J. Health Biol Sci. 2023;11(1):1-3 doi: 10.12662/2317-3206jhbs.v11i1.4726.p1-3.2023

CASE REPORT

Cytomegalovirus Infection-related Immune Thrombocytopenia: A Case Report

Púrpura Trombocitopênica Imune Associada à Infecção por Citomegalovírus: Relato de Caso

Rafael Siqueira Athayde Lima[1,2], Rodrigo Fonseca Halley[2], Tássia Ívila Freitas de Almeida[2], Aglaêrton Silva Pinheiro[2] Maiza Colares de Carvalho[2]

1. Hospital Universitário Walter Cantídio, EBSERH, UFC, Fortaleza, Ceará, Brazil. 2. Hospital Geral de Fortaleza, SESA, Fortaleza, Ceará, Brazil.

Abstract

Immune thrombocytopenia (ITP) is an acquired cause of thrombocytopenia characterized by the presence of autoantibodies against platelets. It may be primary or secondary to several conditions. We present the case of a 63-year-old woman with a diagnosis of immune thrombocytopenia refractory to conventional therapy. After she was tested for secondary causes of ITP, a diagnosis of acute cytomegalovirus (CMV) infection was made. She was treated with ganciclovir and presented normalization of platelet count. CMV-related Immune Thrombocytopenia should always be considered in certain cases of refractory ITP. If the diagnosis of ITP secondary to acute CMV infection is made, specific antiviral therapy with ganciclovir should be considered. In these cases, immunosuppressive agents, such as steroids, may worsen the ITP and should be tapered or withdrawn as rapidly as feasible.

Keywords: immune thrombocytopenia; cytomegalovirus; ganciclovir.

Resumo

A Púrpura Trombocitopênica Imune (PTI) é uma causa de trombocitopenia adquirida caracterizada pela presença de autoanticorpos contra plaquetas. A doença pode ser primária ou secundária a diversas condições. Apresentamos o caso de uma mulher de 63 anos com diagnóstico de PTI refratária à terapêutica convencional. A investigação de causas secundárias evidenciou infecção aguda por citomegalovírus (CMV). A paciente foi tratada com ganciclovir e evoluiu com normalização no nível de plaquetas. A PTI relacionada ao CMV deve sempre ser investigada em pacientes com PTI refratária, sendo a terapia antiviral específica com ganciclovir o tratamento de escolha. Nestes casos, os agentes imunossupressores, como os corticosteroides, podem piorar a PTI e devem ser reduzidos gradualmente ou retirados o mais rapidamente possível.

Palavras-chave púrpura trombocitopênica imune; citomegalovírus; ganciclovir.

INTRODUCTION

Immune thrombocytopenia (ITP), former immune thrombocytopenic purpura, is an autoimmune disorder that occurs in both adults and children characterized by a low platelet count and mucocutaneous bleeding. It is defined as a platelet count < 100,000 per mm³ and immune destruction of platelets[1]. Its incidence among adults is between 1.6 and 3.9 new cases per 10.000 per year[2]. Immune thrombocytopenia can be divided into primary and secondary, which corresponds to 14% of the cases[3]. ITP is a diagnosis of exclusion since there is no laboratory test or any other method that proves immune thrombocytopenia[4]. Steroids and intravenous immunoglobulin (IVIG) are the treatment of choice for immune thrombocytopenia. Splenectomy and rituximab are second-line therapies used in patients with primary ITP who are not responsive to first-line agents or relapsed after treatment[3]. In cases of secondary ITP, treatment of the underlying cause is as important as standard therapy. Cytomegalovirus (CMV) infection is a well-known etiology of secondary ITP and may cause refractory disease[5]. We present a case of a 63-year-old female patient with a history of non-measured fever, petechiae, and low platelets (7,000 per mm³) after CMV infection, with excellent clinical response to specific antiviral therapy.

