


Case Report

## A 5-month patient with ITP secondary to SARS-CoV-2

### SARS-CoV-2' ye ikincil ITP gelişen 5 aylık hasta

Ibrahim Cemal Maslak 

Süleyman Demirel University, Pediatric Immunology and Allergy, Isparta, Türkiye

#### ABSTRACT

Idiopathic thrombocytopenic purpura (ITP) is a hematological disease characterized by the immune-mediated destruction of platelets. It either resolves or becomes chronic. Before the onset of ITP, many children have an antecedent viral illness, which can be an upper respiratory infection or gastroenteritis. Regarding ITP frequency, infancy is the least prevalent age group when compared to older children. In this case report, we present the first infantile case of ITP associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that was successfully treated with intravenous immunoglobulin (IVIg).

**Keywords:** SARS-CoV-2, idiopathic thrombocytopenic purpura, intravenous immunoglobulin

#### ÖZET

İdiopatik trombositopenik purpura (ITP), trombositlerin immün aracılı yıkımı ile karakterize hematolojik bir hastalıktır. Düzelir ya da kronikleşir. ITP'nin başlangıcından önce, birçok çocukta üst solunum yolu enfeksiyonu veya ishale neden olabilen öncül viral hastalık vardır. Bebeklik dönemi, ITP sıklığı açısından daha büyük çocuklara kıyasla hastalığın en az görüldüğü yaş grubudur. Bu olgu çalışmasında, intravenöz immünglobulin (IVIg) ile başarılı bir şekilde tedavi edilen SARS-CoV-2 ile ilişkili ilk infantil ITP vakasını sunuyoruz.

**Keywords:** SARS-CoV-2, idiyopatik trombositopenik purpura, intravenöz immünglobulin

#### INTRODUCTION

ITP is an immune-mediated acquired disorder affecting adults and children and is defined as a temporary or chronic reduction in platelet count (1). It is diagnosed in a patient with isolated thrombocytopenia (peripheral blood platelet count of  $<100 \times 10^9/L$ ) without any other abnormalities in complete blood count or blood cell differentiation who is otherwise healthy (2). The major mechanism is platelet destruction due to a lack of tolerance for the patient's own platelets. T cell abnormalities, such as enhanced Th1 and cytotoxic T

cell activation and reduced Treg activation, are thought to play a role in the immunopathogenesis of ITP (3). Patients may experience clinical symptoms ranging from asymptomatic to life-threatening bleeding, depending on the severity of their thrombocytopenia and individual characteristics (1,4). Before the onset of ITP, the majority of children had a history of infectious illness, which might be upper respiratory infection or gastroenteritis. Specific viral agents (rubella, varicella, mumps, rubeola, or infectious mononucleosis) are responsible

Received: 13.06.2022 · Accepted: 25.07.2022 · Published: 29.09.2022

Correspondence / Yazışma: Ibrahim Cemal Maslak · Süleyman Demirel Üniversitesi, Pediatrik İmmünoloji ve Alerji Bölümü, Isparta, Türkiye · icmaslak@gmail.com

Cite this article as: Maslak IC. A 5-month patient with ITP secondary to SARS-CoV-2. *Pediatr Acad Case Rep.* 2022;1(1):13-6.

in a small number of instances. Acute ITP may also be caused by live vaccinations, particularly the MMR vaccine. The interval between antecedent infection and purpura in children with ITP varies from days to weeks, with the most common gap being around two weeks (5).

A multitude of events may cause the development of autoimmune disorders (AIDs) by causing the immune system to become overly activated. Viruses are a significant part of the environmental elements that have an impact on the immune system. Viruses, such as Epstein-Barr virus (EBV), cytomegalovirus (CMV), human immunodeficiency virus (HIV), and human T lymphotropic virus 1 (HTLV-1), have been linked to many AIDs. As evidenced by different records demonstrating the proclivity of individuals with coronavirus disease 2019 (COVID-19) to develop multiple types of autoantibodies, SARS-CoV-2 is likely to elicit autoantibodies against a person's own platelets (6). Because acute ITP is benign in most children, has a self-limiting course, and life-threatening complications, such as intracranial hemorrhage, are extremely rare, simple follow-up without intervention has been documented to improve platelet counts similarly to those in the intervention group (7). In acute ITP, the platelet count alone should not be utilized as criterion for pharmacological therapy. Patients with active bleeding should be treated if their platelet count is less than  $20 \times 10^9/L$  or if their bleeding is life-threatening regardless of platelet level (8). IVIg, corticosteroids, and anti-D immunoglobulin are among the first-line treatments for both children and adults (9). Oral prednisone at a dosage of 1 to 2 mg/kg per day, administered in split doses and continued for a few weeks, is the corticosteroid treatment regimen used to treat children with newly diagnosed ITP in most published trials and across the world. In a systematic review and network meta-analysis, it was shown that in children with newly diagnosed ITP, IVIg was superior to corticosteroid regarding early response rates defined as platelet

