

The Coexistence of Polycythemia Vera and Iron Deficiency Anemia

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ABSTRACT

Polycythemia vera (PV) is a clonal myeloproliferative neoplasm mainly characterized by an abnormal increase of erythroid precursor cells leading to increased red blood cells (RBC) production that is opposite to iron deficiency anemia (IDA) of which the RBC production is decreased due to iron deficiency. This report was aimed to present one patient who had coexistence of these two opposite entities of the RBC production. She was a 47-year-old Thai who was admitted because of acute coronary syndrome and she was accidentally found to have microcytosis of RBC despite normal hemoglobin (Hb) concentration, Hb 14.7 g%, mean corpuscular volume (MCV) 70.0 fL, white blood cells 12,400/mm³, and platelet 401,000/mm³. The Hb analysis showed only A2A, with normal Hb A2 percentage. The polymerase chain reaction for alpha thalassemia-1 genotype was tested negative. Due to neither alpha- nor beta-thalassemia trait detected, the iron study was performed: Serum ferritin 6.1 ng/mL, serum iron 64 ug/dl, and total iron binding capacity 198 ug/dl. The iron storage was seemingly insufficient; hence, iron supplement was started and continued for 4 months. Her blood tests showed: Hb 18.3 g%, MCV 87.2 fl, serum ferritin 31.7 ng/ml, erythropoietin <1 IU/l, positive JAK2 V617F mutation, and normal oxygen saturation. The diagnosis of PV was definitely concluded and she was finally treated with hydroxyurea and occasional phlebotomy. In case of the coexistence of PV and IDA, only the microcytosis of RBC could be recognized. And with its normal Hb concentration, the microcytosis should not have been simply presumed to be due to thalassemia and/or hemoglobinopathy heterozygosity that does not have any clinical significance outside the antenatal clinic. In contrast, this coexistence needs some proper interventions for better outcome.

Key words: Iron deficiency anemia, microcytosis, polycythemia vera

INTRODUCTION

Polycythemia vera (PV) is one of myeloproliferative neoplasms, a clonal proliferation of hematopoietic stem cell mainly involving the erythroid precursor cells in the bone marrow. It is mainly characterized by increased red blood cell (RBC) mass. WHO revises the criteria for its diagnosis which consist of three major criteria (1) hemoglobin (Hb) concentration >16.5 g% for males, >16.0 g% for females, (2) presence of JAK-2 mutation, and (3) panmyelosis of the bone marrow while the minor criterion is (1) subnormal serum erythropoietin (EPO) level. To make the diagnosis, it needs all three major criteria or

the first two major criteria and minor criterion.^[1] Most cases are asymptomatic or may have non-specific symptoms such as fatigue and headache.^[2] On the contrary, iron deficiency anemia (IDA) is an acquired anemia characterized by the decreased production of Hb due to iron insufficiency leading to microcytic hypochromic anemia.^[3,4] Like PV, patients with IDA may be asymptomatic or may have non-specific symptoms.^[5] These two entities seem to be opposite for the aspect of the RBC production. When they emerge together, the high Hb concentration of PV may be completely masked by the microcytic anemia due to iron deficiency until the patient is concerned as though she had only isolated IDA^[6] or IDA may lower Hb concentration till normal until PV

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has never been suspected.^[7] Herein, we reported a case of coexistence of PV and IDA whose interaction was perfectly appropriate until the definite diagnosis of each entity was not suspected.

CASE PRESENTATION

A 47-year old woman was admitted because of repeated acute chest pain and chest tightness for 4 days. The pain usually originated at the mid of a chest, spread to the left side and lasted for 15 min. It was always triggered by exertion. Her physical examination revealed no anemia and no splenomegaly. The repeated cardiac enzymes and the electrocardiogram study were unremarkable. The cardiac catheterization showed 50% stenosis of the left anterior descending artery. Hence, she was diagnosed as having acute coronary syndrome and treated with medications including isosorbide, aspirin, simvastatin, warfarin, omeprazole, bisoprolol, and clopidogrel.

Her routine complete blood count by the automated hematology analyzer: Hb 14.7 g%, Hct 47.5%, mean corpuscular volume (MCV) 70.0 fL, mean corpuscular hemoglobin (MCH) 21.7 pg, MCH concentration (MCHC) 31.0 g%, red cell distribution width (RDW) 19.5%, white blood cells (WBC) 12,400/mm³, and platelet 401,000/mm³.

Because of the prominence of the microcytosis of RBCs without anemia, thalassemia and/or hemoglobinopathy heterozygosity were first considered and the Hb analysis was performed using the high performance liquid chromatography method and it showed only A₂A, Hb A₂ 3.0% and further investigation was genotype study for alpha thalassemia and it was shown negative for alpha thalassemia-1 genes, both Southeast Asian and Thai deletions.

