International Journal of Research in Medical Sciences
Karpovich Y et al. Int J Res Med Sci. 2023 May;11(5):1796-1800
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20231358

Case Report

A rare case of patient with severe thrombocytopenia associated with sarcoidosis: a case study

Yulia Karpovich[1], Fenilkumar Nitinbhai Ribadiya[1]*, Shalini Suresh Tanna[1], Darshi Yagnesh Trada[1], Yury Karpovich[2], Vladimir Bogdanovich[3]

[1]Department of Internal Medicine, [2]Department of Propaedeutic of Internal Disease, [3]Department of Nephrology, Grodno State Medical University, Grodno, Belarus

Received: 02 March 2023
Accepted: 07 April 2023

***Correspondence:**
Dr. Fenilkumar Nitinbhai Ribadiya,
E-mail: fenilribadiya@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Thrombocytopenia is a problem causing drop in platelet counts through different mechanisms. Patients typically present with petechiae to systemic bleeding, which are indications of a low platelet count. A smaller percentage of drop may be asymptomatic. The major mechanisms include increased sequestration in the spleen, underproduction from the bone marrow, and peripheral destruction. Many etiological factors can cause this. Sarcoidosis is one of the most uncommon etiologies. A careful diagnosis is required because, if the condition is not treated, it can be fatal. Steroid therapy and platelet transfusions remain the mainstay of treatment. Here, we describe a patient who presented with signs and symptoms of severe thrombocytopenia, which further led to the diagnosis of sarcoidosis. An adult male presented to the emergency department with a rash that deteriorated throughout the day. Based on complaints and laboratory testing, severe thrombocytopenia was noted. After a detailed examination and history-taking, he was found to have sarcoidosis. In association with drug administration and sarcoidosis, this could have caused severe thrombocytopenia. Written consent was taken from the patient mentioned in the study. The study was approved by the hospital and institutional ethics committee. Thrombocytopenia is a disorder where platelet counts drop below 150×10^9/l due to many different mechanisms. Among different etiological factors, sarcoidosis is the rarest and may present with very severe thrombocytopenia and lead to fatal complications. Such patients require close monitoring and treatment. Corticosteroids and platelet transfusions can be used as treatments. In the presented case, the patient was successfully treated, and on subsequent follow-up, the patient's condition improved. Manifestations of severe thrombocytopenia can be present even before the diagnosis of sarcoidosis. Further, the history of amoxicillin administration due to infection could have triggered the appearance of thrombocytopenia. Confirmation of sarcoidosis was made via biopsy. Multiple etiological factors that resulted in diagnostic ambiguity in our patient's presentation include the diagnosis of sarcoidosis, a history of infection, amoxicillin, and mild splenomegaly. The patient's treatment and recovery may indicate that corticosteroids, in conjunction with platelet transfusions, are beneficial. This is a novel case report of the presentation of severe thrombocytopenia, which was present even before the diagnosis of sarcoidosis.

Keywords: Sarcoidosis, Severe thrombocytopenia, Thrombocytopenia, Amoxicillin induced thrombocytopenia, Drug-induced thrombocytopenia, Case-study

INTRODUCTION

Thrombocytopenia is a platelet disorder that is indicated if the platelet count is less than 100×10^9/L or less than 150×10^9/l. However, if it is between 100 and 150×10^9/l, it is not considered a disease if it remains stable for more than 6 months; additionally, it is classified as mild ($>70\times10^9$/l), moderate ($20\text{-}70\times10^9$/l), and severe (20×10^9/l) based on the platelet count levels. There are various modes of thrombocytopenia, namely

pseudothrombocytopenia, congenital thrombocytopenia, and acquired thrombocytopenia.[1,2] The most common etiological factors include immune thrombocytopenia (ITP), drug-induced thrombocytopenia (DITP), infections (HCV, CMV, HIV, H. pylori, EBV, parvovirus B19), vaccinations, myelodysplastic syndromes, common variable immunodeficiency, different connective tissue disorders like systemic lupus erythematous (SLE), rheumatoid arthritis, sarcoidosis, antiphospholipid syndrome, hospital acquired infections, TTP/HUS, DITP, DIC, liver diseases, HIT, (macrophage activation syndrome (MAS), bone marrow failure syndromes (aplastic anemia, Fanconi anemia, dyskeratosis congenita, Diamond-Blackfan anemia, Shwachman-Diamond syndrome), chemotherapy-induced thrombocytopenia (CIT), cardiopulmonary bypass, GP2b/3a inhibitors, haematological disorders (leukemia, lymphoma, myelodysplastic syndrome). In pregnancy and postpartum most common being HELLP syndrome (hemolysis, elevated liver enzymes and low platelets), preeclampsia, abruptio placentae, TTP/HUS.[3,4] Major mechanisms for thrombocytopenia include pseudothrombocytopenia, marrow underproduction, peripheral destruction, splenic sequestration. From aformentioned etiologies, diagnosis is based on the history of patient, physical examination, laboratory studies, family history.[4]