count over  $20 \times 10^9/L$  and lack of bleeding at 24 hours, 48 hours, 72 hours, and seven days. Lower adverse events ratio was also a favourable outcome of IVIg (10). A single dose of 0.8 gr/kg IVIg administration has also been suggested as first-line therapy. Subsequent IVIg doses or corticosteroids may be reserved for the children based on the clinical circumstances and follow-up platelet counts (11).

We present a case of acute ITP successfully treated with IVIg in which SARS-CoV-2 was the potentially responsible preceding infectious agent.

### Case Report

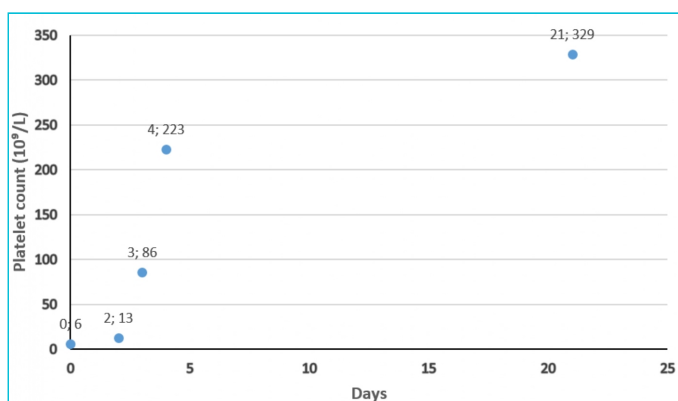
A 5-month-old, previously healthy boy presented to our hospital's emergency department with bruises that started two days ago. His vital signs were normal, and his general condition was good. Physical examination revealed ecchymoses on his knees and forearms, as well as petechial hemorrhages in his mouth but otherwise unremarkable with hepatosplenomegaly or lymphadenopathy (Figures 1 and 2). Laboratory examination showed severe thrombocytopenia (platelet count:  $6 \times 10^9/L$ , MPV: 10.6 fl) with Hb: 13.7 gr/dl and total leukocyte:  $7.7 \times 10^9/L$  (N: 27%, L: 54%, M: 18%). Coagulation and biochemistry tests were all normal. The patient's history revealed real-time polymerase chain reaction (RT-PCR) confirmed COVID-19 infection two weeks earlier with mild pyrexia, cough, and rhinorrhea that lasted two days and required no hospitalization. Owing to mucocutaneous hemorrhagic findings plus platelet count below  $20 \times 10^9/L$ , IVIg was administered (0.8 gr/kg/dose). Platelet count was checked 48 hours after infusion and  $13 \times 10^9/L$ . Due to the ongoing mucocutaneous bleeding, a second IVIg (0.8 gr/kg/dose) was administered again. Clinical and laboratory findings were improved after the second dose. Platelet counts during three weeks are illustrated in Figure 3. The consent of the patient's parents was obtained for this study.



**Figure 1.** Purpura and ecchymoses on arm.



**Figure 2.** Petechiae and ecchymoses on shin.



**Figure 3.** Graph showing platelet trend. The graph reflects the patient's measured platelet count on admission, during hospital course, and post-discharge follow-up.

## DISCUSSION

In this case report, we aimed to display that SARS-CoV-2 might be a preceding pathogen in ITP. Acute ITP linked to SARS-CoV-2 has been recorded in a few case reports, mostly in adults (12-15). Tsao et al. (15) reported the first pediatric case of SARS-CoV-2-associated ITP in a 10-year-old patient. Subsequently, two patients from Greece, aged 15 and 3, were diagnosed with SARS-CoV-2-associated ITP (16). Infancy is the least common age period compared to older children concerning ITP frequency (7.6%) (17). In this context, the current study represents the first infantile case of ITP associated with SARS-CoV-2. In the current case, a single dose of 0.8 g/kg IVIg was administered initially, followed by a second equal dose of IVIg as platelet counts remained below  $20 \times 10^9/L$  at 48 hours after treatment began. Any platelet count of at least  $100 \times 10^9/L$  is considered a full response in the management of ITP, whereas any platelet count of 30 to  $100 \times 10^9/L$ , as well as a doubling of the baseline level, is deemed "response" (1). We achieved response and complete response at 72 and 96 hours, respectively. The aforementioned reports in children with SARS-CoV-2 related ITP, a single dose of 1 gr/kg IVIg was efficacious in improving laboratory and clinical findings (15, 16).

