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Case Report

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MYH9-related diseases in the differential diagnosis of chronic immune thrombocytopenic purpura

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ABSTRACT

Myosin heavy chain 9 (MYH9)-related platelet disorders (MYH9-RD) belong to the group of inherited thrombocytopenias characterized by giant platelets and Döhle bodies. The process leading to the diagnosis of MYH9-RD in a 13-year-old male patient, followed by the diagnosis of chronic immune thrombocytopenic purpura (ITP), is described. The patient had thrombocytopenia with increased mean platelet volume since he was a little boy. Low CD41, CD42 and CD61 levels were detected in blood tests sent to complete missing diagnostic tests. Platelet aggregation tests were also abnormal. The requested genetic test revealed a heterozygous mutation in the MYH9 gene. The patient's audiogram and kidney functions were normal. In conclusion, because MYH9-RD appears to be rare, it is of great importance to maintain a high index of suspicion when managing patients diagnosed with chronic ITP. Additional complaints and findings should be considered at every outpatient clinic examination to make a more accurate diagnosis and prevent unnecessary treatments.

Keywords: Thrombocytopenia, Chronic ITP, MYH9, Mean Platelet Volume, Children

1. INTRODUCTION

Myosin heavy chain 9 (MYH9)-related platelet disorders (MYH9-RD), which have been previously described in four inherited syndromes (Epstein syndrome, Fechtner syndrome, Sebastian syndrome, May-Hegglin anomaly), are a group of hereditary thrombocytopenias characterized by giant platelets and Döhle body [1]. Diagnosis of May-Hegglin and Sebastian syndromes is based on congenital macrothrombocytopenia and characteristic leukocyte inclusions [2]. In contrast, Epstein and Fechtner syndrome diagnosis was defined in patients with additional features such as cataracts, hearing loss, and nephropathy, which usually lead to end-stage renal disease [3]. The disease locus mapped to chromosome 22q12.3-q13.2 in 1999, and a year later, mutations in the MYH9 gene were identified in all four conditions [4]. It was designated as MYH9-RD (OMIM155100) [5]. The MYH9 gene (22q13.1) encodes the heavy chain of the nonmuscular myosin A isoform of class II (myosin-9), a cytoskeletal contractile protein. Myosin-9 is found in most cell types and tissues. There are heterozygous pathogenic variants due to mutations in the MYH9 gene. MYH9-RD is a rare disease with a worldwide prevalence of 1-9:1 million. Mild forms are discovered by chance, and severe conditions are often misdiagnosed. Therefore, the prevalence may be higher than observed. Platelet transfusion should be considered for active bleeding that cannot be stopped otherwise, for life – or organ-threatening bleeding, and bleeding at critical sites. Eltrombopag or platelet transfusion can be used to prepare affected individuals for elective surgery [6]. Antifibrinolytic agents and desmopressin are used to treat bleeding. Hearing loss, kidney complications, and cataracts are treated standardly. People with severe hearing loss benefit from a cochlear implant [7].

In this case, we report a patient's clinical manifestations and management with a c.5593-4G-A mutation in the heterozygous MYH9 NM_002473.5 gene.

2. CASE REPORT

A 13-year-old male patient came with complaints of nosebleeds and easy bruising accompanied by thrombocytopenia. No bleeding, petechiae, purpura or ecchymosis was observed on

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the patient's examination. It was learned that the patient had no history of bleeding more than usual during circumcision. No other features were found in his background. The patient's father had kidney stones.

When the patient's past examinations were examined, it was seen that he had thrombocytopenia with an increase in MPV since 2015. In the peripheral smear, 70% of the neutrophils, 30% of the lymphocytes and 30% of the erythrocytes were normochromic normocytic. Platelets were generally large in each field of the peripheral blood smear, with an average of seven single and clustered platelets in some areas. When the platelet count was 95,000/mm3, MPV was 11 fL. the hemogram was examined in a citrate tube, considering the patient's ethylenediaminetetraacetic acid (EDTA) phenomenon. However, it was observed that thrombocytopenia did not improve. A qualitative platelet disorder panel was analyzed by flow cytometry to exclude Bernard Soulier syndrome due to its mild thrombocytopenic course. Flow cytometry analysis of platelets revealed low CD41, CD42b and CD61 values. Platelet function tests were repeated for Glanzman and Bernard Solier syndrome. In the PFA-100 analysis performed to evaluate bleeding time, the closure time with collagen/ADP and collagen/epinephrine was over 180 seconds; this value was longer than expected. Platelet aggregation was positive with ristocetin. The platelet aggregation test was inadequate for collagen, ADP and epinephrine. With the current results, grey platelet syndrome or MYH9-related macrothrombocytopenia was considered in the patient. Genetic testing was requested because our hospital could not view the electron microscopic image. As a result of genetic analysis, a heterozygous mutation was detected in the MYH9 gene. The result was determined as NM_002473.5 c5593-4G>MYH9-associated thrombocytopenia.

After the patient was diagnosed with macrothrombocytopenia genetically linked to MYH9, an audiogram was taken to detect sensorineural hearing loss and no hearing loss was detected. Renal functions were normal, and nephropathy was not observed. The patient is being followed closely for possible complications in the future.

3. DISCUSSION

In MYH9-RD, the presence and severity of spontaneous bleeding are related to the degree of thrombocytopenia. Most affected individuals do not bleed spontaneously; Fatal bleeding is rare. Symptoms can develop at any time between infancy and adulthood [8]. 72% of patients are diagnosed before the age of 35. Kidney damage begins with proteinuria and microhematuria and gradually progresses to end-stage renal disease (ESRD) [9].

MYH9-RD is a rare disease with approximately 300 cases reported in the literature [10]. The cause of some of the patients followed up with a diagnosis of chronic ITP may be such rare diseases. While investigating the etiological causes of the patient we have been following with the diagnosis of chronic ITP for years, we detected c.5593-4G-A heterozygous mutation in the MYH9 NM_002473.5 gene. Although, various modifications have been associated with the development of nephritis, they were not detected in our patient [9]. Although, sensorineural hearing loss is associated with some platelet defects, it was not detected in our patient [11]. MYH9-RD is inherited in an autosomal dominant manner. The mother or father of the case we identified did not have thrombocytopenia. Denovo mutation is detected in approximately 35% of index cases without family history [12].

In conclusion, although MYH9-RD is rare, the index of suspicion should be kept high in every new complaint or finding in patients. They should be followed up with the diagnosis of chronic ITP, and further examinations should be performed to determine why thrombocytopenia develops.

Compliance with Ethical Standards:

This research was conducted ethically by following per under Helsinki World Medical Association Declaration.

Patient consent: The patient gave her consent for clinical information relating to his case to be reported in a medical publication.

Conflict of interest statement: The authors have no conflict of interest to declare.

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