CASE REPORT – OPEN ACCESS

International Journal of Surgery Case Reports 5 (2014) 1282–1284

Contents lists available at ScienceDirect

International Journal of Surgery Case Reports

journal homepage: www.casereports.com

A case of thrombocytopenia associated with the use of hydroxychloroquine following open heart surgery

Deniz Demir[a,*], Fatih Öcal[b], Mustafa Abanoz[a], Hasan Dermenci[b]

[a] Şanlıurfa Mehmet Akif İnan State Hospital, Cardiovascular Surgery Department, Şanlıurfa, Turkey
[b] Şanlıurfa Mehmet Akif İnan State Hospital, Hematology Department, Şanlıurfa, Turkey

ARTICLE INFO

Article history:
Received 21 August 2014
Received in revised form
10 November 2014
Accepted 10 November 2014
Available online 20 November 2014

Keywords:
Hydroxychloroquine
Cardiac surgery
Thrombocytopenia

ABSTRACT

INTRODUCTION: Thrombocytopenia is a common problem occurring in patients and drug-induced thrombocytopenia is a significant cause of thrombocytopenia.
PRESENTATION OF CASE: We present an unusual case of thrombocytopenia that was considered to be associated with the use of hydroxychloroquine in the late term following open heart surgery.
DISCUSSION: The drug-induced thrombocytopenia, mechanical destruction of the platelets, and hemodilution are common causes of low platelet count. Although drug-induced immune thrombocytopenia has a mild clinical course in most cases (in this case it has severe clinical course), some patients may experience life-threatening hemorrhages. The decision to discontinue the drug that is deemed to be responsible from the drug-induced thrombocytopenia (DITP) relies on the clinical condition of the patient. The diagnosis is mostly established by discontinuation, exclusion, and correlation because the tests performed to detect drug-dependent antibodies (DDAbs) for the diagnosis of DITP are time-consuming, and these tests are also not commonly available. The authors of the current study diagnosed DITP by discontinuation of the drug. We suggest that the use of hydroxychloroquine could be severe thrombocytopenia occurring after open heart surgery.
CONCLUSION: The medication history must be carefully reviewed in patients presenting with thrombocytopenia, and if the medications could cause thrombocytopenia must be discontinued.

1. Introduction

Thrombocytopenia is a common problem occurring in patients hospitalized in cardiology and cardiac surgery units. Platelet count decreases below 100×10^9 cells/L in 2.4–9.2% of the patients who were placed on abciximab, clopidogrel, or acetylsalicylic acid therapy after percutaneous coronary interventions.[1] There is a risk of developing thrombocytopenia in 35–65% of the patients who undergo cardiac surgery.[2]

The idiopathic thrombocytopenic purpura, drug-induced thrombocytopenia, infections (rubella), and pseudo-thrombocytopenia are among the causes of thrombocytopenia.[3]

The current report presents a case of thrombocytopenia that was considered to be associated with the use of hydroxychloroquine in the late term following open heart surgery.

2. Presentation of case

A 55-year-old male patient underwent open heart surgery dye to coronary artery disease that remained unresponsive to medical therapies. The patient was discharged from the hospital with full recovery one week after coronary artery bypass graft surgery. The platelet count at discharge after the operation was 308×10^9 cells/L. The patient was admitted to the outpatient clinics in the Department of Cardiovascular Surgery complaining of nose bleeding, petechiae on the body, and ecchymosis approximately three weeks after surgery (Fig. 1). The laboratory test revealed a platelet count of 7×10^9 cells/L, after which the patient consulted with a hematologist. The peripheral blood smear revealed an insufficient number of platelets and the absence of atypical cells, and the patient was then placed on steroid therapy with the pre-diagnosis of immune thrombocytopenia. The patient underwent bone marrow aspiration biopsy. The bone marrow aspiration biopsy was inconclusive with the exception of slightly increased megakaryocytes. During the follow-up of the patient, platelet count remained at low levels and did not respond to steroid therapy. The patient's medical history was rechecked, and it was revealed that the patient had been using hydroxychloroquine for the last one week erroneously as a pain killer, unbeknownst to the surgeons; hydroxychloroquine use was

