MÆDICA - a Journal of Clinical Medicine

CASE REPORT

MAEDICA – a Journal of Clinical Medicine
2022; 17(1): 234-236
https://doi.org/10.26574/maedica.2022.17.1.234

Immune Thrombocytopenic Purpura Secondary to Sarcoidosis

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ABSTRACT

Sarcoidosis is a systemic granulomatous disease involving multiple organs with predominantly pulmonary manifestations. Severe thrombocytopenia is a relatively rare hematologic manifestation of sarcoidosis. Immune thrombocytopenia is usually characterized by excessive antibody production leading to platelet destruction. There are a few reported cases of immune thrombocytopenic purpura secondary to sarcoidosis, but the pathophysiologic mechanism remains unknown. We report the case of a 65-year-old woman who presented severe thrombocytopenia and was found to have immune thrombocytopenic purpura secondary to sarcoidosis.

Keywords: sarcoidosis, ITP, secondary ITP, immune thrombocytopenic purpura.

INTRODUCTION

Immune thrombocytopenic purpura (ITP) refers to the autoimmune destruction of platelets and can be further classified as primary and secondary. Infectious and autoimmune diseases have been implicated as secondary causes of ITP (1). Sarcoidosis is a rare cause of autoimmune secondary ITP. We describe the case of a patient who presented with severe thrombocytopenia and was diagnosed with sarcoidosis, whose platelet counts improved after sarcoidosis treatment. ❑

CASE REPORT

Our patient was a 65-year-old female with a past medical history of trigeminal neuralgia and mild intermittent asthma who presented to the hospital for one-month history of dry cough and shortness of breath. Her surgical history was remarkable for prior cholecystectomy. Her social history and family history were unremarkable. Her vitals and physical examination were all normal. She also described two weeks of night sweats with occasional fatigue and arthralgias. A computed tomography (CT) scan of the chest done during the admission showed diffuse mediastinal lymphadenopathy, with the largest subcarinal lymph node measuring 5 cm x 2.5 cm, as shown in Figure 1. Complete blood count showed a hemoglobin of 11.9 g/dL, hematocrit of 35.6%, white blood cell count of 9400/µL, and platelet count of 249,000/µL. She was diagnosed with an asthma exacerbation and due to concern for po-

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Article received on the 3rd of December 2021 and accepted for publication on the 9th of March 2022

tential of sarcoidosis, she was discharged home on a longer prednisone taper of 20 mg for two days, 15 mg for two days, 10 mg for two days and 5 mg for two days before stopping altogether. She was scheduled for an outpatient endobronchial ultrasound with biopsy for further evaluation in four weeks. One day prior to the procedure, the patient developed a diffuse petechiae and bruising throughout her legs, arms and her abdomen with nasal bleeding. An urgent complete blood count showed platelets of 3000/µL and the biopsy was subsequently cancelled. Vitals on admission were unremarkable. Physical exam showed a well-nourished Caucasian female in no apparent distress. A diffuse petechial rash as well as ecchymosis on her arms and right flank was noted. No organomegaly was found on abdominal exam. Initial labs showed a normal coagulation profile including PT, PTT and fibrinogen. A complete blood count showed a hemoglobin of 12.4 g/dL, hematocrit of 37.2%, white blood count of 5300/µL and platelet count of 3000/µL. Peripheral smear did not reveal any platelet clumping or fragmentation. The ACE level was 66 mcg/L (14-82U/L) and LDH was elevated at 503 U/L (135-250U/L). Iron studies showed a ferritin level of 169 ng/mL (13-150 ng/mL), iron levels of 63 mcg/dL (60-150 mcg/dL), and TIBC 210 mcg/dL (300-360 mc/dL). Fibrinogen was normal at 433.5 mg/dL (205-522 mg/dL). 25-hydroxy vitamin D was low, measuring only 6.3 ng/mL (30-100 ng/mL). Viral hepatitis serology was negative. TB Gold Quantiferon was also negative. HIT antibodies and serotonin release assay were negative for heparin induced thrombocytopenia. A bone marrow biopsy was done at this point and showed megakaryocyte hyperplasia. Thrombocytopenia was believed to be due to immune destruction, which was consistent with ITP. The patient was treated with intravenous steroids and immunoglobulin for three days. Platelets began improved to 9000/uL and 116,000/uL on day 3 and day 5 after admission. The patient was then transitioned to oral prednisone 25 mg daily. A repeat chest CT showed the thoracic lymphadenopathy had slightly decreased in size compared to the previous CT scan. It also revealed a single enlarged porta hepatis lymph node. No other abdominal or pelvic lymphadenopathy was noted on CT imaging of the abdomen. Given the presence of mediastinal lymphadenopathy and constitutional symptoms,