Further investigation was iron study: Serum ferritin 6.1 ng/ml, serum iron 64 ug/dl, and total iron binding capacity 198 ug/dl. Other blood tests included creatinine 0.96 mg%, cholesterol 169 mg%, low-density lipoprotein 91 mg%, triglyceride 135 mg%, fasting blood sugar 73 mg%, lactate dehydrogenase (LDH) 433 U/L (normal 240–480), and uric acid 7.3 mg%.

Due to the insufficiency of the iron storage, she was continuously supplemented with iron tablets every day for 4 months. The blood tests were performed again: Hb 18.3 g%, Hct 55.8%, MCV 87.2 fL, MCH 28.6 pg, MCHC 32.7 g%, RDW 17.3%, WBC 10,800/mm³, platelet 329,000/mm³, and serum ferritin 31.7 ng/ml. She denied smoking and had no chronic cyanotic heart or lung diseases. Moreover, she did not have excoriation on the additional physical examination. Essential investigations for polycythemia were performed: Serum EPO <1 IU/l (normal 3.7–36 IU/l), positive for JAK2 V617F mutation, ESR 1 mm/h, LDH 1,143 U/L and

normal oxygen saturation. The bone marrow biopsy showed markedly increased cellularity of trilineage particularly erythroid series.

She was definitely diagnosed as having PV and she was treated with oral hydroxyurea and occasional blood phlebotomy until her hematocrit could be kept around 45 g%. Then, the iron supplement was withheld. During follow-up for few years, she had never had any thrombotic event, bleeding diathesis, or splenomegaly whereas the coronary artery disease did not recur.

DISCUSSION

When an individual has the microcytosis without anemia, an attending physician always assumes it could be contributed by the thalassemia and/or hemoglobinopathy heterozygosity^[8] which are highly prevalent in Thailand.^[9] Moreover, if it happens outside the antenatal care unit, it will be mostly left without any recommendation. However, our report showed that the patient who had normal Hb level but low MCV, low ferritin,^[7,10] normal Hb analysis, and no alpha thalassemia 1 heterozygosity needed more concern because she might be presenting the initial stage of more serious disease like PV. However, only low serum ferritin is not valid for investigating JAK2 mutation.^[11]

The diagnosis of IDA in case of PV could be concluded in the initial presentation because her MCV was <76–85 fL while her ferritin was <7.1–29.8 ng/ml.^[12] When iron therapy was accomplished, namely, ferritin 31.7 ng/ml, the MCV became normal whereas her Hb level could access the Hb criterion of PV. This suggests that the IDA can affect the clonal proliferation of erythroid cells of PV. On the contrary, IDA was overlooked in the first presentation because she was free from anemia due to PV and only the microcytosis was recognized. Hence, thalassemia heterozygosity was first expected. Although microcytosis is characteristic of IDA, microcytosis without anemia is hardly possible to be IDA if lack of PV. In contrast, the MCV can be found normal in 40% of IDA^[13] especially among the elderly who always have multiple comorbidities.^[14] Patients who have only iron insufficiency, low serum ferritin, but no anemia and microcytosis, they should be supplemented with iron. Otherwise they may suffer non-specific symptoms such as fatigue, weakness, and poor concentration.^[15]

Gastrointestinal lesions such as erosion, ulcer, and *Helicobacter pylori* positivity are more commonly found in PV than the population.^[16] Many mechanisms proposed for these are altered mucosal blood flow due to hyperviscosity, increased blood histamine from increased basophil count or increased *H. pylori* infection.^[17] These lesions may contribute gastrointestinal bleeding in PV patients.^[18] Hence, PV patients may have IDA at first presentation or during its course.^[19]

Our patient refused to undergo endoscopy, so the cause of IDA in the gastrointestinal tract could not be identified.

History of thrombosis, hematocrit more than 45%, age more than 65 years, and WBC >15,000/mm³ are known as risk factors for thrombosis in PV patients.^[20] Our patient developed acute coronary artery syndrome that is less common than transient ischemic attack^[21] during having only one of these risk factors: Hematocrit >45%. However, after treatment with aspirin and keeping the hematocrit <45%, she never developed any thrombotic event again during follow-up for few years.^[22]

CONCLUSION

The diagnosis of PV in 47-year-old Thai woman was delayed because her initial Hb level appeared normal, did not access the Hb criterion of PV. Due to her prominent microcytosis without beta- and alpha-thalassemia-1 heterozygosities, iron deficiency was explored, diagnosed, and treated. After iron therapy had been accomplished, Hb level was raised, the microcytosis disappeared and polycythemia could be easily recognized and finally PV was definitely diagnosed and properly managed.

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