Case Report

Simultaneous Occurrence of Beta Thalassemia Trait and Polycythemia Vera - A Case Report

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Date of submission: *12/11/2025*
Date of acceptance: *26/12/2025*

ABSTRACT

The coexistence of beta thalassemia trait (also known as heterozygous beta thalassemia, HBT) and polycythemia vera (PV) is extremely rare, with only a few cases reported in medical literature. This combined condition is significant because the two disorders have opposing effects on hemoglobin (Hb) and hematocrit (Hct), which can mask the presence of each other and delay diagnosis. Missing or delaying the diagnosis of PV can lead to deleterious effects due to the high risk of thrombosis. We present a case of an elderly male whose diagnosis of PV was delayed due to the coexistence of HBT and other comorbidities, and review the relevant literature.

Keywords: *Beta thalassemia trait, Polycythemia Vera, JAK2, Stress erythropoiesis.*

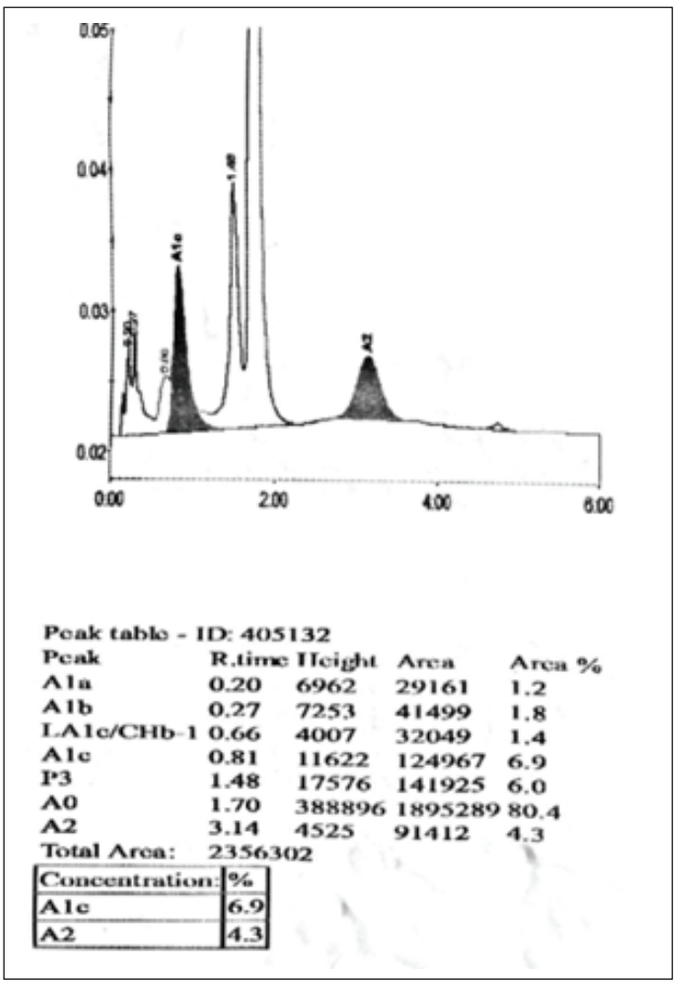
INTRODUCTION

Thalassemia is a group of inherited blood disorders caused by mutations in the globin gene, resulting in defective synthesis of one or more globin chains of hemoglobin (Hb). Alpha thalassemia is caused by deficient production of alpha globin, while beta thalassemia results from deficient production of the beta globin component of Hb. Beta thalassemia is common in the Mediterranean, the Middle East, and North Africa[1]. Beta thalassemia trait/minor manifests as mild anemia, asymptomatic, and does not require transfusion[2]. The complete blood count (CBC) in HBT typically shows microcytosis with erythrocytosis (largely due to stress erythropoiesis)[1]. The diagnosis of beta thalassemia is confirmed by finding an increased percentage of Hb A2 in Hb electrophoresis. Polycythemia vera is a myeloproliferative neoplasm characterized by erythrocytosis caused by the mutant JAK2 protein kinase[3]. It is associated with an increased risk of arterial and venous thromboses, especially in older patients and patients with coexistent cardiovascular risk factors[1]. There are a few case studies showing an association between HBT and PV. It is possible that chronic stress erythropoiesis due to beta thalassemia can lead to ineffective erythropoiesis and also increase the risk of JAK2 mutation[2]. We reviewed the literature regarding the coexistence of HBT and PV, and discussed the hypothesis of a causal relationship between the two conditions.

