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COVID-19-Associated Acute Immune Thrombocytopenic Purpura: An Unusual Pediatric Case

COVİD-19 İlişkili Akut İmmün Trombositopenik Purpura: Sıradışı Pediatrik Bir Olgu

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ABSTRACT

Immune thrombocytopenic purpura (ITP) is a hematological disease manifested by isolated thrombocytopenia. Viral infections in the last month are often found in its etiology. After COVID-19 infection, various hematological complications can be seen, as well as the development of ITP. In this article, a case of pediatric acute ITP who was diagnosed during COVID-19 infection and had no signs of bleeding is presented.

Key Words: COVID-19, Children, Immune thrombocytopenic purpura (ITP), Without petechiae

ÖZ

İmmün trombositopenik purpura (İTP), izole trombositopeni ile kendini gösteren hematolojik bir hastalıktır. Etiyolojisinde son bir aydaki viral enfeksiyonlar sıklıkla bulunur. COVİD-19 enfeksiyonu sonrası çeşitli hematolojik komplikasyonların yanı sıra ITP gelişimi de görülebilmektedir. Bu yazıda COVİD-19 enfeksiyonu sırasında teşhis edilen ve kanama bulgusu olmayan bir çocuk akut ITP olgusu sunulmaktadır.

Anahtar Kelimeler: COVİD-19, Çocuklar, İmmün trombositopenik purpura (İTP), Peteşi olmadan

INTRODUCTION

Immune thrombocytopenic purpura (ITP) is a hematological disorder that generally manifests with petechial/purpuric lesions defined by a platelet count <100000/mm^3. Viral infections in the last month are frequently included in its etiology (1).

ITP has been identified after various viral infections including hepatitis B/C viruses (HBV/HCV), cytomegalovirus (CMV), varicella zoster virus (VZV), human immunodeficiency virus (HIV) (2). A new one has been added to these viral infection agents with the start of reporting of COVID-19 related immune thrombocytopenic purpura cases (3-5).

CASE REPORT

Previously, a healthy 6-month-old baby girl applied to the emergency service with the complaint of fever that had been going on for two days. The patient did not have any other complaints on her application. In her vital signs and physical examination, he had no abnormal findings other than 38°C body temperature. A COVID-19 nasopharyngeal swab PCR test was requested from the patient, as he had a history of close contact with a father, aunt and cousin known to be infected with COVID-19. There was no history of drug use, previous viral infection or vaccination in the past

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month. No hematologic disease was identified in her family history in her first-degree relatives. He was admitted to the pediatric infectious diseases service for observation due to a symptomatic COVID-19 infection. In the hemogram taken on the first day of hospitalization, the white blood cell count was 8240/mm^3, the absolute neutrophil count: 4610/mm^3, the absolute lymphocyte count: 2030/mm^3, hemoglobin: 11.8 g/dL, and the platelet count: 21.000/mm^3. In the hemogram of the patient, which was taken two weeks ago, it was seen that the platelet count was 200.000 /mm^3. In the peripheral smear, the platelet count was consistent with 20.000/mm^3, platelet morphology was normal, and no atypical cells were found. The patient was consulted with the pediatric hematology-oncology department, immune thrombocytopenic purpura (ITP) was considered, and tests for autoimmune and infectious etiology were requested. ANA, anti-double-stranded DNA, indirect and direct Coombs test, antiphospholipid antibody, anti-cardiolipin antibody tests requested for autoimmune etiology were negative. HBsAg, Anti-HIV, Anti HCV, brucella rose bengal, brucella IgM and IgG, CMV IgM and IgG, toxoplasma IgM and IgG, rubella IgM and IgG, salmonella tube agglutination, parvovirus IgM and IgG infectious etiology tests resulted negative. The COVID-19 nasopharyngeal swab PCR test was positive. Fever continued for two more days in clinical follow-up and responded to intravenous paracetamol administration. No fever was observed in the following days. Our patient was accepted as COVID-19-associated acute ITP because of exclusion of other causes and COVID-19 nasopharyngeal swab PCR positivity. Intravenous immunoglobulin (IVIG) infusion (1 g/kg) was administered, and the control platelet count at the 48th hour after the end of the infusion was 162000/mm^3. Response to intravenous immunoglobulin infusion was observed. Her family was advised to apply a two-week home quarantine. After the end of home quarantine, pediatric hematology outpatient clinic and hemogram control were recommended. On the 15th day after discharge, the platelet count checked in the pediatric hematology-oncology outpatient clinic was 196.000/mm^3, and other hemogram values were within normal limits. During the six-month outpatient follow-up period, the patient's platelet count and other hemogram parameters were found to be within normal limits.