Clinical features of thrombocytopenia appear due to impaired platelet plug formation and problems in primary hemostasis. The patient may stay asymptomatic with a small percentage of decreased platelets. If symptomatic, it varies from petechiae to systemic hemorrhage. Moreover, if platelet counts drop below $20–30\times10^9$/l symptoms include mucocutaneous bleeding, and if they drop below $10–20\times10^9$/l they may present with life-threatening severe bleeding like intracranial hemorrhage, bleeding from the GIT, and bleeding from the urinary tract. Patient usually seeks medical attention on appearance of petechial rash or ecchymoses on mucosal membrane and other body parts.[4,5]

Herein, we describe a case of 44-year-old adult male patient with severe thrombocytopenia of about 2×10^9/l most likely secondary to newly diagnosed sarcoidosis which may have manifested after administration of amoxicillin.

CASE REPORT

A 44-year-old male patient, with history of hypertension for the past 10 years, presents with complaint of rash which first appeared on the face and mucous membrane and progressively became worse during the day and appeared throughout the body.

So, he immediately went to the emergency hospital on his own and underwent a clinical and laboratory studies. On CBC, platelet count of 2×10^9/l was noticed for which he received prednisolone 30 mg and 6 doses of platelet transfusion. After treatment, CBC analysis was done on which platelet count improved to 37×10^9/l.

After receiving treatment, the next day he was referred to the haematological department for diagnosis and further evaluation.

On questioning, he reported history of fever few days back. On the following day, he noticed green colored sputum and rhinorrhea with some heaviness on breathing so he independently took antipyretic and amoxicillin 1000 mg 2 tablets a day for duration of 6 days. After 6 days of starting amoxicillin, he noticed rash on the face and on mucous membrane and at the end of the day petechiae were present on the limbs which lead him to emergency department. Patient has no any history of allergy.

On physical examination, icteric sclera, petechiae and ecchymoses were noted on limbs and on oral mucosa (Figure 1). He had body temperature of 36.2 C, blood pressure – 130/80, pulse – 84 /min, respiratory rate – 17 /min with shortness of breath. And absence of neurological symptoms with preserved alertness.

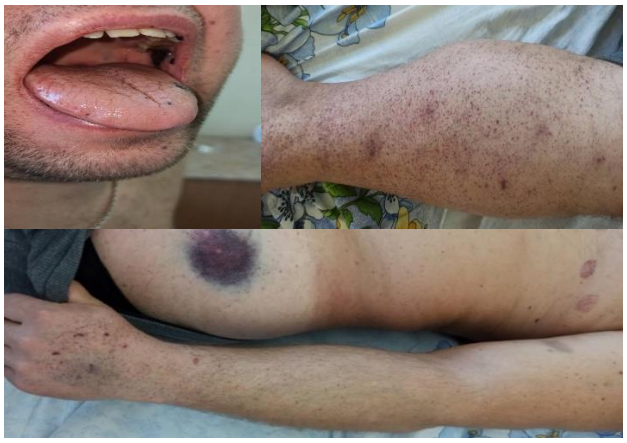

Figure 1: Appearance of petechial rash on mucosal membrane and extremities.

Based on history, physical examination, and lab analysis, a preliminary diagnosis of secondary severe thrombocytopenia was made, to rule out a possible etiology, additional tests for anti-erythrocytic antibodies, an ANA screen, a CT chest, a bone marrow biopsy from the sternum, a USG abdomen, a thyroid hormone test, a coagulogram, and tests for HIV, hepatitis, CMV, and EBV were ordered. Meanwhile, treatment was started with prednisone 90 mg IV drip, omeprazole 20 mg, Losartan 100 mg in the morning for his hypertension, and sodium ethamsylate. Results of viral serology, anti-eythrocytic antibodies, ANA turned out to be negative. Bone marrow biopsy showed normocellular bone marrow and sufficient number of megakaryocytes.

On the ultrasonography (USG) abdomen, mild splenomegaly was present. On the computed tomography (CT) chest, interstitial-nodular changes in the lung parenchyma and enlargement of lymph nodes probably characteristic of sarcoidosis (pulmonary-mediastinal form) were noted, and for a definite diagnosis of

sarcoidosis, an interlobar lymph node biopsy was indicated as soon as platelet counts got into the normal range (Figure 2).