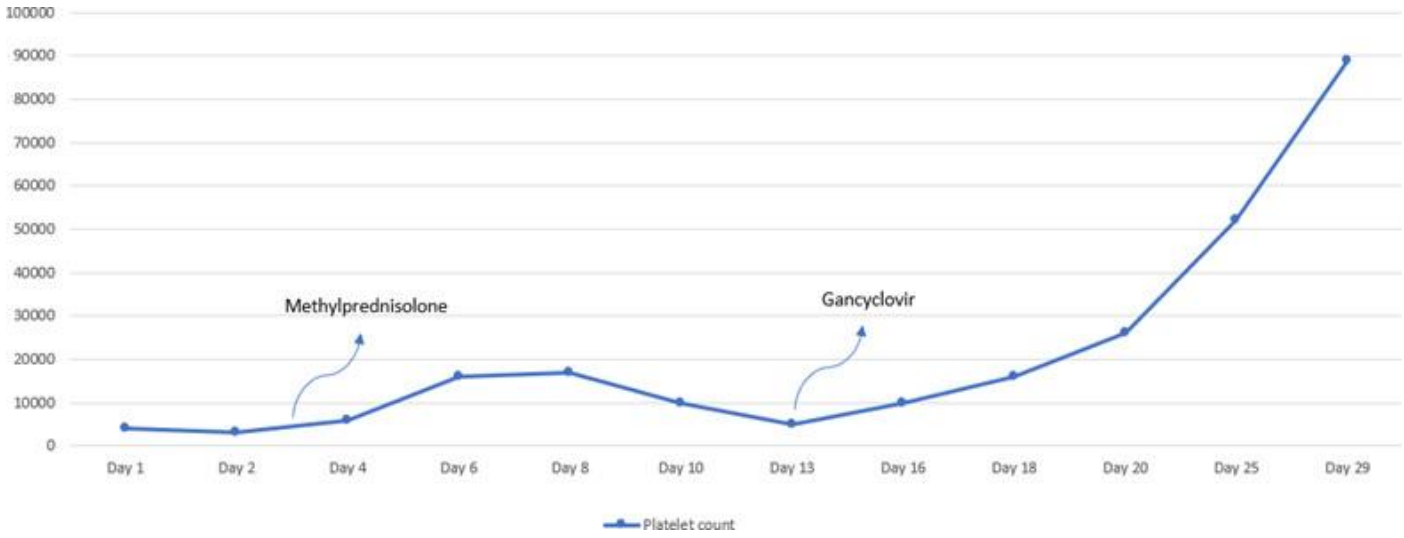
CASE REPORT

A 63-year-old woman presented with a recent 20-day history of non-measured fever, fatigue, and mild temporal headache. After four (4) days of the beginning of the symptoms, she sought medical attention in an emergency department of her city. She had multiple petechiae on her legs, and her physical examination was otherwise normal. She denied a history of bleeding events. Her blood exam showed a low platelet count (7,000 per mm³). Due to these findings, a presumptive diagnosis of Dengue fever was made. However, Dengue antibodies (IgG and IgM) were negative. After nine (9) days, thrombocytopenia persisted, and she was transferred to Hospital Geral de Fortaleza. On admission, she was oriented and afebrile. Heart, lungs, and abdominal physical exams were normal. She had multiple petechiae on her legs and trunk. Her blood pressure was 140 x 80 mmHg. The laboratory revealed severe thrombocytopenia

Correspondence: Rafael Siqueira Athayde Lima. Rua Carolina Sucupira, 81. CEP 60140-120 Fortaleza, CE E-mail: r.siqueira.athayde@gmail.com
Conflict of interesse: There is no conflict of interest on the part of any of the authors.
Received: 2023 Mar 23; Revised: 2023 Sep 1; Accepted: 2023 Sep 15

(4,000 per mm³) without anemia or leukopenia. A presumptive diagnosis of immune thrombocytopenia (ITP) was made. On the 3rd day of hospitalization, intravenous methylprednisolone for three (3) days was started followed by oral prednisone (60 mg daily). Despite corticotherapy, the platelet count did not increase satisfactorily (Figure 1). Tests for secondary causes of ITP were made. Bone marrow aspiration showed no dysplastic changes. Her laboratory exams were negative for antinuclear antibody test, HBV surface antigen, hepatitis C virus antibodies, and nontreponemal test for syphilis and HIV-1 and HIV-2 antibodies. Blood tests for cytomegalovirus antibodies (IgG and IgM) and parvovirus B19 antibodies (IgG and IgM) were positive. Polymerase chain reaction (PCR) was positive for cytomegalovirus and ganciclovir was started on the 13th day for 14 days. After the beginning of the antiviral therapy, platelet levels started to increase, as shown in Figure 1. She was discharged from the hospital on the 29th day with a platelet count of 89,000 per mm³ and tapering off prednisone.

Figure 1. Platelet count (per mL) progression during hospitalization



DISCUSSION

Immune thrombocytopenia (ITP) is an acquired thrombocytopenia caused by autoantibodies against platelet antigens. It is one of the most common causes of thrombocytopenia in adults. Many patients are asymptomatic. For those who have symptoms, these are normally related to primary coagulation features, such as petechia, oral mucosa bleeding, and epistaxis. However, severe hemorrhage may occur, such as intracranial hemorrhage, gastrointestinal bleeding, and hematuria. Laboratorially, ITP usually presents as isolated thrombocytopenia, although variable degrees of anemia may occur due to bleeding or associated autoimmune hemolytic anemia (Evans Syndrome). ITP may be primary (also called idiopathic) or secondary. Secondary causes of ITP include drugs (e.g., methyldopa), autoimmune diseases (e.g., systemic erythematosus lupus), malignancies disorders (e.g., lymphoproliferative disorders, such as chronic lymphocytic leukemia) and infections (e.g., HIV, CMV, hepatitis C virus, Helicobacter pylori)[4].

