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Case Report

A Pediatric Case Report with Immune Thrombocytopenic Purpura Associated with COVID-19

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Abstract

Immune Thrombocytopenic Purpura (ITP) of childhood is identified as isolated thrombocytopenia. While it can be triggered by a viral infection such as hepatitis B, hepatitis C, cytomegalovirus, Epstein-Barr, influenza, herpes, varicella-zoster, and HIV or other immune causes, the reason for ITP remains unknown in most patients. We reported a pediatric case with ITP whose COVID-19 total antibody test was positive. Despite the poor response of high dose intravenous immunoglobulin (IVIG), steroid treatment generated a good result. Our patient had an asymptomatic Severe Acute Respiratory Syndrome Coronavirus 2, SARS-CoV-2 infection (COVID-19 infection) and COVID-19 PCR was negative. Since we are in the period of the COVID-19-related pandemic, SARS-CoV-2 should be kept in mind in the etiology of ITP. This case raises awareness of both PCR and antibody screening for COVID-19 in patients with ITP, especially in the pandemic season.

Keywords: SARS-CoV-2; ITP; IVIG; Steroid; Hematology

Introductıon

Immune Thrombocytopenic Purpura (ITP) is defined by isolated platelet count below 100,000/microL without abnormal hemoglobin and white blood cell count [1]. Primary ITP is identified as the absence of disorders or other known causes that may be related to thrombocytopenia. Autoantibodies related to commonly immunoglobulin G [IgG] directed against platelet membrane antigens such as glycoprotein (GP) IIb/IIIa complex, GP Ib/IX, GP Ia/IIa, and GP VI are associated with thrombocytopenia in ITP. Because of accelerated clearance of the antibody-coated platelets in the spleen, platelets' half-life has shortened, and in addition, platelet production has decreased by the same antibodies. As a result of these, the platelet count has fallen [2,3]. ITP is one of the most frequent causes of symptomatic thrombocytopenia in children. The yearly incidence of ITP is predicted to be between 1 and 6.4 cases per 100,000 children [4,5]. ITP can present at any age in children, but there is a peak in frequency between two and five years and a smaller peak in adolescence. ITP frequently exists with the rapid manifestation of a petechial rash, bruising, and/or bleeding in a healthy individual. Approximately 60 percent of children with newly diagnosed ITP have a background of a preceding viral illness within the past month [6]. Numerous viruses have been identified as triggers of ITP, including influenza, Epstein-Barr virus, hepatitis B, hepatitis C, varicella zoster virus, and HIV [7]. ITP occurring in association with Severe Acute Respiratory Syndrome Coronavirus 2, SARS-CoV-2 infection (COVID-19 infection) has been described [8]. Bone marrow examination (aspirate and biopsy) is not necessary for children with ITP unless atypical features are present. Important indications for bone marrow aspiration and biopsy include the following such as insufficient or no response to treatment with steroids, intravenous immune globulin [IVIG], and/or anti-D immune globulin given at appropriate doses. Children with no or mild bleeding is only

observed regardless of the platelet count. A single dose of IVIG [0.8-1 g/kg] or a short course of corticosteroids are used as first-line treatment for pediatric patients requiring treatment in acute ITP [9].

We reported a case of a pediatric patient with ITP whose total antibody test was positive and PCR test was negative for COVID-19. When the disease history was detailed, it was obtained that signs and symptoms related with COVID-19 such as loss of taste and smell in the family four or five weeks before. The patient's laboratory and physical examination findings did not meet the PIMS criteria. So, COVID-19 associated ITP was diagnosed to the patient. Pulse steroid treatment (five days 30 mg/kg/dose, four days 20 mg/kg/dose) was used as first-line because of the poor response to two-dose of IVIG [1 gr/kg/dose].

Case Presentatıon

A 5-year-old girl admitted to the emergency department due to sudden onset rash and ecchymosis on the body for five days. The patient had not any history of a known COVID-19 exposure. She had not any complaints such as cough, difficulty breathing, or chest pain. She received no medications, and had no family history of hematologic or autoimmune disorders. On physical examination, her vital signs were body temperature 39°C, heart rate 120 beats per minute, respiratory rate 25 breaths per minute, and blood pressure 100/60 mm Hg. The case was malnourished. Skin examination appeared petechiae on her lower extremities, buttocks, head and ecchymoses in the sacral regions and lower and upper extremities. Cardiac, pulmonary, abdominal, and lymph node examinations were normal. Testing showed normal partial thromboplastin time, prothrombin time, and electrolytes. Complete blood count revealed high white blood cell count (15.2 x 10^9 /L [71 % neutrophils, 10 % lymphocytes, 11 % monocytes]), low hemoglobin (9.6 g/dL), low hematocrit (26.7 %), and low platelets (2x 10^9 /L). Acute phase reactants showed high C-reactive protein (CRP) (52 mg/L), high erythrocyte sedimentation rate (ESR) (49 mm/hour). We assessed the levels of plasma 25-hydroxyvitamin D3 (25(OH)D3), ferritin and vitamin B12. Blood 25(OH) D3 (10 µg/L) and vitamin B12 levels (198 µg/L) were low. While ferritin (86 µg/L) was normal, total iron binding capacity was high (380 ug/dL). All viral serological tests were normal. Reverse transcriptase–polymerase chain reaction (PCR) testing was negative for COVID-19. COVID-19 total antibody was positive (29.96 reactive). COVID-19 immune globuline (IgA-IgM) was intermediate (6.65 intermediate value). The patient was also evaluated in terms of COVID-19-related Pediatric Inflammatory Multisystem Syndrome (PIMS) criteria identified during the COVID-19 pandemic. PIMS diagnosis was excluded. She followed by the hematology service. She received 4x10 mg/kg acetaminophen as pretreatment and antipiretic, followed by 1 gr/kg/dose intravenous immunoglobulin [IVIG] twice was given. During this period, 50 mg/kg cefotaxime every 8 hours was started after obtaining the blood and urine cultures. Despite IVIG administration, she appeared recurrent epistaxis on day 3. Her repeat complete blood count was normal white blood cell count (6.1 x10 ^{9} /L), low hemoglobin (7.7 g/dL), low hematocrit (22 %), and low platelets (7x 10^9 /L). She had no response to IVIG. She received five days 30 mg/kg/dose, four days 20 mg/kg/dose iv methylprednisolone as a single daily. Then seven days 10 mg/kg/dose oral methylprednisolone as a single daily was treated. She was succesfully treated with pulse steroid. On day 16, platelet count had increased to 278 x 10^9 /L (Figure 1).