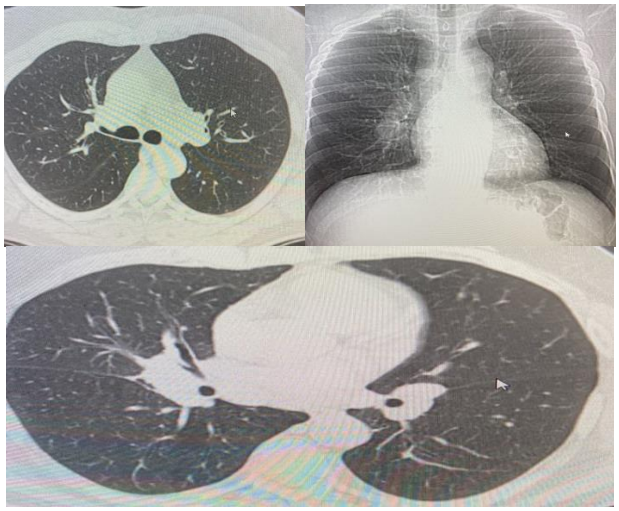

Figure 2: Showing interstitial-nodular changes in the lung parenchyma and enlargement of lymph nodes.

During his hospital stay, the patient received multiple platelet transfusions and steroids. Serial CBCs were ordered during his hospitalization; a summary of his platelets is shown in Figure 3.

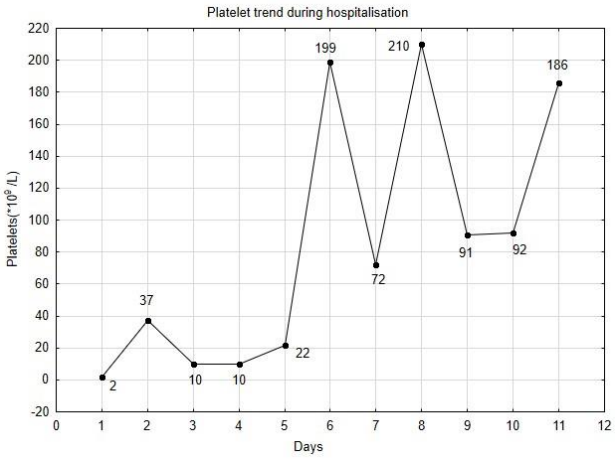

Figure 3: Summary of platelet count from day of hospitalization.

The patient's condition improved in about 10–11 days. As his condition improved, a video-assisted thoracoscopy (VATS) biopsy of S8 of the lower lobe of the right lung and a biopsy of the interlobar lymph node on the right were indicated. Histopathological examination of the interlobar lymph node showed evidence of granulomatous inflammation, were as in lung fragment, focal peribronchial and perivascular fibrosis, focal emphysema, and focal thickening of the pleura due to fibrosis. Inflammatory changes were not detected. Based on this, he was diagnosed with severe thrombocytopenia, probably secondary to sarcoidosis, which may have manifested after the administration of amoxicillin. At the time of discharge, the patient's condition was satisfactory, and platelet counts improved to 186×10^9/l. Additionally, patient was instructed to take methylprednisolone 32 mg in the morning, 8 mg in the afternoon with a reduction to 4 mg after 5 days.

DISCUSSION

Thrombocytopenia is a disorder of platelet, indicated if it is less than 100×10^9/l or less than 150×10^9/l. However, Sometimes, if it is between 100-150×10^9/l it is not considered as a disease if it remains stable for more than 6 months; further based on levels of platelet count it is divided into mild (>70×10^9/l), moderate (20-70×10^9/l) and severe (<20×10^9/l).[2] Among different etiological factors, sarcoidosis is a disease that is characterized by the presence of non-caseating granulomatous lesions in multiple organ systems. Hematological disorders like thrombocytopenia caused by sarcoidosis are extremely rare among pulmonary and extrapulmonary complications. The incidence of thrombocytopenia in cases of sarcoidosis is estimated to be between 1-2%.[6]