CASE PRESENTATION

78-year-old male, diabetic, hypertensive, CKD with a history of ischemic stroke, referred to Hematology OPD for persistent leukocytosis. He had mild dizziness and occasional vertigo. His CBC showed Hb 13.5 gm/dl, RBC count 8.0x1012/L, HCT 42.8%, MCV 53.5fl, WBC 32.65x109/L, neutrophils 49.6%, lymphocytes 21.8%, eosinophils 26%, and platelets 332x109/L. Iron profile & Hb electrophoresis were checked for microcytosis, which revealed Iron deficiency and beta thalassemia trait (HPLC showed HbA2 4.3% (normal range: 0-3.5%), Fig. 1). Family screening revealed his daughter also has beta thalassemia trait. Reactive causes of leukocyto-

sis and erythrocytosis were excluded. Normal hemoglobin level with erythrocytosis despite having iron deficiency and beta thalassemia trait raises the suspicion of Polycythemia Vera (PV). Myeloproliferative neoplasm (MPN) panel and Chronic Eosinophilic Leukemia (CEL) panel were done for the evaluation of erythrocytosis and leukocytosis with eosinophilia. The diagnosis of polycythemia vera was confirmed by identifying the JAK2 V617F mutation; the CEL panel was negative. Abdominal ultrasound showed no organomegaly. The patient was on low-dose aspirin and clopidogrel for his underlying conditions. Hydroxyurea



Peak table - ID: 405132

Peak	R.time	Height	Area	Area %
A1a	0.20	6962	29161	1.2
A1b	0.27	7253	41499	1.8
LA1c/CHb-1	0.66	4007	32049	1.4
A1c	0.81	11622	124967	6.9
P3	1.48	17576	141925	6.0
A0	1.70	388896	1895289	80.4
A2	3.14	4525	91412	4.3
Total Area:			2356302	

Concentration:	%
A1c	6.9
A2	4.3

Figure 1: HPLC shows HbA2 4.3%

was added. On regular follow-up, he showed a good response to HU and low-dose Aspirin. On his last follow-up (8 months after initiation of HU), CBC showed Hb 12.2 gm/dl, RBC 4.4x1012/L, Hct 38.3%, MCV 86fl, WBC 10.46x109/L, neutrophils 53%, lymphocytes 30%, eosinophils 11%, and platelets 160x109/L.

DISSCUSSION

Beta thalassemia is characterized by a decreased production of the beta subunit of Hb[1]. Phenotypically, it is of three types: thalassemia major, thalassemia intermedia, and thalassemia minor/trait. Beta thalassemia major is usually diagnosed during the first two years of life, and these patients are transfusion dependent. Beta thalassemia intermedia presents later and does not require regular blood transfusions. Beta thalassemia trait causes mild or asymptomatic anemia, rarely requiring transfusion or any treatment[1].

Paterakis et al. showed that individuals with HBT had significantly higher reticulocyte counts, which were proportional to the degree of anemia[4]. This statement is in agreement with the findings of Vedovato et al., who found that levels of serum Erythropoietin (Epo) were higher in HBT subjects than in normal controls[5]. It can be postulated that higher levels of Epo result in increased stimulation of the EpoR/JAK2/STAT signaling pathway, thus increasing the probability of JAK2 mutations[5].