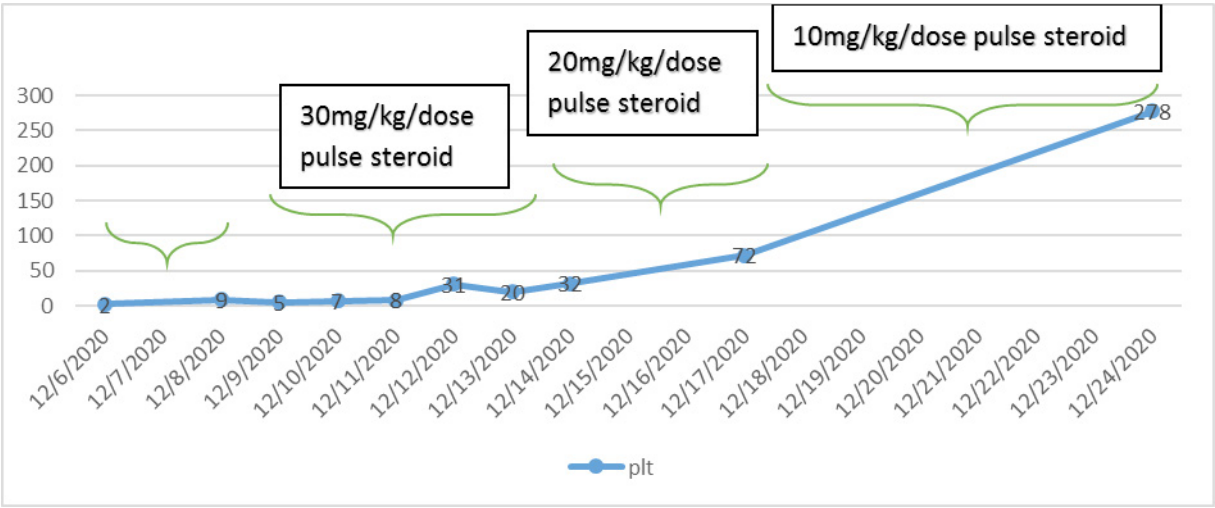

Figure 1: Improvements in blood count levels of platelets (Plt) during IVIG and steroid treatment (Plt: x 10^9).

Discussıon

Here we report a pediatric case of acute ITP with positive COVID-19 total antibody following asymptomatic COVID-19. To our knowledge, no cases of COVID-19-associated acute ITP have been previously reported in children or adolescents.

The laboratory findings such as thrombocytopenia, elevated D-dimer, prolonged prothrombin time, and disseminated intravascular coagulation are frequently hematological manifestations of COVID-19 [10]. Our case presents an extraordinary difference to these findings, in COVID-19 related ITP infection, and the negative COVID-19 PCR test, and the positive of COVID-19 total antibody. COVID-19 must be a diagnosis of exclusion in the evaluation of thrombocytopenia especially acute ITP during the COVID-19 pandemic. With this case report, we emphasize the requirement for clinicians to be aware of elevated COVID-19 infection rates and mild COVID-19 symptomatology in children.

There are few adult case reports in the literature about ITP caused by COVID-19. We wanted to review some of these cases. A 65-year-old woman with autoimmune hypothyroidism and hypertension who presented with 4 days of fever, cough, and fatigue, had positive COVID-19 testing on admission. Epistaxis and lower extremity purpura were appearred on day 4 of hospitalization. She had isolated thrombocytopenia on laboratory results. Because she was considered as ITP, she were treated with IVIG, prednisolone, and eltrombopag. Her platelet counts resolved by day 13 of hospitalization [11]. A recent study reported that A 39-year-old man who has Evans syndrome and positive rapid COVID-19 PCR assay treated IVIG. At the same time, steroid treatment was avoided due to the active infection period [12]. At the sametime, an 86-year-old man who had findings compatible with severe COVID-19 pneumonia treated IVIG and oral prednisolone [13]. While many reported cases had an active COVID-19 infection and positive COVID-19 PCR, we report firstly our pediatric case that had an asymptomatic COVID-19 infection, negative COVID-19 PCR, and positive COVID-19 antibody. In addition, we received a good response from steroid treatment in spite she had a poor response to IVIG similar to the literature.

We described the presentation and response to treatment of ITP associated with COVID-19 in a pediatric patient who had COVID-19 asymptomatically four or five weeks before. We think that COVID-19 plays a triggering role for ITP. As we are in a pandemic period full of unknowns and gaining new information every day, in various cases presenting with any hematological disease during this period, it is critical for health care to be aware of COVID-19 and to consider viral testing in these patients.

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