Chuvash polycythemia in a 53-year-old male: A case report

Timothy Hall

ABSTRACT

Introduction: Chuvash polycythemia is a rare autosomal recessive hypoxia-sensing disease and is characterized by increased serum erythropoietin and red blood cells. Although it is relatively more common in the Chuvashia Republic of the Russian Federation, cases have been occurred worldwide.

Case Report: The case reported here is a 53-year-old male who presented with unprovoked left lower extremity deep vein thrombosis (DVT). After excluding other hypercoagulative and myeloproliferative disorders, the diagnosis of Chuvash polycythemia was confirmed by locating the VHL P81S mutation. The DVT was treated and other malignant syndromes were ruled out.

Conclusion: Chuvash polycythemia can present similarly to other myeloproliferative diseases, like polycythemia vera. However, treatment modalities, like phlebotomy and chemotherapy, used for those diseases were not needed in this case of Chuvash polycythemia. Careful monitoring and prevention of possible thrombotic events may be enough to manage such patients.

Keywords: Chuvash, Erythrocytosis, Hypoxia, Polycythemia, Thrombotic

INTRODUCTION

Chuvash polycythemia is a hereditary augmented hypoxia sensing disorder [1]. The mutation causing this disorder appears more commonly in the Chuvashia Republic of the Russian Federation, however cases have been reported worldwide [1, 2]. Patients typically present with increased serum erythropoietin and red blood cells. The mutation responsible for this disorder is located on the von Hippel Landau (VHL) gene [3]. This gene is involved in the production of hypoxia-inducible factor (HIFs), which are important regulators in the response to hypoxia. In hypoxic conditions, HIFs stimulate increased production of erythropoietin, whereas in normoxic conditions, the VHL protein will degrade HIFs. The mutation in the VHL protein prevents the degradation of HIFs leading to increased serum erythropoietin even in normoxic conditions [4]. Malignancies like renal cell carcinoma, pheochromocytoma, neuroendocrine tumors, and hemangioblastomas are usually seen with heterozygous mutations of VHL. Despite involving a VHL mutation, Chuvash polycythemia has not been associated with malignancies seen in classic VHL tumor predisposition syndromes [3]. However, Chuvash polycythemia, similar to other forms of polycythemia, has been associated with arterial and venous thrombosis, bleeding episodes, cerebral vascular events, and premature mortality.

CASE REPORT

A 53-year-old male presented with an unprovoked lower left extremity deep vein thrombosis (DVT). The patient had already experienced another DVT that was treated about a year ago. He complained of pain and swelling of the leg and stated that he felt fatigued by some time. Past medical history includes hypertension, gastroesophageal reflex disease, and diverticulitis. Past
surgeries include open reduction and internal fixation of the fibula and tonsillectomy. Hematocrit of the initial visit was 49% (ref: 41.5–50.4%) and erythropoietin levels were 18.7 μU/mL (ref: 2.6–18.5 μU/mL). Other lab values from the initial visit showed that the patient had iron deficiency which could have contributed to the fatigue, but attempts to treat it did not result in an increase in ferritin or resolution of symptoms (Table 1).

The DVT was treated with Rivaroxaban 10 mg once a day. Bone marrow biopsy showed mildly hypercellular (60–70%) bone marrow with trilineage hematopoiesis. Analysis showed that this patient was negative for JAK 2 V617F mutation as well as exon 12, and negative for calreticulin (CALR) and myeloproliferative leukemia (MPL) mutation. In addition, erythropoietin receptor (EPOR) mutation analysis also returned negative. Being negative for this mutation, polycythemia vera was ruled out for this patient. Insulin-like growth factor receptor 1 (IGF 1R) analysis was inconclusive and eventually a mutation on VHL P81S was found. Although abnormal, as seen in Table 2, his hematocrit and hemoglobin remained stable throughout the time we followed the patient (Table 2).

Following the discovery of the VHL mutation, a magnetic resonance imaging (MRI) was performed to screen for central nervous system (CNS) vascular malformations and possible malignancy syndromes. Other than finding a chronic T12 compression fracture that was previously documented, the MRI was negative for vascular malformations and showed no malignancies. The patient continues his dose of Rivaroxaban 10 mg once a day and his complete blood count (CBC) values and symptoms are monitored closely approximately once a month at our outpatient hematology clinic for any changes.

**DISCUSSION**

In our patient, the diagnosis of Chuvash polycythemia was made by finding the VHL mutation. Chuvash polycythemia presented similarly to other myeloproliferative diseases, like polycythemia vera. Both diseases present with high red blood cell count and hypercellular bone marrow with trilineage growth [5]. Clinically, both can present with increased frequency of unprovoked thrombotic events, like deep vein thrombosis. However, in our patient and in Chuvash polycythemia because of differing pathophysiology of the disease, erythropoietin levels are normal to high and, despite the high RBC count, low levels of hemoglobin was present. Because of relative rarity of this disorder, the proper treatment course for this disease is not widely agreed on. Phlebotomy and chemotherapy are some proposed modalities of treatment [1, 3]. However, based on our patient’s lab values, it was decided that those treatments were unnecessary and monitoring was sufficient. After ruling out any malignancy syndromes, direct oral anticoagulants were felt to be the only necessary intervention for the patient’s thrombotic event.

This report is limited by short period of time that this patient was followed. In order to see if our interventions are sufficient to prevent further adverse outcomes, our patient needs to follow by a longer period of time. In addition, a more comprehensive coagulation panel is needed to monitor the progression of the patient’s condition and to see if the patient is on proper anticoagulation. Further studies needs to be done with a larger sample size to properly determine what treatment course can alleviate the symptoms of Chuvash polycythemia and improve lab values.

<table>
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<tr>
<th>Table 1: Laboratory values on initial visit</th>
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<tr>
<td>Hemoglobin (14–17.5 gm/dL)</td>
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<tr>
<td>Red blood cell (RBC) (4.5–5.9 million cells/mcL)</td>
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<tr>
<td>White blood cell (WBC) (4.5–11.0 × 10^9 cells/L)</td>
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<tr>
<td>Platelet (150–450 × 10^9 platelets/L)</td>
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<tr>
<td>Ferritin (30–400 ng/mL)</td>
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<td>Mean corpuscular volume (MCV) (80–96 fl)</td>
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<th>Table 2: Hematocrit and hemoglobin over the course of 6 months</th>
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<tr>
<td>RBC (4.5–5.9 million cells/mcL)</td>
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<tr>
<td>HGB (14–17.5 gm/dL)</td>
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<td>HCT (41.5–50.4%)</td>
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<td>MCV (80–96 fl)</td>
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RBC: red blood cell; HGB: hemoglobin; HCT: hematocrit; MCV: mean corpuscular volume.
CONCLUSION

Chuvash polycythemia is a rare autosomal recessive hypoxia-sensing disease and is characterized by increased serum erythropoietin and red blood cells. This case report demonstrates that individuals diagnosed with this disease do not necessarily need to be treated with phlebotomy or chemotherapy. Instead careful monitoring of laboratory values and prevention of thrombotic events may be sufficient to treat these patients. In addition, despite possessing a VHL mutation, there is no evidence of any associated malignancy syndromes.

REFERENCES


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Author Contributions
Timothy Hall – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Guarantor of Submission
The corresponding author is the guarantor of submission.

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Conflict of Interest
Author declares no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.

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