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CASE REPORT

Infant case of severe immune thrombocytopenia caused by COVID-19 infection

Tatsuya Anzai[1,2] | Naomi Nakashima[2] | Hiroyuki Betsui[1] | Yuta Kawahara[1] | Yuriko Hayashi[3] | Hirokazu Kimura[3] | Akira Shimada[1]

[1]Department of Pediatrics, Jichi Medical University, Shimotsuke, Tochigi, Japan

[2]Department of Pediatrics, Koga Red Cross Hospital, Koga, Ibaraki, Japan

[3]Department of Health Science, Gunma Paz University Graduate School, Takasaki, Gunma, Japan

Correspondence
Akira Shimada, Department of Pediatrics, Jichi Medical University, 3311-1 Yakushiji, Shimotsuke, Tochigi 329-0498, Japan.
Email: shimada.akira@jichi.ac.jp

Abstract

Immune thrombocytopenia (ITP) is a common childhood acute autoimmune bleeding disorder caused by numerous viruses and characterized by isolated thrombocytopenia. Although cases of ITP caused by coronavirus disease 2019 (COVID-19) infection have been reported in adults, pediatric reports are limited. We present the case of a 1-year-old girl who developed COVID-19-infection-related ITP with a very low platelet count ($0.0 \times 10^4/\mu$L). We searched for COVID-19-related pediatric ITP cases and found 10 other cases, with the majority having platelet counts of $<1.0 \times 10^4/\mu$L. Although pediatric ITP cases caused by COVID-19 infection may be severe, further studies are needed.

KEYWORDS
child, coronavirus disease 2019 (COVID-19), immune thrombocytopenia (ITP)

1 | INTRODUCTION

Immune thrombocytopenia (ITP) is a common childhood acute autoimmune bleeding disorder characterized by isolated thrombocytopenia, petechiae, bruising, and bleeding. Children with newly diagnosed ITP typically have a history of a preceding viral illness within the preceding month. Numerous viruses have been identified as triggers of ITP, including Epstein–Barr virus, influenza, varicella zoster virus, and human immunodeficiency virus [1].

Recently, ITP was reported to be triggered by coronavirus disease 2019 (COVID-19) infection [2] or vaccination [3]; however, the majority of cases were in adults. Herein, we report a case of ITP in an infant caused by COVID-19 infection.

2 | CASE REPORT

A 1-year-old girl presented with fever, cough, and rhinorrhea and was diagnosed with COVID-19 infection the day after taking a SARS-CoV-2 antigen test at home. Her fever subsided 5 days after infection. She came to our hospital at 8 days post-COVID-19 infection because she showed signs of oral mucosal bleeding and petechiae of the extremities. She did not have a history of vaccination against COVID-19 or allergies. Her vital signs were stable. Physical examination showed oral mucosal bleeding, tongue hematoma, and petechiae of the face, back, and extremities (Figure 1). A physical examination of the heart, lung, liver, and spleen showed no abnormalities. There were no symptoms suggestive of multisystem inflammatory syndrome in children, such as lymphadenopathy, bulbar conjunctival injection, or brawny edema of the hands. Echocardiography did not show cardiac dysfunction, pericardial effusion, or coronary abnormalities. A blood test showed thrombocytopenia ($0.0 \times 10^4/\mu$L) without leukopenia or anemia [white blood cell (WBC) 6320/μL, hemoglobine (Hb) 11.4 g/dL]. Renal and liver function and coagulation tests were normal [Creatinine (Cr) 0.22 mg/dL, aspartate aminotransferase (AST) 36 IU/L, alanine aminotransferase (ALT) 11 IU/L, Prothrombin Time-International Normalized Ratio (PT-INR) 1.1, activated partial thromboplastin time (APTT) 29.0 s]. Platelet-associated IgG was elevated to 873 ng/10^7