* Corresponding author. Tel.: +90 5054571988.
E-mail addresses: denizzdr@msn.com (D. Demir), fthocal@yahoo.com (F. Öcal), mustafaabanozdr@hotmail.com (M. Abanoz), hasandermenci@yahoo.com (H. Dermenci).

http://dx.doi.org/10.1016/j.ijscr.2014.11.052

Fig. 1. Images showing petechiae on the chest of the patient.

discontinued. The platelet counts increased over a period of several days, and petechia and ecchymosis on the body disappeared. The platelet count at 1 month control visit was 300×10^9 cells/L. The patient is under follow up for 3 months and who was healthy in that time.

3. Discussion

The drug-induced thrombocytopenia, mechanical destruction of the platelets, and hemodilution are common causes of low platelet count encountered after open heart surgery.[1]

Although drug-induced immune thrombocytopenia has a mild clinical course in most cases, in this case it was severe may depend of cross-reaction between acetyl salicylic acid and hydroxychloroquine. Many drugs can induce the development of immune thrombocytopenia such as antibiotics, anticonvulsants, and anti-inflammatory drugs. However, the most common type of drug-induced thrombocytopenia is heparin-induced thrombocytopenia.[4]

Treatment varies depending on the causes of thrombocytopenia. For instance, steroids and intravenous immunoglobulin (IVIG) therapy are used in the treatment of immune thrombocytopenic purpura, whereas direct thrombin inhibitors (bivalirudin, argatroban, lepirudin) are used in the treatment of heparin-induced thrombocytopenia.[5,6]

Drug-induced thrombocytopenia occurs as a non-immune-mediated suppression of bone marrow or immune-mediated destruction of the platelets by specific antibodies to the drug. Thrombocytopenia is caused by myelosuppressive substances are dose-dependent and not difficult to recognize. However, immune-mediated thrombocytopenia is not dose-dependent and the diagnosis is challenging; the reason is that these patients use multiple medications.[7]

The decision to discontinue the drug that is deemed to be responsible from the drug-induced thrombocytopenia (DITP) relies on the clinical condition of the patient. The diagnosis is mostly established by discontinuation, exclusion, and correlation because the tests performed to detect drug-dependent antibodies (DDAbs) for the diagnosis of DITP are time-consuming, and these tests are also not commonly available.[4,7]

Transfusions and steroid therapy have been used in the treatment of DITP; however, there is no evidence on the efficiency of these therapies. The drug is eliminated from the body in a couple days in hospitalized patients, and this is followed by gradual increase in the platelet count. Thrombocytopenia and bleeding symptoms rarely persist for weeks. The patients with persistent symptoms can be administered therapies such as IVIG and plasma exchange therapy; however, the efficiency of these therapies has not been clearly demonstrated.[4]

Hydroxychloroquine is used in the treatment of malaria, rheumatic disorders, and systemic lupus erythematosus.[8] Many side effects have been reported associated with the use of hydroxychloroquine. Among these side effects, there is a particular concern regarding the development of cardiomyopathy and thrombocytopenia.[9,10]

The patient was discharged with full recovery after open heart surgery. However, the patient was re-admitted at postoperative 3 weeks complaining of nose bleeding, petechiae, and ecchymosis on the body. The platelet count was very low upon admission. The peripheral blood smear revealed a low platelet count and the absence of atypical cells. The patient was deemed to have immune thrombocytopenia, for which he was placed on steroid therapy. However, the patient did not respond to therapy. Meanwhile, a more comprehensive medical history was obtained. It was revealed that the patient had been using hydroxychloroquine as a pain killer outside the knowledge of the surgeons. Hydroxychloroquine use was discontinued, and platelet count showed a gradual increase in the following days. The platelet count was 300×10^9 cells/L at the 1 month control visit. The patient is still under follow-up at 3 months without exhibiting any hemorrhage and other problems.

