



# A Case of Deep Thrombocytopenia which had Successfully Received Prolonged Trimethoprim Sulfametaxazole Treatment for Nocardiosis

Derin Trombositopeniye Rağmen Uzun Süreli Trimetoprim Sülfametaksazol Tedavisini Başarıyla Tamamlayan Bir Nokardiyoz Olgusu

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## ABSTRACT

Thrimethoprim sulfametaxazole (TMP/SMZ), is usually not preferred to use long time because of its potential to lead thrombocytopenia. But especially in chronic infections which require long lasting treatments, it is an important choice because its oral form is available. We present a case of nocardiosis which had been treated and survived succesfully despite his concomitant deep thrombocytopenia due to idiopathic thrombocytopenic purpura.

**Keywords:** Trimethoprim/sulfamethoxazole, thrombocytopenia

## INTRODUCTION

Sulfonamides are among the earliest antimicrobials. Today their representative in common practice is the trimethoprim-sulfamethoxazole (TMP/SMZ) compound(1). It is active against many microorganisms, but some serious side effects like renal dysfunction, thrombocytopenia, and dermatological reactions are not rare and make it less prescribed than it could be. In some cases, it can be a great challenge to a clinician when obliged to use TMP/SMZ because of the shortness of other alternatives. We present such a case with prolonged use of TMP/SMZ despite profound thrombocytopenia.

## ÖZ

Trimetoprim sülfometaksazol (TMP/SMZ), trombositopeni yapma potansiyeli nedeni ile kullanımından çekinilen bir antibiyotiktir. Ancak nokardiyoz gibi bazı uzun süreli tedavi gerektiren enfeksiyonlarda, oral kullanılabilmesi nedeni ile vazgeçilmez bir ajandır. Biz de olgumuzda uzun süreli oral tedaviyi eşlik eden, idiyopatik trombositopenik purpura(ITP) tablosuna bağlı bağıli derin trombositopenisine rağmen başarı ile sürdüren ve tamamlayan bir nokardiyoz olgusu sunmaktayız.

**Anahtar Kelimeler:** Trimetoprim/sülfametoksazol, trombositopeni

## CASE REPORT

A 65 years old male patient, who was followed in hematology clinics for severe thrombocytopenia had been diagnosed with ITP and given 48mg/day methylprednisolone for 2 months. Because his thrombocytopenia did not improve and persisted at the level of  $11 \times 10^9/L$ , He was assessed as a non-responder to steroid treatment and splenectomy was planned after IVIG treatment.

While his platelets returned to normal after discontinuation of steroid treatment, he has been diagnosed with pneumonia plus central nervous system infection due to Nocardia spp unfortunately. He was initially given intravenous triple agents treatment of TMP/SMZ, imipenem, and amikacin for 21 days, and then oral TMP/SMZ as a

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sequential treatment alone. Folic acid was started simultaneously with TMP/SMZ. But his platelets decreased to  $1 \times 10^9/L$  on the 24th day of treatment and he couldn't tolerate the drug orally because of gastrointestinal discomfort. Again imipenem and amikacin for nocardiosis and thrombopoietin receptor agonist (TRA) for supporting thrombopoiesis were started while TMP/SMZ was stopped. After 1 month of alteration, his platelets were still under  $3 \times 10^9/L$ . This decrease was assessed as due to TMP/SMZ.

When 2,5 months of the treatment was attained, infection has been recovering, but his platelet levels were still very low despite TRA and other treatments. As good news, the platelets were large at the peripheral blood smear and the patient had no bleeding. He had a persistent demand for discharge and his only reason for hospitalization was nocardiosis treatment which had to continue for at least 6 months.

Because the only oral treatment choice for nocardiosis was TMP/SMZ, the team decided to discharge the patient with that antibiotic. The patient was informed about the importance of regular use of drugs, preventing himself from trauma, and coming to frequent policlinic control and was sent home.

One month later, he was seen in a policlinic control visit at the end of 3,5 months of the nocardiosis treatment. His platelets were determined as  $2 \times 10^9/L$  but he had no bleeding in this period and his general condition was well with no other symptoms. He told that oral TMP/SMZ had caused a mildly itchy rash but antihistaminics did well. Hematologists had stopped his TRA treatment because they thought it had no benefit.

