

## IMMUNE THROMBOCYTOPENIC PURPURA FOLLOWING CORONAVAC VACCINATION: A CASE REPORT

Giulia Eduarda Aimi<sup>1</sup> , Guilherme Rasia Bosi<sup>1</sup> ,  
Larissa Beatriz Guerra<sup>1</sup> , Lessandra Michelin<sup>1</sup> 

### ABSTRACT

Immune thrombocytopenic purpura (ITP), an autoimmune disorder, has been documented as a result of SARS-CoV-2 infection and a vaccination side effect. The COVID-19 pandemic has led to the creation of CoronaVac vaccine and has been widely administered in Brazil.

Patient, in the case, is an 82-years-old female who received the vaccine two days before an acute episode of gingivorrhagia and diffuse cutaneous petechiae. Other exams were made to look for other causes of secondary thrombocytopenia and all the results were normal. The patient showed improvement on the platelet levels three day after the beginning of the treatment with high dosage methylprednisolone.

Knowing that other kinds of vaccine can generate ITP, the SARS-CoV-2 vaccine could be related to the symptoms.

**Keywords:** *Covid-19; Coronavac; trombocitopenia*

*Clin Biomed Res.* 2022;42(4):407-409

1 Unimed Nordeste. Caxias do Sul, RS, Brasil

#### Corresponding author:

Larissa Beatriz Guerra  
larissab.guerra@hotmail.com  
Universidade de Caxias do Sul,  
Campus Sede  
R. Francisco Getúlio Vargas, 1130 -  
Petrópolis, Caxias do Sul - RS  
95070-560

### INTRODUCTION

The ongoing COVID-19 pandemic caused by SARS-CoV-2 has led to high morbidity and mortality worldwide<sup>1</sup>. Since the onset of the pandemic, researchers worldwide have been trying to develop vaccines for this disease. Different vaccine platforms were tested for pre-clinical trials, including live attenuated virus vaccines, inactivated virus vaccines, recombinant viral vector vaccines, DNA vaccines, mRNA vaccines, virus-like particle vaccines, and subunit vaccines. In the meantime, the development of SARS-CoV-2 vaccines has increased our knowledge of new technologies for future control of globally relevant pathogenic microorganisms.

The use of new vaccines to prevent the disease has revealed some adverse events, such as local reactions (pain, itching, redness, swelling, and induration) and systemic reactions (coughing, diarrhea, fatigue, fever, headache, nausea and vomiting, pruritus, muscle pain, joint pain, malaise, anorexia, and immune thrombocytopenic purpura [ITP], which is the case of the patient mentioned in this report). Vector vaccines were the first to be associated with adverse events such as those described, but these events were eventually associated with other vaccines, such as the inactivated one.

ITP is an autoimmune disorder characterized by a reduction in platelet count due to platelet destruction and decreased platelet production. ITP was associated with COVID-19 infection in a small number of patients and has been associated with other infectious diseases and other vaccines<sup>2</sup>.

The pathogenesis of vaccine-related thrombocytopenia is not well understood. Studies presume that the disease is immune-mediated and may be related to the hyperfunction of B-cells observed in ITP<sup>3,4</sup>. Thus, thrombocytopenia may be induced by enhancement of macrophage-mediated clearance or impaired platelet production as part of a systemic inflammatory response to vaccination<sup>5,6</sup>.

We report a case of secondary ITP after the first dose of an inactivated SARS-CoV-2 vaccine.

## CASE REPORT

An 82-year-old female with a previous history of mild hypothyroidism presented an acute episode of gingival bleeding and diffuse cutaneous petechiae 48 hours after receiving the first dose of the inactivated vaccine for SARS-CoV-2. The inactivated SARS-CoV-2 vaccine (CoronaVac) was developed in China and has been widely administered in Brazil since January 2021. The vaccine is administered intramuscularly in two doses, 28 days apart. Few adverse events have been reported to the National Pharmacovigilance System, and those related to clinical hematological manifestations are even rarer<sup>7</sup>.