Before the patient presenting thrombocytopenia, who was using 100 mg acetyl salicylic acid, antibiotic and anti-inflammatory drug. During in this period, the patient's platelet count was within normal range. However, after one weak, severe thrombocytopenia was observed in the patient duo to erroneously using hydroxychloroquine. In several days, after cessation of the drug platelet levels in the patient has become the normal range. Thrombocytopenia was observed while the patient was using acetylsalicylic acid and hydroxychloroquine. Both drugs can cause this case.[1,10] The diagnosis was established by discontinuation and exclusion of hydroxychloroquine. After hydroxychloroquine was ceased, the patient was become health. But who still using acetylsalicylic acid 100 mg and thrombocytopenia was not seen in controls. Therefore acetylsalicylic acid was not considered as a cause of thrombocytopenia in this patient. Also role of 100 mg acetyl salicylic in this case was considered as increasing of thrombocytopenia severity. In order to determination drug-dependent thrombocytopenia, mostly drug cessation and exclusion methods are used.[7] Also in this case, drug cessation was used as exclusion method. We believe that the use of hydroxychloroquine is cause of thrombocytopenia.

4. Conclusion

The medication history must be carefully assessed in the differential diagnosis of patients presenting with isolated thrombocytopenia, and the drugs that might be possibly related to thrombocytopenia must be discontinued.

Conflict of interest

Each author certifies that he has no commercial associations that might pose a conflict of interest in connection with the submitted article.

Funding

No funding support.

Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Author contributions

Dr. Deniz Demir Operation surgeon 1 and correspondence. Dr. Fatih Öcal Haematologist and review of literature. Dr. Mustafa Abanoz operation surgeon 2. Dr. Hasan Dermenci Haematologist and review of literature.

References

1. Matthai Jr WH. Thrombocytopenia in cardiovascular patients: diagnosis and management. *Chest* 2005;**127**(2):46–52.
2. Rezende E, Morais G, Silva Junior JM, Oliveira AM, Souza JM, Toledo DO, et al. Thrombocytopenia in cardiac surgery: diagnostic and prognostic importance. *Rev Bras Cir Cardiovasc* 2011;**26**(1):47–53.
3. Ashoub A, Lakshmanan S, Luckraz H. Cardiac surgery in a patient with severe thrombocytopenia: how low is too low? *Ann Card Anaesth* 2013;**16**(3):215–7.
4. Aster RH, Curtis BR, McFarland JG, Bougie DW. Drug-induced immune thrombocytopenia: pathogenesis, diagnosis, and management. *J Thromb Haemost* 2009;**7**(6):911–8.
5. LugaoRdos S, Motta MP, de Azevedo MF, de Lima RG, AbrantesFde A, Abdala E, et al. Immune thrombocytopenic purpura induced by intestinal tuberculosis in a liver transplant recipient. *World J Gastroenterol* 2014;**20**(25):8304–8.
6. Velagic V, Samardzic J, Baricevic Z, Skoric B, Cikes M, Gasparovic H, et al. Management of heparin-induced thrombocytopenia with fondaparinux in a patient with left ventricular assist device. *Int J Organ Transplant Med* 2014;**5**(2):83–6.
7. Bansal R, Sharma PK, Sharma A. A case of thrombocytopenia caused by rifampicin and pyrazinamide. *Indian J Pharmacol* 2013;**45**(4):405–7.
8. Cohen PR. Hydroxychloroquine associated hyperpigmentation mimicking elder abuse. *Dermatol Ther (Heidelb)* 2013;**3**(2):203–10.
9. Abbasi S, Tarter L, Farzaneh-Far R, Farzaneh-Far A. Hydroxychloroquine: a treatable cause of cardiomyopathy. *J Am Coll Cardiol* 2012;**60**(8):786.
10. Nieweg HO, Bouma HG, Devries K, Jansz A. Haematological side-effects of some anti-rheumatic drugs. *Ann Rheum Dis* 1963;**22**:440–3.