Immune Thrombocytopenia Secondary to COVID-19 Infection

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KEY WORDS: coronavirus disease-2019 (COVID-19), hematologic manifestation, immune thrombocytopenia (ITP), severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2)

IMAJ 2021; 23: 342–343

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Immune thrombocytopenia (ITP) is a relatively rare condition characterized by low platelet counts and a tendency for spontaneous bleeding, and is assumed to be autoimmune mediated. Viral infections have been described as potential triggers for this condition. We describe a case of a sudden and severe thrombocytopenia in a 70-year-old patient who tested positive coronavirus disease-2019 (COVID-19).

Since first described in December 2019, in Wuhan (China), the global pandemic of the novel severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has been reported to cause the COVID-19 disease. Among many other clinical and laboratory manifestations of this virus, thrombocytopenia has been described as a common laboratory finding in COVID-19 patients affecting up to one-third of patients, although the thrombocytopenia described is usually mild and asymptomatic [1]. Immune thrombocytopenia (ITP) is characterized by a platelet count that is less than 100×10^9/L and is assumed to be autoimmune mediated. The clinical manifestation is usually skin and mucosal bleeding found in up to 2/3 of patients [2]. Several case reports of ITP secondary to COVID-19 infection have been described in the literature [3]. We report here a case of a sudden severe thrombocytopenia in a 70-year-old patient in the recovery stages of COVID-19.

PATIENT DESCRIPTION

During the COVID-19 pandemic a 70-year-old man presented to our emergency department with 14 days of a worsening dry cough and dyspnea. Ten days prior to his current admission, the patient was diagnosed with a severe COVID-19 infection. His initial blood test showed normal platelet count (150×10^9 cells per liter), and his COVID-19 polymerase chain reaction (PCR) obtained from a nasopharyngeal swab was positive. After improvement in his saturation, he was discharged home with a preventive dose of SC enoxaparin sodium 40 mg/d.

At admission, he was afebrile and had a respiratory rate of 22 breaths per minute and an oxygen saturation of 90% while he was breathing ambient air. Breath sounds were diminished bilaterally and the rest of his physical examination was unremarkable without signs of petechiae or mucosal bleeding.

Laboratory tests showed an isolated severely decreased platelet count of 10×10^9 platelets per liter with elevated mean platelet volume, while the rest of his blood count was within the normal limits (hemoglobin level was 14.2 g/dl, and the white blood cell count was 8000/µl). The patient had an increased C-reactive protein (CRP) level of 6.4 mg/dl (reference range 0–0.5), increased levels of fibrinogen concentration of 511.5 mg% (reference range 170–420), and a D-dimer level within the normal range (0.37 mg/L). All other laboratory tests were within normal limits. A chest computed tomography scan showed multiple ground glass opacities, right pleural thickening and a mediastinal lymphadenopathy less than 1 cm. Nasopharyngeal swab for COVID-19 PCR remained positive.

His past medical history included hypertension, chronic obstructive pulmonary disease, ischemic heart disease, and past smoking. His medical history was negative for any hematological or autoimmune diseases. He also has no family history of such diseases.

The patient was admitted to the COVID-19 ward and antimicrobial treatment (ceftriaxone followed by piperacillin/tazobactam and azithromycin) and oxygen supplementation with nasal cannula was started. A peripheral blood smear showed no platelet clumping and a true thrombocytopenia was evident. Large thrombocytes were seen without schistocytes. A workup for possible causes of thrombocytopenia, including disseminated intravascular coagulation, other viral infections (human immunodeficiency virus, Epstein–Barr virus, cytomegalovirus, hepatitis C virus, hepatitis B virus), bacterial sepsis, and heparin-induced thrombocytopenia where all negative, while an autoimmune antibody analysis was positive for anticardiolipin IgM (11.6 U/ml) and was negative for anticardiolipin IgG, anti-beta 2-glycoprotein IgM and IgG, antinuclear antibodies, and lupus anticoagulants. Lactate dehydrogenase levels were normal and there was no evidence of hepatosplenomegaly or lymphadenopathy. A diagnosis of ITP, most probably secondary to COVID-19 infection was made, and treatment with hydrocortisone (100 mg three times a

day) was started. Under this treatment the platelet count remained low, reaching a nadir of 3×10^9 cells per liter on his 6th day of hospitalization. However, there were no signs of bleeding or thrombosis. The patient's respiratory symptoms improved, his CRP levels subsided. His nasopharyngeal swab PCR was negative twice for COVID-19 on his ninth and tenth day of admission. The patient met the discharge criteria for the ward and was transferred to the hematologic department. He received a treatment of intravenous dexamethasone (20 mg daily) for 5 days along with two doses of Intravenous immune globulin (IVIG) at a dosage of 1 g per kilogram of body weight, within 48 hours, resulting in slight improvement in his platelet count(14×10^9 cells per/L). The patient was then discharged and continued ambulatory hematologic follow up. Treatment with prednisone 60 mg/day was recommended, and his platelet count was back to normal (150×10^9 cells/L) one month following discharge.

COMMENT

Secondary ITP, occurring amidst other diseases, has been described in the literature in the past, mainly in the context of viral infections including the human immunodeficiency virus, hepatitis C and B viruses, cytomegalovirus and the Epstein-Barr virus. Autoimmune disorders and rarely hematological malignancies could also be associated with this condition [2,4]. Bhattacharjee and Banerjee [3] analyzed and described 45 cases of new-onset ITP secondary to COVID-19 infection in a thorough systematic review. They found that the diagnosis of ITP, in just about 80% of the cases, is within the first 3 weeks after the onset of the COVID-19, was seen in our patient as well. The chronological sequence in this case suggests that the ITP in this patient was secondary to his COVID-19 infection, as well as the initial response to a short course of glucocorticoids and intravenous immunoglobulin, as seen in most of the other case reports. Although our patient tested positive for Anti cardiolipin IgM, this finding is quite common among COVID-19 patients, found in 6.6% of patients and likely to be clinically irrelevant [5]. As so few cases of ITP have been described secondary to COVID 19 infection, we believe that this report can contribute to the current literature and understanding of the new evolving autoimmune complications of SARS coronavirus-2.

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There are years that ask questions and years that answer.
Zora Neale Hurston (1891–1960), American author, anthropologist, and filmmaker

Capsule

Microglia use TAM receptors to detect and engulf amyloid β plaques

Two microglial TAM receptor tyrosine kinases, Axl and Mer, have been linked to Alzheimer's disease, but their roles in disease have not been tested experimentally. **Huang** et al. found that in Alzheimer's disease and its mouse models, induced expression of Axl and Mer in amyloid plaque-associated microglia was coupled to induced plaque decoration by the TAM ligand Gas6 and its co-ligand phosphatidylserine. In the *APP/PS1* mouse model of Alzheimer's disease, genetic ablation of Axl and Mer resulted in microglia that were unable to normally detect, respond to, organize or phagocytose amyloid-β plaques. These major deficits notwithstanding, TAM-deficient *APP/PS1* mice developed fewer dense-core plaques than *APP/PS1* mice with normal microglia. These findings reveal that the TAM system is an essential mediator of microglial recognition and engulfment of amyloid plaques and that TAM-driven microglial phagocytosis does not inhibit, but rather promotes, dense-core plaque development.

Nature Immunol 2021; 22: 586
Eitan Israeli