The next month's control peripheral blood smear showed that platelets couldn't save their large forms without TRA treatment, so it was begun again.

The patients' lung and CNS lesions were seen in resolution at follow-up visits while he had no bleeding despite insisting platelet levels of  $3 \times 10^9/L$ . The treatment was stopped after 6,5 months of total antibiotic use and 4 months of TMP/SMZ alone and continuously; because he was assumed as cured.

The first post-treatment control visit was on the 15th day and his platelets were  $2 \times 10^9/L$ .

Elective splenectomy was made 2 months after nocardiosis treatment had been stopped and his platelets reached to the level of  $316 \times 10^9/L$ .

## DISCUSSION

Thrombocytopenia is one of the most recognized adverse events due to TMP/SMZ and is closely related to discontinuation, even exclusion from treatment (2). Although the main mechanism of thrombocytopenia is due to impaired folate use, drug-induced immune thrombocytopenia is also reported (1,3-5). But our patient

had received this treatment for a long time despite his thrombocytopenia and survived by partial support of thrombocyte increasing agents and close follow-up. There are some reports of immune thrombocytopenia patients who received TMP/SMZ for infection prophylaxis during rituximab treatment but the dose is low: double-strength (160/800 mg) tablets q12 h, two times a week (6). Another report is about cutaneous nocardiosis of an immune thrombocytopenia patient treated with TMP/SMZ for three months. The platelet count is mentioned as  $35 \times 10^9/L$  at the beginning of the treatment but there is no information about platelet levels during follow-up (7). Another else report is the treatment of an HIV patient with toxoplasmosis by TMP/SMX+ clindamycin regimen for 4-6 weeks: they report that none of the 25 patients had severe thrombocytopenia during treatment (8). Our patient seems the longest treatment receiving one with the deepest thrombocytopenia.

## CONCLUSION

Especially, long-time treatment necessities with no other options may lead to such risky decisions, and in well-chosen patients, this treatment approach may be useful.

## ETHICAL DECLARATIONS

**Informed Consent:** All patients signed the free and informed consent form.

**Referee Evaluation Process:** Externally peer-reviewed.

**Conflict of Interest Statement:** The authors have no conflicts of interest to declare.

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## REFERENCES

1. Zinner SH, Mayer KH. Sulfonamides and Trimethoprim; Trimethoprim-Sulfamethoxazole. In: Mandell GL, Dolin R, Blaser MJ, editors. Principles and Practice of Infectious Disease. Philadelphia: Elsevier; 2020. p. 416-25.
2. Ho JM-W, Juurlink DN. Considerations when prescribing trimethoprim-sulfamethoxazole. CMAJ. 2011; 183:1851-7.
3. Hayashi M, Strouse JJ, Veltri MA, Curtis BR, Takemoto CM. Immune thrombocytopenia due to Trimethoprim-Sulfamethoxazole; under-recognized adverse drug reaction in children? *Pediatr Blood Cancer*. 2015;62(5):922-3.
4. Nixon CP, Cheves TA, Sweeney JD. Sulfamethoxazole-induced thrombocytopenia masquerading as posttransfusion purpura: a case report. *Transfusion*. 2015;55(11): 2738-41.
5. Caluwé R, Van Laecke S, Emonds MP, Peeters P, Vanholder R. Immediate posttransplantation cotrimoxazole-induced immune thrombocytopenia. *Am J Transplant*. 2010;10(4):943-6.
6. Raso S, Napolitano M, Arrigo G, et al. Antimicrobial prophylaxis in patients with immune thrombocytopenia treated with rituximab: a retrospective multicenter analysis. *Ann Hematol*. 2021;100(3):653-9.



7. Kofteridis D, Mantadakis E, Mixaki I, et al. Primary cutaneous nocardiosis in 2 patients on immunosuppressants. *Scand J Infect Dis.* 2005;37(6-7):507-10.
8. Goswami RP, Goswami RP, Rahman M, Ray Y, Tripathi SK. Alternative treatment approach to cerebral toxoplasmosis in HIV/AIDS: experience from a resource-poor setting. *Int J STD AIDS.* 2015;26(12):864-9.