Two months prior to the vaccination, the patient had a platelet count of  $189 \times 10^9/L$ . The vaccine was administered on March 17, 2021 and, after 2 days, the patient developed epistaxis and oral bleeding. On the day after the clinical manifestations, the patient was admitted to the emergency room with active bleeding, manifested by uncontrolled gingival bleeding and the appearance of petechiae and purpura. Platelet count was  $1 \times 10^9/L$ . Serological, biochemical, and imaging tests were performed to search for other causes of secondary thrombocytopenia. All results were normal, including thyroid function. In addition, pseudothrombocytopenia was ruled out by confirming platelet levels after the citrate control test. The patient was hospitalized for four days, with adequate clinical evolution and no bleeding episodes, and was discharged with guidance on the use of intravenous methylprednisolone (1 g per day for three days). Immunological suppression with prednisone 1 mg/kg/day was maintained at hospital discharge. One day after the end of methylprednisolone treatment, the patient had partial recovery of platelet levels ( $55 \times 10^9/L$ ). After 15 days from the onset of clinical manifestations, platelet levels improved to  $262 \times 10^9/L$ , with a complete response to steroid treatment. The dose of prednisone was reduced until its interruption after 30 days, and the patient still had a normal platelet count after seven months of follow-up.

## DISCUSSION

Immune-mediated platelet destruction associated with SARS-CoV-2 vaccination has been described, although it has only been presented in a few case reports. ITP is a well-known adverse reaction related to other vaccines, especially rubella, pneumococcus, and influenza vaccines, even though it is a rare adverse event<sup>2</sup>. The mechanism of post-vaccination thrombocytopenia may be related to increased B-cell function, which also occurs in the pathophysiology of ITP<sup>3,4</sup>.

A study about vaccination with the recombinant adenoviral vector encoding the spike protein antigen of SARS-CoV-2 was published on April 2021 in the *New England Journal of Medicine*. The study investigates ITP after vaccination with ChAdOx1 nCov-19, analyzing patients who presented thrombotic events. The authors reported that post-vaccination immune thrombocytopenia is mediated by platelet-activating antibodies against PF4, which clinically mimics autoimmune heparin-induced thrombocytopenia, that is severely associated with patients with unusual thrombocytopenia, increased frequency of disseminated intravascular coagulation, and atypical thrombotic events— clinical elements observed in some patients after vaccination<sup>8</sup>.

In the case described above, the patient developed severe thrombocytopenia within 48 hours of receiving the first dose of the inactivated SARS-CoV-2 vaccine. Despite experiencing a serious adverse event, the patient fully recovered after the administration of standard ITP treatment with high-dose methylprednisolone. The risk of using a new vaccine is often questioned by the population, but the benefits of immunization against SARS-CoV-2 are greater. In Brazil, mass immunization began with an inactivated vaccine called CoronaVac, developed with shared technology between Sinovac and the Butantan Institute. After the first dose, this vaccine presents an effectiveness of 15.5% against COVID-19, 37.4% against hospitalization, 44.7% against intensive care unit (ICU) admission, and 45.7% against deaths by COVID-19. In addition, vaccine effectiveness in fully immunized people was 65.9% against COVID-19, 87.5% against hospitalization, 90.3% against ICU admission, and 86.3% against deaths by COVID-19<sup>9</sup>.

Thrombocytopenia can be facilitated by old age, as well as by some other diseases as lupus, antiphospholipid syndrome, thyroid disease, an Evans syndrome, infectious agents, and vaccination. This condition can also be induced by medications, although the patient in this case report did not have any risk factors for ITP and was immunized with the inactivated vaccine. Patients who experienced ITP after the COVID-19 vaccine were urgently treated with intravenous immunoglobulin (IVIG), corticosteroids, and platelet transfusion. Rituximab and romiplostim or eltrombopag olamine (thrombopoietin receptor agonist [TPO-RA] agents) were used in cases in which the patient did not show any response to first- and second-line treatments. Based on these results, we suggest the administration of IVIG and high doses of steroids; in addition to that, other treatments should be considered, such as continuous corticosteroid immunosuppression until clinical resolution. Most outcomes were favorable with combination therapy, but death after cerebral hemorrhage has been reported even after adequate treatment<sup>7</sup>.