In the present case, the patient is a case of beta thalassemia trait and polycythemia vera (JAK2 mutation positive). Polycythemia vera is a myeloproliferative neoplasm caused by a mutation in JAK2 (95% cases), which leads to an uncontrolled, neoplastic proliferation of hematopoietic stem cells. This leads to an increase in the proliferation of RBCs with a secondary increase in WBCs and platelets due to simultaneous stimulation of these cell lines. The presenting feature includes headache, vertigo, dizziness, claudication, thrombosis, itching, and visual disturbances as a result of the increased viscosity of blood4. Few case studies showed an association between beta thalassemia and polycythemia vera[6].

A list of the literature showing cases of HBT with PV is shown in Table 1[1,7-11]. A patient with beta thalassemia trait who suddenly experiences a rise in

	present case	Khan AA[2]	Kontas K[1]	De Sloovere et al.[7]	Lopes da Silva and Silva[8]	Ifran et al.[9]	Thomas[10]	Castro[11]
Age	78	70	84	60	75	68	71	48
Gender	M	M	F	F	F	F	F	F
Hyperviscosity	Yes	No	Yes	Yes	No	Yes	Yes	No
Splenomegaly	No	No	No	Yes	Yes	Yes	No	Yes
RBC (x10^{12}/L)	8.0	6.0	7.0	10.5	9.0	9.3	7.4	8.0
Hb (g/dl)	13.5	14.8	15.8	19.8	15.4	15.5	15.6	14.4
Hct (%)	42.5	44.7	50.4	58.6	51.8	59.0	48.1	42.0
MCV (fl)	53.5	63.7	69.0	56	59.2	NA	65	70
HbA2 (%)	4.3	5.3	3.8	4.1	4.3	4.7	5.5	4.9*
EPO	ND	Low	Low	Low	Low	Low	Low	ND
JAK2 mutation	Yes	Yes	Yes	Yes	Yes	ND	ND	ND
Treatment given	Aspirin HU	Aspirin HU	Aspirin HU	Aspirin HU	Aspirin HU	Phlebotomy	Phlebotomy	Busulfan Phlebotomy Mustard

Table1: Clinical and laboratory parameters of the reported cases of co-occurrence of HBT and PV

* The patient was heterozygous for both beta thalassemia and sickle cell disease.
RBC: red blood cell; Hb: hemoglobin; Hct: hematocrit; MCV: mean corpuscular volume; EPO: erythropoietin; NA: not available; ND: not done; HU: Hydroxyurea; HBT: heterozygous beta thalassemia; PV: polycythemia vera

hemoglobin and hematocrit levels should have a differential diagnosis of myeloproliferative neoplasm.

Iron deficiency is found in most of the polycythemia patients, either at diagnosis or during the course of the disease[12]. Reasons include overutilization of iron by the hyperplastic erythropoiesis, blood loss from the gastrointestinal tract, and or therapeutic venesection[12]. Our patient is also having an iron deficiency, likely due to hyperplastic erythropoiesis.

There are no published data regarding the prevalence of JAK2 mutations in HBT. Studies showed conflicting results: Taher et al. did not find the JAK2 V617F mutation in any of the 36 Lebanese thalassemia intermedia patients[13]. Similarly, Vlachaki et al. detected no JAK2 V617F mutation in 20 Greek beta thalassemia patients[6]. On the contrary, Asadi et al. have detected this mutation in 19% of patients with beta thalassemia major[14]. Interestingly, most of the HBT patients who developed PV were female. This statement is supported by the findings of Vedovato et al., who observed that women with HBT had significantly higher levels of serum Epo than men with HBT[5]. All of these findings suggest that a causal relationship between HBT and PV is possible. More prospective studies are needed to find out the correlation between HBT and PV.

CONCLUSION

Polycythemia vera coexisting with Beta Thalassemia Trait may elude diagnosis for a considerable time due to the masking effect of one another, exposing the patient to the risk of serious complications, including fatal thrombotic complications. Timely diagnosis of PV in this population requires a high index of suspicion (sudden increase in Hb and Hct level in beta thalassemia patients) and a low threshold for investigation, including search for JAK2 mutations. The prevalence of the latter in individuals with HBT, and vice versa, should be the subject of future research.

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