Cytomegalovirus is a cause of morbidity and mortality in immunosuppressed patients and a well-known cause and perpetuating factor of ITP in pediatric as well as adult populations[6,7]. Various mechanisms have been proposed to explain ITP after a viral infection. A virus-antivirus complex may adhere to the platelets and cause them to be removed by the reticuloendothelial system. Furthermore, the virus could directly damage the bone marrow megakaryocyte and induce defective platelet formation that stimulates antibody formation[5]. This theory may explain why CMV infection-induced ITP has limited or no response to conventional therapy. Other theories support that the virus directly affects platelets so that they become antigenic, inducing the production of antiplatelet antibodies[5]. Some signs and symptoms are suggestive of CMV-related ITP, such as transaminitis, hepatomegaly, fever of unknown origin, atypical lymphocytes on blood smear shown, and unresponsiveness or refractory nature to standard therapy[8]. If CMV-related ITP is suspected, a polymerase chain reaction for cytomegalovirus should be ordered. If the diagnosis of immune thrombocytopenia secondary to cytomegalovirus is made, specific antiviral therapy with ganciclovir should be considered[9]. The recommended dose is 5 mg/kg 2 times/day for two (2) weeks after CMV PCR becomes undetectable. Then, the dose should be reduced to once daily. The discontinuation of antiviral therapy depends upon the clinical setting and the platelet count. In cases of myelosuppression due to ganciclovir, therapy should be switched to foscarnet. Some authors suggest reducing immunosuppressive agents, including steroids, as rapidly as feasible. Aggressive immunosuppressive therapy may exacerbate the primary CMV infection and worsen the ITP. If platelet-specific treatment is required while awaiting anti-CMV

therapy response, intravenous immunoglobulin (IVIG) can be useful in order to avoid immunosuppression[8].

CONCLUSION

Clinicians should consider CMV infection as a cause of immune thrombocytopenia, especially when some signs and symptoms (such as fever, myalgia, hepatomegaly) or some laboratory findings (such as atypical lymphocytes on smear) are present. Furthermore, a limited or no response to ITP-specific therapy (such as steroids) is another pitfall that should prompt physicians to test for CMV infection and other causes of secondary ITP. In cases of CMV infection-related ITP, antiviral treatment with ganciclovir may be more effective and important than standard ITP therapy and should be considered a first-line therapy in these cases. There is limited data about the benefits of steroids in ITP secondary to CMV infection, and some authors believe that it should be avoided, especially in immunocompromised hosts.

REFERENCES

1. Lambert MP, Gernsheimer TB. Clinical updates in adult immune thrombocytopenia. Blood. 2017 May; 129(21): 2829-2835. doi 10.1182/blood-2017- 03-754119.

2. Abrahamson PE, Hall SA, Feudjo-Tepie M, Mitrani-Gold FS, Logie J. The incidence of idiopathic thrombocytopenic purpura among adults: a population-based study and literature review. Eur J Haematol. 2009 Aug; 83(2): 83-89. doi 10.1111/j.1600-0609.2009.01247.x.

3. Ozelo MC, Colella MP, de Paula EV, Nascimento ACKV, Vilaça PR, Bernardo WM. Guideline on immune thrombocytopenia in adults: Associação Brasileira de Hematologia, Hemoterapia e Terapia Celular. Project guidelines: Associação Médica Brasileira – 2018. Hematol Transfus. Cell Ther. 2018 Jan-Mar; 40(1): 50-74. doi: 10.1016/j.htct.2017.11.001.

4. Matzdorff A, Meyer O, Ostermann H, Kiefel V, Eberl W, Kühne T, et al. Immune Thrombocytopenia – Current Diagnostics and Therapy: Recommendations of a Joint Working Group of DGHO, ÖGHO, SGH, GPOH, and DGTI. Oncol Res Treat. 2018; 41(Suppl 5): 1–30. doi: 10.1159/000492187.

5. Yenicesu I, Yetgin S, Ozyurek E, Aslan D. Virus-associated Immune Thrombocytopenic Purpura in Childhood. Pediatr Hematol Oncol. 2002 Sep; 19(6): 433-437. doi: 10.1080/08880010290097233.

6. Flores-Chang BS, Arias-Morales CE, Wadskier FG, Gupta S, Stoicea N. Immune thrombocytopenic purpura secondary to cytomegalovirus infection: a case report. Front. Med (Lausanne).2015 Nov; 2: 79. doi 10.3389/fmed.2015.0007.

7. Shrestha R, Rondelli D, Sherpa MT. Cytomegalovirus: A possible cause of Persistent Refractory Immune Thrombocytopenic Purpura. JAIM. 2014 Jan-Jun; 03(01): 42-45. doi http://dx.doi.org/10.3126/jaim.v3i1.10704.

8. DiMaggio D, Anderson A, Bussel JB. Cytomegalovirus can make immune thrombocytopenic purpura refractory. Br J Haematol. 2009 Jun; 146(1): 104–112. doi 10.1111/j.1365-2141.2009.07714.x.

9. Shimanovsky A, Patel D, Wasser J. Refractory immune thrombocytopenic purpura and cytomegalovirus infection: a call for a change in the current guidelines. Mediterr J Hematol Infect Dis. 2016, 8(1): e2016010. doi: http://dx.doi.org/10.4084/MJHID.2016.010

How to cite this article/ Como citar este artigo:
Lima RSA, Halley RF, Almeida TIF, Pinheiro AS, Carvalho MC. Cytomegalovirus Infection-related Immune Thrombocytopenia: A Case Report . J Health Biol Sci. 2023; 11(1):1-3.