Knowing that COVID-19 vaccines are new, pharmacovigilance reports are important in the discovery and guidance of the possible adverse events from each vaccine. The main adverse events reported for the various vaccines used include pain, itching, redness, swelling, induration, cough, diarrhea, fatigue, fever, headache, nausea and vomiting, muscle pain, joint pain, malaise, anorexia, and, although rare, ITP. However, these adverse events should not discourage immunization since their effectiveness is essential for the control of serious disease and mortality in the population<sup>2</sup>.

Since COVID-19 vaccines are new, additional surveillance is needed to determine the true incidence

of thrombocytopenia after vaccination. Although ITP is a rare post-vaccine adverse event, this case report should not be seen as a reason to avoid vaccination, but a signal to closely monitor patients for any suspected symptoms after vaccination. It is important to report any complications that may arise with new vaccines to extend our knowledge about possible side effects and ways to avoid potential complications. In addition, the number of people who developed ITP as a side effect is much smaller than the number of people in whom the vaccine was effective, those who present decreased risk of death and morbidity due to SARS-CoV-2 infection.

## REFERENCES

- Walker PGT, Whittaker C, Watson OJ, Baguelin M, Winskill P, Hamlet A, et al. The impact of COVID-19 and strategies for mitigation and suppression in low- and middle-income countries. *Science*. 2020;369(6502):413-22.
- Helms JM, Ansteatt KT, Roberts JC, Kamatam S, Foong KS, Labayog JS, et al. Severe, refractory immune thrombocytopenia occurring after SARS-CoV-2 vaccine. *J Blood Med*. 2021;12:221-4.
- Giordano P, Cascioli S, Lassandro G, Marcellini V, Cardinale F, Valente F, et al. B-cell hyperfunction in children with immune thrombocytopenic purpura persists after splenectomy. *Pediatr Res*. 2016;79(2):262-70.
- Yokomichi H, Tanaka-Taya K, Koshida R, Nakano T, Yasui Y, Mori M, et al. Immune thrombocytopenic purpura risk by live, inactivated and simultaneous vaccinations among Japanese adults, children and infants: a matched case-control study. *Int J Hematol*. 2020;112(1):105-14.
- Rinaldi M, Perricone C, Ortega-Hernandez OD, Perricone R, Shoenfeld Y. Immune thrombocytopenic purpura: an autoimmune cross-link between infections and vaccines. *Lupus*. 2014;23(6):554-67.
- Perricone C, Ceccarelli F, Neshet G, Borella E, Odeh Q, Conti F, et al. Immune thrombocytopenic purpura (ITP) associated with vaccinations: a review of reported cases. *Immunol Res*. 2014;60(2-3):226-35.
- Lee EJ, Cines DB, Gernsheimer T, Kessler C, Michel M, Tarantino MD, et al. Thrombocytopenia following Pfizer and Moderna SARS-CoV-2 vaccination. *Am J Hematol*. 2021;96(5):534-7.
- Greinacher A, Thiele T, Warkentin TE, Weisser K, Kyrle PA, Eichinger S. Thrombotic thrombocytopenia after ChAdOx1 nCov-19 vaccination. *N Engl J Med*. 2021;384(22):2092-101.
- Jara A, Undurraga EA, González C, Paredes F, Fontecilla T, Jara G, et al. Effectiveness of an inactivated SARS-CoV-2 vaccine in Chile. *N Engl J Med*. 2021;385(10):875-84.

*Received: Jan 30, 2022*

*Accepted: May 30, 2022*