Paroxysmal nocturnal hemoglobinuria in the differential diagnosis of thrombocytopenia

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Abstract

Paroxysmal nocturnal hemoglobinuria (PNH) is a disease which diagnosis may be delayed due to variable clinical findings. We describe herein a case of PNH in a 21 year old woman who admitted with complaints of chronic weakness, intermittent spontaneous ecchymoses, and an intermittent abdominal pain. On laboratory tests thrombocytopenia and iron deficiency anemia without any clinical findings were found. Flow cytometric evaluations showed a PNH clone of 15% for erythrocytes, 64% for monocytes, and 60% for granulocytes. The patient was diagnosed with PNH and an eculizumab therapy was initiated. Following initiation of eculizumab therapy, the frequency of abdominal pain attacks decreased, hemoglobin level normalized, and platelet values increased slightly. In patients submitting with a triad of symptoms such as thrombocytopenia, iron deficiency anemia, and abdominal pain attacks of unknown etiology we suggest considering PNH. We also encourage physicians to share their similar observations in order to raise the knowledge on infrequent presentations of PNH.

Introduction

Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, life-threatening, hematological disorder characterized by hemolysis of the red blood cells due to activation of the complement system.1 The prevalence of the disease is estimated as 1 to 5 cases per million worldwide. Clinical triad of hemolytic anemia, bone marrow failure and thrombophilia is typical for PNH.2 The complex pathogenic mechanism of the disease is mostly discovered while some biological aspects are still under investigations. Clonal expansion of hematopoietic stem cells (HSCs) with a somatic mutation in X-linked phosphatidylinositol glycan class A (PIG-A) gene are considered to be the main cause of the disease.3 Due to this mutational PNH is considered to be a genetic hematological disorder. However this genetic abnormality is insufficient to explain the pathogenesis of bone marrow failure and thromboembolism, therefore investigations and discussions are ongoing.4 The absence of complement regulators on erythrocytes is the main reason of chronic hemolysis patients with PNH. Anemia, hemoglobinuria, fatigue, painful abdominal crises, dysphagia and erectile dysfunction are other symptoms related to intravascular hemolysis.5 The thromboembolism is consider to be also linked to hemolysis however the true pathophysiology is not clear yet. Thrombosis and renal failure are leading causes of death in PNH patients.6 Thrombocytopenia is a rare and unusual manifestation of PNH. In the literature there are insufficient data about the thrombocytopenia as initial presentation of PNH. Herein we report a 21 year-old woman with PNH presenting with thrombocytopenia misdiagnosed as immune thromocytopenic purpura.

Case Report

Twenty-one year-old woman was referred to our department at November 2014 from a medical center where she was followed for 2 years with diagnosis of immune thrombocytopenia and iron deficiency anemia. During that follow-up period she did not experience any bleeding and had moderate thrombocytopenia required not any treatment with antithrombotic drugs. However an oral iron supplementation on an occasional basis was given for anemia. Therefore she was referred to our clinic for further diagnosis and treatment. Her medical history showed that, she had been recovering while she was receiving oral iron supplementation; however her hemoglobin (Hb) levels were decreasing soon after cessation of treatment. Her thrombocytopenia ( ranged from 45,000 to 55,000/mm3) persisted and there were no clinical findings consistent with blood loss that can explain a possible iron deficiency anemia. Also according to her anamnesis she reported complaints of chronic weakness, intermittent spontaneous ecchymoses, and an intermittent abdominal pain of unknown etiology. All necessary evaluations including abdominal ultrasound, and also assessments regarding thrombosis and FMF were performed however no clinical evidence was found for her abdominal pain.

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Table 1. Laboratory results of the patient before and after Eculizumab treatment.

| Parameter                        | Pre-treatment | 2 months post-treatment |
|----------------------------------|---------------|------------------------|
| White blood cells (/mm³)          | 4800          | 6700                   |
| Hemoglobin (g/dL)                | 10.1          | 12.0                   |
| Platelets (/mm³)                  | 58,000        | 78,000                 |
| Reticulocyte (%)                 | 5.9           | 3.2                    |
| Lactate dehydrogenase (U/L)      | 547           | 227                    |
| Direct Coombs test               | (-)           | (-)                    |
| Mean corpuscular volume (fl)     | 88            | 92                     |
| Haptoglobin (mg/dL)              | 12            | 42                     |
| Serum ferritin levels (ng/mL)    | 12            | 124                    |
| Antinuclear antibodies           | (-)           | (-)                    |
| Anti-dsDNA antibodies            | (-)           | (-)                    |
| HBsAg, Hepatitis C virus and HIV serology | (-) | (-) |
| Lupus anticoagulant (lupus antibody) | (-) | (-) |

Conclusions

In conclusion, we suggest considering PNH diagnosis in patients submitting with a triad of symptoms: thrombocytopenia, iron deficiency anemia, and abdominal pain attacks of unknown etiology. We also encourage physicians to share their similar observations in order to raise the knowledge on this unusual presentation of PNH.

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