Journal of the Turkish Academy of Dermatology
eISSN 1307-394X

Case Report

Cyclosporine-Induced Immune Thrombocytopenia in a Patient with Psoriasis Vulgaris

Savaş Yaylı*, MD, Sevgi Bahadır*, MD, Nergiz Erkut**, MD, Mehmet Sönmez**, MD

Address: *Department of Dermatology, Karadeniz Technical University, School of Medicine, Trabzon, Turkey
** Department of Hematology, Karadeniz Technical University, School of Medicine, Trabzon, Turkey
E-mail: savasyayli@gmail.com
* *Corresponding Author:* * Savas Yayli, MD, Karadeniz Teknik Üniversitesi Tıp Fakültesi Dermatoloji AD 61080 Trabzon/Turkey

Published:
J Turk Acad Dermatol 2011; **5 (3)**: 1153c2
This article is available from: http://www.jtad.org/2011/3/jtad1153c2.pdf
Key Words: Cyclosporine, psoriasis, thrombocytopenia

Abstract

Observation: Drug-induced thrombocytopenia is a rare, but serious, adverse effect of treatment with many drugs. Cyclosporine is not a well-known cause. We show that cyclosporine which is an effective treatment option for immune thrombocytopenia may also responsible for immune thrombocytopenia in a 58-year-old patient with psoriasis. Our patient experienced thrombocytopenia with a platelet count of 20000, after four months of the therapy with cyclosporine. It was detected in regular examination of complete blood cell analyse and it was confirmed by assessment of blood smear. Because of the lack of another possible cause, cyclosporine was the probable cause of the thrombocytopenia. It was withdrawn promptly. Both of platelet count and blood smear were completely normal after ten days. As an immunoregulator on T cells, cyclosporine may cause immune thrombocytopenia by leading dysregulation of T cell immunity and increasing the number of autoreactive peripheral T lymphocytes. We point out that cyclosporine as an effective drug for treatment of psoriasis vulgaris and immune thrombocytopenia may also induce immune thrombocytopenia even after four months.

Introduction

Drug-induced thrombocytopenia (DIT) is a rare, but serious, adverse effect of treatment with a wide range of drugs. Many of these medications induce thrombocytopenia by immune mechanisms [1]. Cyclosporine is not a well-known cause of drug-induced immune thrombocytopenia (DIIT) [2]. To our knowledge, this is the first case of cyclosporine-induced immune thrombocytopenia in a patient with psoriasis vulgaris.

Case Report

A 58-year-old patient with psoriasis vulgaris was admitted to our clinic for follow-up control. She has been on cyclosporine therapy for four months. Before cyclosporine, she had used topical treatments for many years, and a short course of acitretin therapy which had been withdrawn because of the intolerance to therapy. Cyclosporine was initially administered at a dosage of 2.5 mg/kg/d, which was gradually decreased to 1.5 mg/kg/d, the current dosage. She had no psoriatic lesions and any complaints. Besides cyclosporine therapy, she had been on amlodipine and citalopram for seven and four years, for hypertension and depression, respectively.

Physical examination revealed no psoriatic lesions, and no pathologic signs on her skin and mucosal surfaces. Regular laboratory investigations for cyclosporine including renal function tests, elect-

rolytes, and complete blood cell analyses showed normal results except for platelet count which was 20.000/μL. Erythrocyte sedimentation rate (ESR) was mildly increased (35 mm/hour) and level of C-reactive protein was also normal. Her last platelet count which was done at 3rd month was 150.000/μL, and she did not have any petechia, bruising, and epistaxis or more severe bleedings in last days. There was no clinical sign of any viral or bacterial infections, serologic tests for Epstein-Barr virus, cytomegalovirus, and parvovirus B19 which may cause thrombocytopenia were negative. After hematology consultation, examination of peripheral blood smear test showed no abnormality except for thrombocytopenia [**Figure 1**].

Although pure thrombocytopenia is not a well-known side effect of cyclosporine, it was the probable cause of thrombocytopenia in our patient. Cyclosporine was withdrawn promptly with the diagnosis of drug-induced immune thrombocytopenia (DIIT). After withdrawal of the cyclosporine, no new symptoms due to thrombocytopenia occurred on follow-up period. Platelet count increased to 120.000/ μL after one week, and it reached normal values after a few days (> 150.000/ μL).

Discussion

According to the established criteria for drug causality assessment in thrombocytopenia, cyclosporine is the probable cause of thrombocytopenia in our patient [**2**]. The causal association is strongly suggested, because of the lack of another possible cause for pure thrombocytopenia, and the complete normalization of the platelet counts of the patient after cyclosporine withdrawal. In addition, cyclosporine was the drug which was administrated at last period, even it was four months ago. Although other drugs she used, either amlodipine or citalopram were also reported as a cause of thrombocytopenia in one case [**3, 4**], our patient had been on amlodipine and citalopram for seven and four years, respectively. After cyclosporine withdrawal, while she continued using these drugs, the platelet counts increased to the normal values.

