Immune thrombocytopenic purpura associated with coronavirus disease 2019 infection in an asymptomatic young healthy patient.

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INTRODUCTION

Cutaneous findings in patients with severe acute respiratory syndrome coronavirus 2 infection (SARS-CoV-2) are more common every day. Findings include, among others, pseudo-chilblains, vesicular, urticarial, and maculopapular eruptions. Livedo or necrosis is less common and, most importantly, suggests occlusive vascular disease usually related to severe coronavirus infection.[1] Petechiae/purpuric rash can resemble dengue fever or appear as a morbilliform rash. This rash can spare palmoplantar skin and mucosa or presents with confluent erythematous macules, papules, and petechiae in asymmetric peri flexural distribution. It could represent a sign of milder coronavirus disease 2019 (COVID-19) disease in which differential diagnosis includes drug-induced or viral rash and not necessarily a warning sign of thrombocytopenia.[2]

Immune thrombocytopenic purpura (ITP) is an unusual form of COVID-19 presentation. In most cases, it appears in the context of an active coronavirus infection with skin petechiae or purpura being the only or more prominent sign of the disease.

CASE REPORT

A 22-year-old healthy man presented with a 2-day history of an acute-onset petechial rash on his lower extremities. He was strictly following government COVID-19 quarantine directions.

During this time, he vigorously worked out on a daily basis. Because the lesions did not fade away and were more prominent each day, he decided to seek medical assistance through telemedicine with a specialist in dermatology. He provided photos showing petechial and purpuric lesions in both lower extremities, some of them with a linear distribution (Figs 1 and 2). During the video conference, he also showed petechial-like lesions on the dorsum of both hands. A day before the petechial eruption, he reported gingival bleeding and a buccal hematoma occurring after a dental procedure.

He denied respiratory symptoms, fever, anosmia, hyposmia, headache, or any other symptoms.

Suspecting a COVID-19–related acute platelet disarrangement, he was immediately instructed to stop any physical activity, and a full laboratory workup was requested. Findings were in the normal ranges except for the platelet count which was severely decreased:1000/μL (reference range, 150,000-400,000/μL). An oropharyngeal swab for SARS-Cov-2 testing was positive.

The peripheral film showed isolated thrombocytopenia without platelet clumps, normal neutrophils, and red blood cells, suggesting ITP. Prothrombin time, activated partial thromboplastin times, and fibrinogen level were within the normal range. The renal function was normal.

He started treatment with endovenous immunoglobulins (flebogamma, 1 g/d for 2 days) and

Abbreviations used:

COVID-19:	coronavirus disease 2019
ITP:	immune thrombocytopenic purpura
SARS-CoV-2:	severe acute respiratory syndrome coronavirus 2 infection

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Fig 1. Multiple petechial skin lesions in left foot.

thrombopoietin receptor agonists (Revolade, 50 mg/d). Corticosteroid use was deferred.

The etiologic ITP study was negative for HIV, hepatitis B virus, anti-DNA and lupus anticoagulant. Only antinuclear antibodies were positive at 1/640. The complement within the normal range. The thyroid function was normal. Chest radiograph showed no abnormalities.

He remained in good health, presenting only on the fifth day with a mild episode of headache, which resolved with acetaminophen. Laboratory findings showed a progressive increase in the platelet count (83,000/μL), and the purpuric lesions began to disappear, so he was discharged on the sixth day. Three months later, the patient is doing very well, with his platelet count within the normal range. The temporal sequence in this case suggests, but does not prove, that COVID-19 was a causal factor in immune thrombocytopenia in this patient.

DISCUSSION

It is well known that COVID-19 infection can predispose to arterial and venous thrombosis.[3] COVID-19–associated ITP is a rare presentation with very few cases published.[4-7] Our case is very interesting because it appears in an asymptomatic young healthy patient with no symptoms or signs of COVID-19 infection, showing severe ITP with an elevated risk of internal bleeding. The rest of the cases appeared in the context of COVID-19 infection with respiratory illness,[4,6] except for 2 cases, 1 with a moderate decrease in the patient's platelet count but no skin signs of bleeding[5] and the other of a young man with only mild symptoms (fever and runny nose) that unfortunately had an intracerebral hemorrhage.[7]

Fig 2. Petechial and purpuric lesions in left thigh.

Similar to the other viral infections,[8] SARS-CoV-2 can also trigger ITP. The etiology of COVID-19–related thrombocytopenia could be multifactorial—maybe a direct effect of SARS-CoV-2 on hematopoietic and bone marrow stromal cells leading to hematopoietic dysfunction and bone marrow growth inhibition or a cytokine storm, which, in turn, leads to the destruction of bone marrow progenitor cells, both of which result in decreased platelet production.[9] Alternatively, it can trigger an autoimmune response against blood cells by inducing autoantibodies and immune complex, a consequence of which is augmented platelet destruction. Recently, publications report that autoantibodies are positive in almost 70% of severely ill patients with COVID-19.[10] None of these patients had a history of systemic autoimmune rheumatic disease, and antinuclear antibodies were positive in 34.5% of patients, suggesting

autoimmune activation. This finding is not surprising, as cytokines present in the cytokine storm, such as interleukin-6, can drive autoinflammatory reactions and also autoimmunity, probably via preexisting natural B-cell clones or molecular mimicry. The possible autoimmune mechanism merits further investigation.

During this pandemic, the findings of petechiae and purpura have usually been associated with milder COVID-19 infection, but this is not always true, so dermatologists must be aware of this warning sign to promptly rule out COVID-19–associated ITP, a potentially life-threatening disease. Treatment issues may exist, however, because corticosteroid use in these patients is not fully supported.

As SARS-CoV-2 is now widespread, we encourage testing for SARS-CoV-2 in patients suspected of a thrombocytopenic purpura or its relapsing, even in the absence of respiratory symptoms.

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