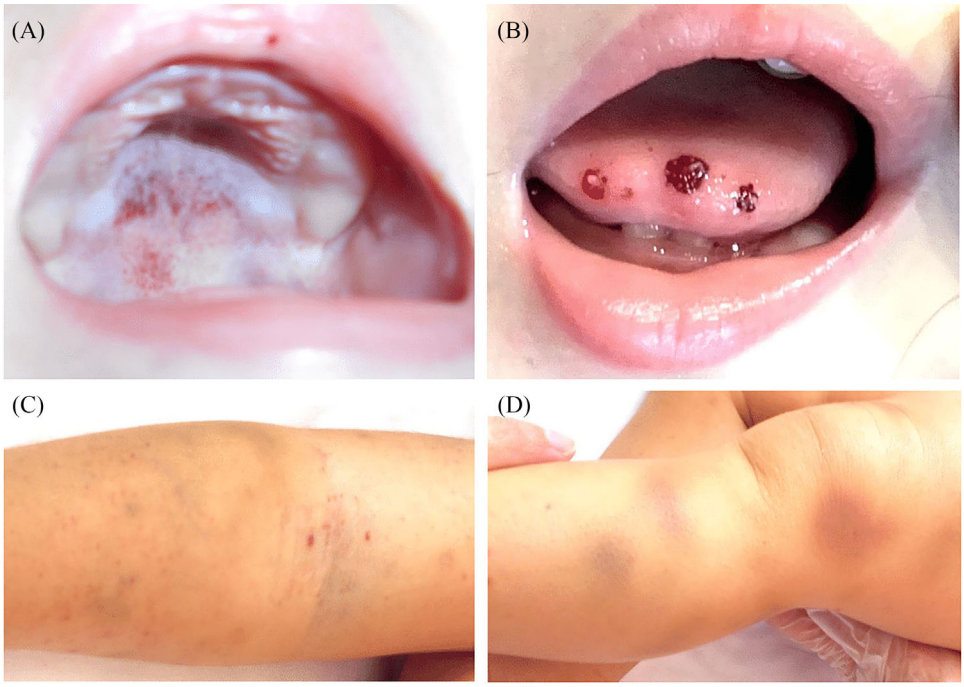

FIGURE 1 Appearance of the patient's oral mucosal bleeding (A), tongue hematoma (B), and petechiae of the upper and lower extremities (C and D).

cells. A SARS-CoV-2 quantitative antigen test given at admission was positive. She was diagnosed with ITP caused by COVID-19 infection on the basis of clinical symptoms and laboratory data.

After hospitalization, she was treated with intravenous immunoglobulin (IVIG, 1 g/kg/day) because her modified Buchanan and Adix bleeding score was moderate. Two days after IVIG treatment, her platelet count increased slightly ($0.3 \times 10^4/\mu L$). However, the platelet count dropped again to $0.0 \times 10^4/\mu L$ the next day, so she was treated with secondary IVIG (at the same dose as in the first treatment) and 2 mg/kg/day of oral prednisolone (PSL). After IVIG + PSL treatment, the platelet count improved. The patient's condition also improved, and the petechiae were significantly reduced. Four days after IVIG + PSL treatment, the platelet count was elevated to $4.9 \times 10^4/\mu L$. She was discharged after 8 days of treatment. Fortunately, she did not show intracranial hemorrhage or life-threatening hemorrhage. PSL was tapered and stopped 2 months after discharge. She showed no recurrence 1 year after the initial diagnosis.