The exact mechanism by which sarcoidosis causes severe thrombocytopenia is still unclear, but as of now, mainly three mechanisms have been identified as being behind this. Among these three, thrombocytopenia caused by one or multiple mechanisms can be present in the same patient. Mechanisms include involvement of bone marrow, splenomegaly, and immunological. First is splenomegaly, where the spleen leads to sequestration and destruction of platelets. However, thrombocytopenia due to hypersplenism in sarcoidosis must always be suspected if the patient presents with splenomegaly and thrombocytopenia. In bone marrow involvement, non-caseating granulomatous infiltration is rare and may not be associated with thrombocytopenia. The third mechanism is immunological, where platelet destruction is mediated by TH1 cells and IgG antibodies.[7-10] our patient presented with severe thrombocytopenia of 2×10^9/l and upon workup of his condition, he was found to have sarcoidosis of the lung, which was confirmed by the presence of non-caseating granulomas on biopsy. Bone marrow biopsy was conducted to check if any specific findings were present. In cases where bone marrow was involved in sarcoidosis, non-caseating granulomas were observed. Moreover, there have been reported cases with increased megakaryocytes, emperipolesis, and normal cellularity of bone marrow. Further on CBC, anemia and leukopenia is seen in bone marrow involvement.[11,12] In our case, the patient had normal cellularity of the bone marrow with sufficient number of megakaryocytes and the absence of anemia and leukopenia, signifying no bone marrow involvement. Furthermore, our patient's history of fever, rhinorrhea, and green-colored sputum, for which he received amoxicillin 2000 mg for 6 days, could have triggered drug-induced thrombocytopenia. Thus, despite having a definite diagnosis of sarcoidosis, the history of drug administration

makes the etiology of secondary severe thrombocytopenia uncertain. So far, no cases have been reported where the diagnosis of secondary severe thrombocytopenia was made, followed by a newly diagnosed case of sarcoidosis and a history of amoxicillin administration.

As Dr. Matthieu Mahévas mentions in his case series, treatment of thrombocytopenia in patients with sarcoidosis includes steroids as a first line and IVIG, rituximab, as a second line. Although splenectomy is indicated if the platelet count doesn't resolve even after the first and second lines of treatment.[13] A definite treatment for drug-induced thrombocytopenia (DITP) is not available, but it is sometimes treated as immune-mediated thrombocytopenia. As in the initial steps of management of DITP, discontinuation of the drugs started within the last 5–10 days is recommended. After cessation of the medications, platelet transfusion therapy can be done as a primary treatment to treat the thrombocytopenia if the patient is symptomatic. This shows no benefit in managing underlying pathogenesis, but it is very effective in preventing further progression of symptoms to severe bleeding. As DITP is sometimes difficult to differentiate from ITP, corticosteroids are also often recommended, but they are still controversial to use in treatment.[14] Here, based on CT-findings, which justifies sarcoidosis and history of drug administration, our patient was given prednisolone 90 mg IV drip in his starting days of hospitalization and also multiple episodes of platelet transfusion were done. So the mainstay of treatment was corticosteroids and platelet transfusions, which led to a recovery in platelet counts. Once our patient achieved a platelet count of 210.5×10^9/l biopsy of interlobar lymph node and a video-assisted thoracoscopy (VATS) biopsy of the S8 of the right lung were indicated. Histopathological examination of the biopsy showed granulomatous inflammation, which is most characteristic of sarcoidosis. Steroid therapy in sarcoidosis helps to prevent the progression of granulomas by inhibiting autoimmunity.[15] Here, the use of steroids and platelet transfusions in the first place might have inhibited the progression of diseases to some extent and helped in achieving platelet counts. At the time of discharge, his platelet counts were 186×10^9/l and his general condition was satisfactory. Upon discharge, he was instructed to take methylprednisolone 32 mg in the morning, 8 mg in the afternoon, with a decrease to 4 mg after 5 days, and omeprazole 20 mg.

As described above, our patient presented with history of amoxicillin administration, followed by acute severe thrombocytopenia and a diagnosis of sarcoidosis during investigation was made. This is a novel case in which thrombocytopenia led to the diagnosis of sarcoidosis, and possibly a history of drug administration could have triggered the appearance of thrombocytopenia.

Based on our case we are proposing several hypotheses. Whenever patient presents with symptoms of secondary severe thrombocytopenia, sarcoidosis may also be the etiology behind this until proven otherwise. The combined therapeutic approach in the treatment of this patient with the use of glucocorticoids and platelet transfusion was successful and is recommended in clinical practice.

Limitations

For rule out drug-induced thrombocytopenia, tests for hapten-dependent antibody, drug-dependent antibody and drug-dependent platelet reactive antibodies (DDAb) were not done in this case.