In the light of the current reported case, it should be noted that SARS-CoV-2 may be a potential trigger of ITP like other infections. As a result, when evaluating individuals with ITP, it is recommended that the previous history question be expanded to include COVID-19 infection.

### Conflict of Interest / Çıkar Çatışması

The authors declared no conflicts of interest with respect to authorship and/or publication of the article.

### Financial Disclosure / Finansal Destek

The authors received no financial support for the research and/or publication of this article.

## REFERENCES

- Rodeghiero F, Stasi R, Gernsheimer T, Michel M, Provan D, Arnold DM, et al. Standardization of terminology, definitions and outcome criteria in immune thrombocytopenic purpura of adults and children: report from an international working group. *Blood* 2009; 113: 2386-93.
- Kuhne T. Diagnosis and management of immune thrombocytopenia in childhood. *Hamostaseologie* 2017; 37: 36-44.
- Kuhne T. Update on the Intercontinental Cooperative ITP Study Group (ICIS) and on the Pediatric and Adult Registry on Chronic ITP (PARC ITP). *Pediatr Blood Cancer* 2013; 60: 15-8.
- Imbach P. Treatment of immune thrombocytopenia with intravenous immunoglobulin and insights for other diseases. A historical review. *Swiss Med Wkly* 2012; 142: 13593.
- Blanchette V, Bolton-Maggs P. Childhood immune thrombocytopenic purpura: diagnosis and management. *Pediatr Clin North Am* 2008; 55: 393-420.
- Dotan A, Muller S, Kanduc D, David P, Halpert G, Shoenfeld Y. The SARS-CoV-2 as an instrumental trigger of autoimmunity. *Autoimmun Rev* 2021; 20 (4).
- Bolton-Maggs PH, Dickerhoff R, Vora AJ. The nontreatment of childhood ITP (or "the art of medicine consists of amusing the patient until nature cures the disease"). *Semin Thromb Hemost* 2001; 27: 269-75.
- British Committee for Standards in Haematology General Haematology Task F. Guidelines for the investigation and management of idiopathic thrombocytopenic purpura in adults, children and in pregnancy. *Br J Haematol* 2003; 120: 574-96.
- Provan D, Stasi R, Newland AC, Blanchette VS, Bolton-Maggs P, Bussel JB, et al. International consensus report on the investigation and management of primary immune thrombocytopenia. *Blood* 2010; 115: 168-86.
- Acero-Garces DO, Garcia-Perdomo HA. First Line Treatments for Newly Diagnosed Primary Immune Thrombocytopenia in Children: A Systematic Review and Network Meta-analysis. *Curr Pediatr Rev* 2020; 16: 61-70.
- Blanchette V, Imbach P, Andrew M, Adams M, Mcmillan J, Wang E, et al. Randomized Trial of Intravenous Immunoglobulin-G, Intravenous Anti-D, and Oral Prednisone in Childhood Acute Immune Thrombocytopenic Purpura. *Lancet* 1994; 344: 703-7.
- Gonze A, Hanneke C, Coppens N, Vellemans H, Maury G. SARS-CoV-2-Induced Severe Immune Thrombocytopenic Purpura. *J Med Cases* 2020; 11: 166-8.
- Guirguis N, Rehman T, Shams Y, Gordon M, Mekhaieel E, Rozell S, et al. SARS-CoV-2 Infection Inducing Immune Thrombocytopenic Purpura: Case Series. *Ochsner J* 2021; 21: 187-9.
- Revuz S, Vernier N, Saadi L, Campagne J, Poussing S, Maurier F. Immune Thrombocytopenic Purpura in Patients with COVID-19. *Eur J Case Rep Intern Med* 2020; 7: 001751.
- Tsao HS, Chason HM, Fearon DM. Immune Thrombocytopenia (ITP) in a Pediatric Patient Positive for SARS-CoV-2. *Pediatrics* 2020; 146(2).
- Behlivi E, Tragiannidis A, Hatzipantelis E, Panagopoulou P. Immune thrombocytopenia secondary to COVID-19 infection: Report of two cases. *Pediatr Blood Cancer* 2021; 68: 29175.
- Kuhne T, Buchanan GR, Zimmerman S, Michaels LA, Kohan R, Berchtold W, et al. A prospective comparative study of 2540 infants and children with newly diagnosed idiopathic thrombocytopenic purpura (ITP) from the Intercontinental Childhood ITP Study Group. *J Pediatr* 2003; 143: 605-8.