DISCUSSION

Viral infections and other immunological triggers can be counted among the causes of ITP that can be detected (6). Approximately two-thirds of newly diagnosed ITPs have a history of viral infection in the past month (1). In our case, there was no history of viral infection in the last month, but there was a history of close contact with family members and relatives infected with COVID-19 at home, and the diagnosis was made with a positive nasopharyngeal swab PCR test. Especially after the measles-mumps-rubella (MMR) vaccine, which is one of the early childhood vaccines, ITP development can be seen with a small percentage, and ITP development is not expected after other early childhood vaccines (7). In our case, there was no history of vaccination in the last month before hospitalization.

Immune thrombocytopenic purpura is a diagnosis made by excluding other causes (8). Viral infections (HIV, HCV, CMV, parvovirus), hematological diseases (leukemia, autoimmune hemolytic anemia, etc.), systemic autoimmune diseases (systemic lupus erythematosus, etc.) are diagnoses that should be excluded (9). In our case, the tests requested for autoimmune etiology for other causes of ITP were negative, except for the COVID-19 nasopharyngeal swab PCR test, which is one of the tests requested for infectious etiology, all others were negative. IVIG infusion was given to our case due to near-severe thrombocytopenia, and a positive platelet count response was observed in the hemogram control after the infusion, supporting the diagnosis of ITP. In the six-month follow-up of our patient after discharge, it was observed that the platelet count and other hemogram parameters were normal. All these findings supported the diagnosis of acute ITP associated with COVID-19 in our case.

The platelet count <100.000/mm^3 is used to define thrombocytopenia in ITP. The platelet count of our patient was 21.000/mm^3 and platelet morphology was normal in the peripheral smear. Mild thrombocytopenia can usually be seen in COVID-19 infection (10). However, in severe COVID-19 infection, severe thrombocytopenia can be seen in proportion to the severity of the disease (11). However, in cases where the platelet count is <100.000/mm^3 or the platelet count has decreased by more than 50%, autoimmune causes (especially ITP) should be considered first.

In a systematic review (15), three pediatric cases (12-14) presenting as COVID-19-related ITP in different age groups were mentioned. The clinical features of these cases, their treatments for ITP and clinical follow-up information will be given below, respectively.

A 10-year-old female patient, who was healthy before the first case, applied to the emergency department with the complaint of a one-day rash. The rash has spread from his lower extremities bilaterally to his chest and neck within 24 hours. On the morning of admission, he had purple lesions and new bruises in his mouth. 3 weeks ago, the patient had been mildly ill with 2 days of fatigue, non-productive cough and fever up to 38.3°C in the setting of SARS-CoV-2 exposure. She then felt completely fine for 2.5 weeks until the rash developed. She had severe thrombocytopenia (5000/mm^3) at her admission. SARS-CoV-2 nasopharyngeal swab PCR test was positive. (1g/kg) received an intravenous IVIG infusion. He was discharged from the hospital the next morning. The hemogram control after two weeks and at the second month was normal (12).