CONCLUSION

A 44-year-old male patient presents to the emergency department with complaint of rash that progressively became worse during the day and appeared throughout the body. On examination, petechiae and echhymoses were present on the legs, and the CBC showed severe thrombocytopenia of 2×10^9/l. A thorough review of the patient's history reveals that the patient took amoxicillin 2 g/day for 6 days. On an extensive workup, including a CT scan and intralobar lymph node biopsy, a confirmed diagnosis of sarcoidosis was made, which raised a high suspicion regarding the etiology of secondary severe thrombocytopenia. Based on this and the elimination of every other possible etiological factor, the cumulative cause behind the presentation of severe thrombocytopenia could be sarcoidosis and/or drug administration. Multiple etiological factors that resulted in diagnostic ambiguity in our patient's presentation include a history of infection, the diagnosis of sarcoidosis, amoxicillin, and mild splenomegaly. Corticosteroids and platelet transfusions were used in the treatment to improve the patient's condition. Further studies are required to find a possible correlation among sarcoidosis, thrombocytopenia, and amoxicillin.

ACKNOWLEDGEMENTS

Authors would like to thank the patients, without whom, the entire case study would have amounted to nothing. Also, they would like to thank fellow researcher Mehul Hitesh Sadadiwala for his teaching and encouraging young budding researchers.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Stasi R, Amadori S, Osborn J, Newland AC, Provan D. Long-Term Outcome of Otherwise Healthy Individuals with Incidentally Discovered Borderline Thrombocytopenia. PLoS Med. 2006;3:e24.
2. Diz-Küçükkaya R, López JA. Thrombocytopenia. In Williams Hematology. McGraw-Hill Education. 2015.
3. Stasi R. How to approach thrombocytopenia. Hematology. 2012;191-7.

4. Lee EJ, Lee AI. Thrombocytopenia. Primary Care: Clinics in Office Practice. 2016;43:543-57.
5. Moss RA. Drug-induced immune thrombocytopenia. Am J Hematol. 1980;9:439-46.
6. Dąbrowska M, Krenke R, Maskey-Warzęchowska M, Boguradzki P, Waszczuk-Gajda A, Jędrzejczak WW, et al. Primary immune thrombocytopenia in a patient with sarcoidosis. Pneumonol Alergol Pol. 2011;79(5):371-6.
7. Fordice J, Katras T, Jackson RE, Cagle PT, Jackson D, Zaleski H, et al. Massive splenomegaly in sarcoidosis. South Med J. 1992;85(7):775-8.
8. Mahévas M, Le Page L, Salle V, Lescure FX, Smail A, Cevallos R, et al. Thrombocytopenia in sarcoidosis. Sarcoidosis Vasc Diffuse Lung Dis. 2006;23(3):229-35.
9. Judson MA, Baughman RP, Teirstein AS, Terrin ML, Yeager H Jr. Defining organ involvement in sarcoidosis: the ACCESS proposed instrument. ACCESS Research Group. A Case Control Etiologic Study of Sarcoidosis. Sarcoidosis Vasc Diffuse Lung Dis. 1999;16(1):75-86.
10. Korogodina A, Kaur N, Kumthekar A. Sarcoidosis-Associated Immune Thrombocytopenic Purpura and Focal Segmental Glomerulosclerosis. J Investig Med High Impact Case Rep. 2022;10:23247096221097522.
11. Medhat BM, Behiry ME, Fateen M, El-Ghobashy N, Fouda R, Embaby A, et al. Sarcoidosis beyond pulmonary involvement: A case series of unusual presentations. Respir Med Case Rep. 2021;34:101495.
12. Yanardağ H, Pamuk GE, Karayel T, Demirci S. Bone marrow involvement in sarcoidosis: an analysis of 50 bone marrow samples. Haematologia (Budap). 2002;32(4):419-25.
13. Mahévas M, Chiche L, Uzunhan Y, Khellaf M, Morin AS, Le Guenno G, et al. Association of sarcoidosis and immune thrombocytopenia: presentation and outcome in a series of 20 patients. Medicine (Baltimore). 2011;90(4):269-78.
14. George JN, Aster RH. Drug-induced thrombocytopenia: pathogenesis, evaluation, and management. Hematology Am Soc Hematol Educ Program. 2009;153-8.
15. Starshinova AA, Malkova MM, Basantsova NY, Zinchenko YS, Kudryavtsev YV, Ershov GA, et al. Sarcoidosis as an Autoimmune Disease. Front Immunol. 2020;10.

Cite this article as: Karpovich Y, Ribadiya FN, Tanna SS, Trada DY, Karpovich Y, Bogdanovich V. A rare case of patient with severe thrombocytopenia associated with sarcoidosis: a case study. Int J Res Med Sci 2023;11:1796-800.