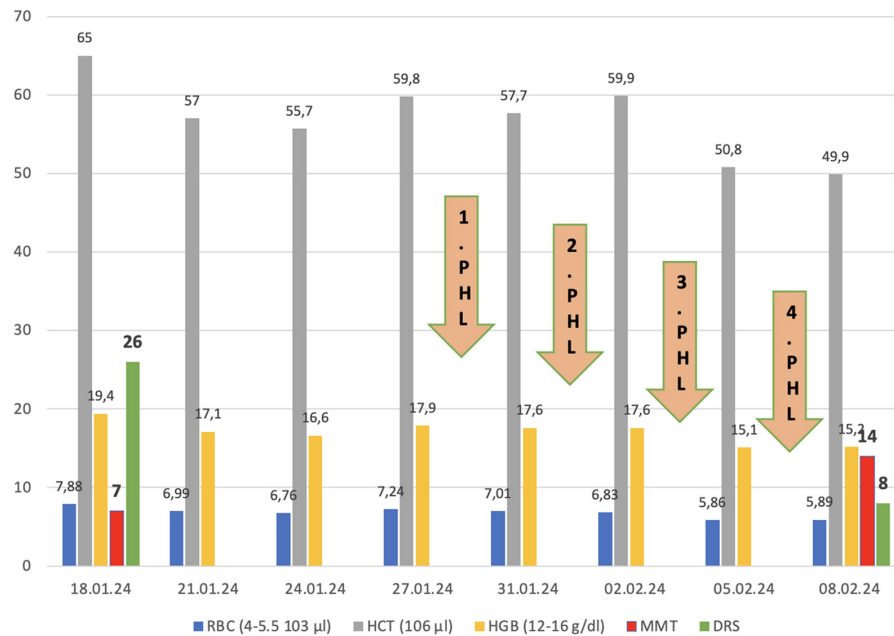
A 68-year-old retired man with a prior stable work history presented with a 4-month history of left-hand weakness, followed by progressive cognitive decline over the past month. His symptoms included disorientation, worsening forgetfulness, suspiciousness toward his wife (jealous delusions), grandiose delusions (claiming to be the president), and escalating verbal and physical aggression. These symptoms prompted an initial admission to the neurology department for further investigation.

The patient had been diagnosed with PV 7 years prior, confirmed by *JAK2* mutation positivity. He had been treated with phlebotomy and hydroxyurea for 2 years, but he discontinued treatment 5 years ago. He had no prior psychiatric history or significant medical conditions until the onset of

the aforementioned symptoms and had not been taking any medications. Brain magnetic resonance imaging conducted during his admission revealed chronic ischemic hyperintensities in the bilateral white matter and an encephalomalacic area in the right parieto-occipital lobe. Laboratory tests showed elevated hemoglobin levels of 19.4 g/dL, hematocrit of 65%, white blood cell count of  $16.5 \times 10^3/\mu\text{L}$ , and platelets of  $791 \times 10^3/\mu\text{L}$ . On psychiatric evaluation, the patient scored 28/30 on the Delirium Rating Scale (DRS) and 7/30 on the Mini Mental State Examination (MMSE). Based on his clinical presentation and test results, the patient was diagnosed with delirium secondary to PV.

Initial treatment with haloperidol at 5 mg/day was initiated but yielded no significant improvement in symptoms. Hematology consultation was sought and alternate-day phlebotomy was started. After five sessions, the patient's hematocrit levels decreased to 49%. Given his age and history of stroke, the patient was classified as high risk and started on hydroxyurea and aspirin therapy along with phlebotomy [7]. Following hematological intervention, there was a marked improvement in his psychotic symptoms and resolution of delirium (DRS score improved to 6/30; Figure 1). However, cognitive dysfunction persisted, with only partial improvement noted (MMSE score improved to 15/30; Figure 1). After 13 days of haloperidol treatment, the patient's psychiatric medication was switched to risperidone at a dose of 2 mg/day. The patient was discharged with ongoing hematological treatment and risperidone at 2 mg/day for residual psychiatric symptoms.

The mechanisms underlying neuropsychiatric symptoms in PV remain unclear. Cerebral hyperviscosity and reduced brain metabolism due to slowed cerebral circulation have



**Figure 1.** Temporal changes in hematological parameters and neuropsychiatric scale scores during sequential phlebotomy sessions. RBC: Red blood cells; HCT: hematocrit; HGB: hemoglobin; MMT: Mini-Mental Test; DRS: Delirium Rating Scale; PHL: phlebotomy.

been proposed as possible contributors [6,8]. The presence of microischemic areas may also play a role. Consistent with prior reports, our patient's psychiatric symptoms were resistant to conventional treatments but showed significant improvement with hematological management [1,2,3,5]. This supports the hypothesis that such symptoms are a result of the disease's progression and are reversible with appropriate hematological intervention.

Our findings align with studies suggesting that psychiatric manifestations in PV may indicate advanced disease or progression to myelofibrosis [3]. However, the persistence of cognitive impairment despite the improvement in delirium in our patient supports hypotheses suggesting an uncertain relationship between the reduction in hematocrit levels and the recovery of cognitive functions [9]. While PV treatment may reverse the decreased cerebral blood flow caused by increased blood viscosity and improve certain cognitive functions [10], in some cases the permanent cognitive deficits may be explained by lacunar infarcts resulting from prolonged elevated hematocrit levels [11], although no such infarcts were observed in our patient. Early recognition and collaboration with hematologists are crucial for managing these cases effectively and preventing unnecessary psychotropic interventions.

In patients with no prior psychiatric history, late-onset, atypical, and treatment-resistant psychiatric symptoms should prompt consideration of PV as an underlying cause. Psychiatric manifestations during the course of PV require

immediate interdisciplinary collaboration, with hematological management prioritized to address the root cause of symptoms. Furthermore, from a hematological perspective, monitoring and assessing psychiatric symptoms during the course of PV can provide valuable insight into disease severity and guide timely interventions.

**Keywords:** Polycythemia vera, Delirium, Psychosis, Phlebotomy

**Anahtar Sözcükler:** Polisitemia vera, Deliryum, Psikoz, Flebotomi

### Ethics

**Informed Consent:** Written informed consent was obtained from the patient and the patient's legal guardian for the publication of this case report and any accompanying images.

### Footnotes

#### Authorship Contributions

Surgical and Medical Practices: Y.E.Y., H.I.E., E.G., N.Ç.T., Ö.D.B.; Concept: Y.E.Y., H.I.E., E.G., N.Ç.T., Ö.D.B.; Design: Y.E.Y., H.I.E., E.G., N.Ç.T., Ö.D.B.; Data Collection or Processing: Y.E.Y., H.I.E.; Analysis or Interpretation: Y.E.Y., H.I.E., E.G., N.Ç.T., Ö.D.B.; Literature Search: Y.E.Y., H.I.E.; Writing: Y.E.Y., H.I.E., E.G., N.Ç.T., Ö.D.B.

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