3 | DISCUSSION

ITP is one of the most common causes of symptomatic thrombocytopenia in children. ITP is a clinical diagnosis largely made in patients with mucocutaneous bleeding and laboratory confirmation of isolated thrombocytopenia (platelet count $< 10.0 \times 10^4/\mu L$). Other causes of thrombocytopenia must be ruled out. ITP is categorized into three phases, depending on duration: newly diagnosed (within 3 months of diagnosis), persistent (between 3 and 12 months after diagnosis), and chronic (for more than 12 months). Numerous viruses have been identified as triggers of ITP, including Epstein–Barr virus, influenza, varicella zoster virus, and human immunodeficiency virus [1]. ITP caused by COVID-19 infection has been reported more frequently in elderly patients with a median age above 60 years of age [4]. Although the first pediatric patient with ITP caused by COVID-19 infection was reported in July 2020 [5], 11 pediatric ITP patients have been reported to date, including our case [6–13] (Table 1). Almost all were treated with IVIG. Two cases were treated with IVIG + methylprednisolone (mPSL), and one case was treated with mPSL. In our case, the patient was treated with IVIG + PSL. No intracranial hemorrhage or life-threatening hemorrhage occurred in any of the patients. In adult cases, ITP caused by COVID-19 infection has been reported to cause more severe thrombocytopenia, significantly lower platelet counts, more bleeding episodes, and more intracranial hemorrhages compared with ITP caused by non-COVID-19 infections [14]. Because of the small number of reported cases, it is unknown whether patients with pediatric ITP caused by COVID-19 infection develop severe symptoms or not. Kühne et al. reported a review of pediatric ITP caused by non-COVID-19 infection that included three groups (<1 year, 1–10 years, 10–16 years of age) [15]. The mean platelet counts at diagnosis were not different between the groups (1.46 ± 1.65, 1.50 ± 1.83, and $1.84 \pm 2.47 \times 10^4/\mu L$, respectively). Intracranial hemorrhage occurred in three of 1742 children during the first 6 months after the diagnosis of ITP. Previously, 10 pediatric patients with ITP caused by COVID-19 infection were reported, six of whom had a low platelet count ($<1.0 \times 10^4/\mu L$) (Table 1). Although pediatric ITP cases caused by COVID-19 infection may become severe, further studies are needed to clarify the severity and long-term prognosis.

TABLE 1 Reported cases of pediatric immune thrombocytopenia (ITP) caused by coronavirus disease 2019 (COVID-19).

Author	Age	Male/female	Onset of COVID-19 illness to diagnosis of ITP	Platelet count at diagnosis	Treatment	Complication
Patel et al. [5]	12 years	F	5 days	$<1.0 \times 10^4/\mu L$	IVIG, mPSL	Respiratory failure
Tsao et al. [6]	10 years	F	3 weeks	$0.5 \times 10^4/\mu L$	IVIG	No
Soares et al. [7]	2 years	F	25 days	$2.8 \times 10^4/\mu L$	IVIG	No
Ringoringo and Hartoyo [8]	9 months	M	3 days	$1.6 \times 10^4/\mu L$	mPSL	No
Behlivani et al. [9]	15 years	M	5 weeks	$0.1 \times 10^4/\mu L$	IVIG	No
	3 years	F	3 weeks	$2.6 \times 10^4/\mu L$	IVIG	No
Ceglie et al. [10]	11 years	M	4 weeks	$0.5 \times 10^4/\mu L$	IVIG	No
Marinescu et al. [11]	8 years	F	<24 h	$0.0 \times 10^4/\mu L$	IVIG, mPSL	Renal and liver dysfunction
Vadakkekara et al. [12]	1 year	F	5 weeks	$2.0 \times 10^4/\mu L$	IVIG	No
Hirate et al. [13]	13 years	F	2 weeks	$0.2 \times 10^4/\mu L$	IVIG	No
The patient	1 year	F	8 days	$0.0 \times 10^4/\mu L$	IVIG, PSL	No

Abbreviations: IVIG, intravenous immunoglobulin; mPSL, methylprednisolone; PSL, prednisolone.

Even though most pediatric COVID-19 infections are mild, care should be taken with respect to ITP caused by COVID-19 infection in the post-COVID-19 pandemic era.

AUTHOR CONTRIBUTIONS

Conception, design, and draft preparation: Tatsuya Anzai and Akira Shimada. All authors critically reviewed and revised the manuscript and gave final approval of the published version. All authors agree to be accountable for all aspects of the work.

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CONFLICT OF INTEREST STATEMENT

The authors declare they have no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this study as no new data were created or analyzed in this study.

ETHICS STATEMENT

Because this is a case report, ethics committee approval is not required for this study, in accordance with the national ethical guidelines in Japan.

PATIENT CONSENT STATEMENT

Verbal consent was obtained from the patient's parents.

CLINICAL TRIAL REGISTRATION

The authors have confirmed clinical trial registration is not needed for this submission.

ORCID

Tatsuya Anzai https://orcid.org/0009-0005-9852-560X
Akira Shimada https://orcid.org/0000-0001-5207-3779

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