The second case, a 16-year-old male patient, presented with rash and mouth sores. SARS-CoV-2 nasopharyngeal

swab PCR test could not be performed, COVID-19 IgG test was positive. Both of her parents reported flu-like symptoms that they had quarantined at home 3-4 weeks ago. At her admission, she had extensive petechiae of the skin and oral mucosal purpura, and moderate thrombocytopenia (45.000/mm^3). One day after discharge, petechiae and purpura, and platelet count decreased to 4000/mm^3. It started with clinical improvement with corticosteroid treatment, and the platelet count increased to 73.000/mm^3 after one week (13).

The third case, a 12-year-old girl, presented with complaints of fever, cough and vomiting for 5 days. In her application, the SARS-CoV-2 nasopharyngeal swab PCR test was positive. He was treated with IVIG (1 g/kg) and steroids (1.5 mg/kg MPZ). While the platelet count was 10.000/mm^3 at admission, it increased to 143.000/mm^3 after the treatments. Because the patient had severe acute respiratory distress syndrome, mechanical ventilation support, tocilizumab and remdesivir were given. The patient was discharged on the 14th day of hospitalization (14).

Apart from the three pediatric cases mentioned in the systematic review, two more pediatric cases (fourth and fifth cases) were reported. The clinical features of these cases (16,17), treatments applied for ITP, and clinical follow-up information are given below.

The fourth case, an 11-year-old male patient, was admitted with the complaint of diffuse petechiae and ecchymosis. She had severe thrombocytopenia (5000/mm^3) on her admission and SARS-CoV-2 nasopharyngeal swab PCR test was positive. Fever and cough preceded the onset of petechial rash approximately 4 weeks. Intravenous immunoglobulin infusion was administered (800 mg/kg), partial response was initially obtained (platelet count 45.000/mm^3) 48 hours after the end of the infusion. A second IVIG infusion was administered four days after the first infusion, resulting in a complete response (platelet count 216.000/mm^3 48 hours after the end of the infusion). Three weeks later, the patient was discharged and followed up in the outpatient clinic. It was reported that he was in optimal clinical condition and his complete blood count was normal in his nine-month follow-up (16).

The fifth case, a 1-year-old 5-month-old female patient, presented with fever and ecchymosis that had been going on for two weeks in her limbs. She had a mild history of COVID-19 five weeks ago. In her application, her platelet count was 20.000/mm^3. COVID-19 IgG antibodies were positive. A single dose of intravenous IVIG (1 g/kg) was administered. One week later, the platelet count was 100.000/mm^3 in the hemogram control. Platelet count completely normalized in 10 weeks. He completed his three-month follow-up and was in full remission (17).

In our case, there was no sign of bleeding in the physical examination at admission and during the follow-up period. At the time of admission, the platelet count was 21.000/mm^3, and the SARS-CoV2 nasopharyngeal swab test was positive. The duration of symptoms before admission was two days. Complete response to intravenous immunoglobulin treatment was obtained, and in the 6-month follow-up after discharge, she was clinically stable and her platelet count was within normal limits.

Although the diagnosis of ITP was made in the second and third weeks after the onset of COVID-19 disease, there were cases of ITP that started in the first week. This may be due to the inability of patients to recognize or report the symptoms of COVID-19 disease (15). In a systematic review, ITP is among the autoimmune diseases that can develop after COVID-19 infection, and the time between the symptoms of COVID-19 disease and the onset of autoimmune symptoms ranges from 2 days to 33 days (18). In our case, the time between the onset of symptoms and diagnosis was as short as two days.

It is remarkable that our case was diagnosed with ITP very soon after the symptoms of COVID-19 appeared and there was no sign of bleeding at the time of diagnosis.

In conclusion, when sudden thrombocytopenia is detected in children diagnosed with COVID-19 disease, the diagnosis of COVID-19 associated with ITP should be kept in mind even if there is no evidence of bleeding. Although the development of ITP is expected 2-3 weeks after the diagnosis of COVID-19 infection, it should be kept in mind that the development of ITP may occur days after the onset of symptoms.

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