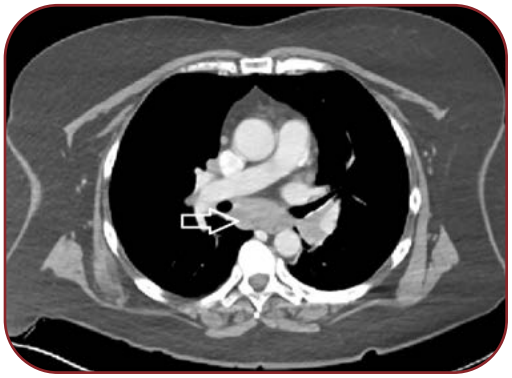

FIGURE 1. Chest computed tomography showing lymphadenopathy (white arrow)

ITP was thought to be secondary to a possible lymphoproliferative disorder. Due to concerns of endobronchial ultrasound not providing adequate tissue for diagnostic purposes, the patient underwent cervical mediastinoscopy & biopsy by cardiothoracic surgery once her platelets had stabilized. Grocott-Gomori's Methenamine Silver and Periodic Acid-Schiff stains from the mediastinal lymph node biopsy samples were negative for fungal organisms. Acid fast stain was also negative for mycobacteria. The frozen sections of the lymph nodes obtained showed evidence of granulomas. Pathology confirmed lymphoid tissue with multiple non-necrotizing granulomas. Based on these findings, the patient was diagnosed with sarcoidosis. She was discharged on prednisone 25 mg daily. Platelets remained stable for a month but began to drop as attempts were made to wean down her steroid dose. The dosage had to be increased back to prednisone 25 mg daily. The patient was also started on rituximab, after which platelet counts gradually recovered to 250,000/µL. ❑

DISCUSSION

Sarcoidosis is a multisystem disease characterized by granulomatous lesions. Thrombocytopenia is a rare extrapulmonary complication of sarcoidosis. The exact incidence of thrombocytopenia in sarcoidosis is unknown, but retrospective studies report an estimated incidence of 1-2% among patients with sarcoidosis (2). While abnormalities such as leukopenia, lymphopenia and anemia may be commonly seen, severe thrombocytopenia seems to be rare. A review of 381 cases of thrombocytopenia showed five pa-

tients with sarcoidosis (1%) and in another series of 324 patients with sarcoidosis, 2% had platelet count <100,000/ µL (3).

Although the exact relationship between sarcoidosis and thrombocytopenia is poorly understood, thrombocytopenia is believed to stem from three main mechanisms, including hypersplenism, bone marrow infiltration, and immune thrombocytopenia (ITP), with the latter one accounting for more than 80% of cases (4). In the first mechanism, sarcoidosis causes splenic granulomas, leading to splenic sequestration and subsequent platelet destruction. In a review of 6,074 cases of sarcoidosis in 29 publications, the prevalence of splenomegaly was found to be 10% (5). Splenomegaly was absent in our case, making this mechanism unlikely. The second mechanism is bone marrow involvement secondary to granulomatous infiltration. This is also less likely in our case as other cell lines were unaffected. Moreover, our patient's bone marrow biopsy did not show any other abnormalities besides megakaryocytes, which were likely a natural response for the thrombocytopenia.

The exact molecular mechanism by which sarcoidosis leads to ITP remains unclear. CD8+T cells have been shown to participate in apoptosis of platelets in ITP. (6) The number of CD8+T cells expressing cytolytic molecules such as perforin, granzyme B and granulysin were shown to be increased in patients with sarcoidosis when compared to those without sarcoidosis (7). Immune thrombocytopenic purpura in sarcoidosis also appears to be particularly severe, often complicated by bleeding, unresponsiveness to therapy, and death in up to 15% of patients (8). A study conducted in 2011 looked at 20 patients with sarcoidosis and ITP and concluded that while patients with sarcoidosis had severe thrombocytopenia at presentation and often needed longer duration of prednisone, overall response to treatment was favorable (9). Our patient had refractory ITP needing rituximab therapy before sustained improvement of platelets. ❑

CONCLUSION

We present this case to highlight the importance of recognizing sarcoidosis as a differential for ITP. Hematological manifestations of sarcoidosis, while uncommon, can be life threatening and require early recognition and prompt management. ❑

Conflicts of interest: none declared.
Financial support: none declared.

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