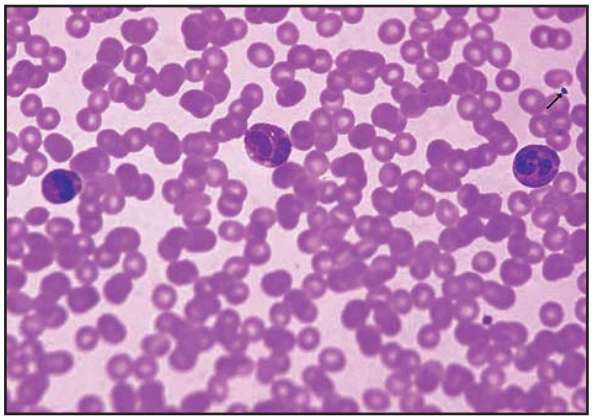

Figure 1. Peripheral blood smear of the patient that shows thrombocytopenia. Arrow shows thrombocytes

Cyclosporine is a powerful suppressor of T-cell function [**5**]. Cyclosporine binds to and inhibits calcineurin, a calcium and calmodulin dependent phosphatase, which selectively inhibits both antigen-induced activation of CD4+ lymphocytes and the production by these cells of interleukin 2 (IL-2) and other cytokines. This results in an indirect effect on the growth and differentiation of B lymphocytes. Cyclosporine can induce and maintain remission in autoimmune diseases, particularly in those with mechanisms mediated by T cells [**6**]. It has proven effectiveness in psoriasis and other autoimmune diseases [**7**]. It is also an effective drug for the treatment of patients with chronic idiopathic thrombocytopenic purpura refractory to corticosteroids or splenectomy [**8**].

DIT is generally manifested petechia, bruising, and epistaxis. Bleeding may become more severe as gastrointestinal or genitourinary mucosal bleeding or even intracranial or pulmonary hemorrhage [**9**]. The major bleeding rate in reported case of DIT was shown as 9%. An additional 67% of patients demonstrated bleeding that was considered less than severe, 24% of patients had no bleeding symptoms [**2**]. Most patients with DIT experience moderate to severe thrombocytopenia (platelet count less than 50.000/μL), with the majority reaching nadir levels below 20.000/μL [**9**]. Our patient did not have any petechia, bruising, and epistaxis or more severe bleedings although platelet count was 20.000/ μL. Thrombocytopenia was detected in the regular examination of complete blood cell analyses which was routinely done as a follow up criteria for patients with psoriasis vulgaris on cyclosporine therapy at 4th month. Cyclosporine was withdrawn promptly. After ten days, platelet count was in normal range.

Table 1. Medications Commonly Implicated in Drug-induced Immune Thrombocytopenia

Heparin
Quinine
Quinidine
Penicillin
Sulfonamids
Non-steroidal anti-inflammatory drugs
Oral antidiabetic drugs
Carbamazepine
Phenytoin
Valproate
Gold salts
Rifampicin
Ranitidine
Hydrochlorothiazide
Cephalosporins
Eptifibatide
Abciximab
Lotrafiban
Procainamide

Cyclosporine is not a well-known cause of DIIT. Most commonly reported medications implicated in DIIT were listed in **Table 1** [**2**]. Cyclosporine is rather reported as a cause of thrombotic microangiopathy includes hemolytic uremic syndrome and thrombotic thombocytopenia purpura, but is even a rare complication [**10**]. As an immunoregulator on T cells, cyclosporin may cause immune thrombocytopenia by leading dysregulation of T cell immunity, which results in decreased regulatory T cells, and increasing the number of autoreactive peripheral T lymphocytes [**11**].

We point out that cyclosporine, an effective drug for the treatment of psoriasis, and also immune thrombocytopenia, may also induce immune thrombocytopenia even after four months of therapy. Because of the frequent use of cyclosporine in psoriasis, and the other inflammatory skin diseases, this should be kept in mind on dermatological practice.

References

1. Kenney B, Stack G. Drug-induced thrombocytopenia. Arch Pathol Lab Med 2009; 133: 309-314. PMID: 19195976
2. George JN, Raskob GE, Shah SR, Rizvi MA, Hamilton SA, Osborne S, et al. Drug-induced thrombocytopenia: a systematic review of published case reports. Ann Intern Med 1998; 129: 886-890. PMID: 9867731
3. Garbe E, Meyer O, Andersohn F, Aslan T, Kiesewetter H, Salama A. Amlodipine-induced immune thrombocytopenia. Vox Sang 2004; 86: 75-76. PMID: 14984564
4. Andersohn F, Konzen C, Bronder E, Klimpel A, Garbe E. Citalopram-induced bleeding due to severe thrombocytopenia. Psychosomatics 2009; 50: 297-298. PMID: 19567773
5. Kahan BD. Cyclosporine. New Eng J Med 1989; 321: 1725-1738. PMID: 2687689
6. Kappers-Klunne MC, Van't Veer MB. Cyclosporin A for the treatment of patients with chronic idiopahic thrombocytopenic purpura refractory to corticosteroids or splenectomy. Br J Haematol 2001; 114: 121-125. PMID: 11472356
7. Ellis CN, Fradin MS, Messana JM, Brown MD, Siegel MT, Hartley AH, et al. Cyclosporin for plaque-type psoriasis: results of a multidose, double-blind, trial. New Eng J Med 1991; 324: 277-284. PMID: 1986287
8. Cines DB, McKenzie SE, Siegel DL. Mechanisms of action of therapeutics in idiopathic thrombocytopenic purpura. J Pediatr Hematol Oncol 2003; 25: 52-56. PMID: 14668641
9. Visentin GP, Liu CY. Drug-induced thrombocytopenia. Hematol Oncol Clin North Am 2007; 21: 685-696. PMID: 17666285
10. Chen WS, Young AH, Wang H, Huang DF. Hemolytic uremic syndrome with ischemic glomerulonepropathy and obliterative vasculopathy in a systemic sclerosis patient treated with cyclosporine-A. Rheumatol Int 2009; 29: 821-824. PMID: 19156422
11. Noris M, Casiraghi F, Todeschini M, Cravedi P, Cugini D, Monteferrante G. Regulatory T cells and T cell depletion: role of immunosuppressive drugs. J AmSoc Nephrol 2007; 18: 1007-1018. PMID: 17287424