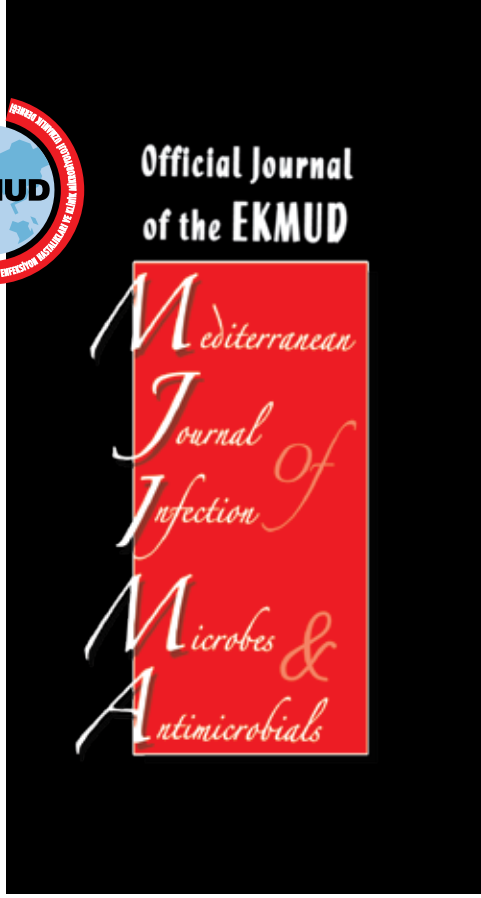
URL: http://www.mjima.org/

OLGU SUNUMU ● CASE REPORT



Piperacillin/Tazobactam-Induced Neutropenia: A Case Report

Piperasilin/Tazobaktam Tarafından Uyarılmış Nötropeni: Bir Olgu Sunumu

Hayati DEMİRASLAN[1], Sibel GÜRBÜZ[2], Zehra DOĞAN TOMUL[2], İlhami ÇELİK[2]

[1] Erciyes Üniversitesi Tıp Fakültesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Anabilim Dalı, Kayseri, Türkiye
[2] SB Kayseri Eğitim ve Araştırma Hastanesi, Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği, Kayseri, Türkiye

ABSTRACT

Neutropenia, secondary to immune destruction or maturation arrest, is commonly described as an adverse hematological effect of beta-lactam antibiotics. A 29-year-old woman was being treated with piperacillin/tazobactam due to draining heel osteomyelitis. Herein, we present a case of reversible neutropenia occurring on the 25th day of treatment. Neutropenia resolved six days after discontinuation of piperacillin/tazobactam. We think that patients receiving prolonged treatment with piperacillin/tazobactam should be followed cautiously for neutropenia.

Key words: Piperacillin, tazobactam, neutropenia, adverse effect

Received: 15.11.2011 • ***Accepted:*** 17.02.2012 • ***Published:*** 29.03.2012

ÖZET

İmmün yıkıma veya olgunlaşma durmasına sekonder nötropeni beta-laktam antibiyotiklerin yaygın tanımlanan yan etkisidir. Yirmi dokuz yaşında kadın, akıntılı topuk osteomiyeliti nedeniyle piperasilin/tazobaktam tedavisi alıyordu. Burada, tedavisinin 25. gününde ortaya çıkan geri dönüşümlü nötropeni olgusunu sunuyoruz. Piperasilin/tazobaktam kesildikten altı gün sonra nötropeni düzeldi. Uzamış piperasilin/tazobaktam tedavisi alan hastaların nötropeni açısından dikkatle izlenmeleri gerektiğini düşünüyoruz.

Anahtar kelimeler: Piperasilin, tazobaktam, nötropeni, yan etki

Geliş Tarihi: 15.11.2011 • ***Kabul Ediliş Tarihi:*** 17.02.2012 • ***Yayınlanma Tarihi:*** 29.03.2012

INTRODUCTION

Piperacillin/tazobactam (PT) is a beta-lactamase inhibitor that is a semi-synthetic ureidopenicillin with broad spectrum. Bone marrow suppression is a recognized adverse drug reaction of beta-lactam antibiotics[1]. A recent systematic review supported the assumption that piperacillin can also have such adverse effects[2]. We report a case of reversible neutropenia associated with PT. This report reinforces previous suggestions that monitoring of hematological parameters is important in patients receiving prolonged treatment with PT.

CASE REPORT

We report herein the case of a 29-year-old woman with a history of paralysis of the lower extremities caused by lumbar 1-2 compression fracture due to a traffic accident 10 years ago. Her right heel had been burned one year ago, after which a foul-smelling wound drainage developed. She was admitted due to the right heel osteomyelitis. Gram-negative rods and gram-positive cocci were seen on Gram staining of the wound drainage sample. PT (4.5 g q8h) was given to the patient. Complete blood count (CBC) at baseline showed: hemoglobin 9.4 g/dL, white blood cell (WBC) count 18.800/mm^3 and platelet count 461.000/mm^3. Levels of creatinine, serum aminotransaminases and lactate dehydrogenase were in normal limits, but the level of albumin was 3.3 g/dL. Aerobic wound culture was negative. Teicoplanin was added on the 10th day of antimicrobial therapy because of wound drainage. On the 23rd day of antimicrobial therapy, the patient's body temperature rose to 38.0°C. She complained of periumbilical pain and cramping during PT infusion, and her samples were analyzed for the infectious source. The blood and wound culture were negative, urine sample was sterile, and chest radiograph was normal. Meanwhile, the treatment remained unchanged; however, for two days, the patient's temperature was increased, at 38.9°C and 38.6°C. On the 25th day of antimicrobial therapy, the leukocyte count dropped to 1400/mm^3 (absolute neutrophil count was 100/mm^3) and platelet count to 194.000/mm^3, and hemoglobin level was 10.4 g/dL. Neither eosinophilia nor rashes were detected. Daily CBC count was performed to monitor the leukocyte count. The courses of leukocyte and neutrophil counts including the PT discontinuation day are shown in Figure 1; teicoplanin was carried over. The patient's fever resolved one day after PT was discontinued, and the leukocyte and absolute neutrophil counts reverted to normal six days after discontinuation. On the 28th day of hospitalization, wound drainage had completely ceased and healing was observed; she was discharged on the 30th day of hospitalization.

DISCUSSION

There is some information in the literature about the toxicity of prolonged PT treatment for conditions such as bone-related infections and empyema[3,4]. In non-neutropenic fever studies, the occurrence of piperacillin-related neutropenia is rare (0.04%)[2]. A high incidence of antibiotic-induced neutropenia among patients receiving prolonged PT therapy for bone-related infections has been reported, with toxicity related to the cumulative dose. It was noticed that clinical findings like fever and rash should be considered as

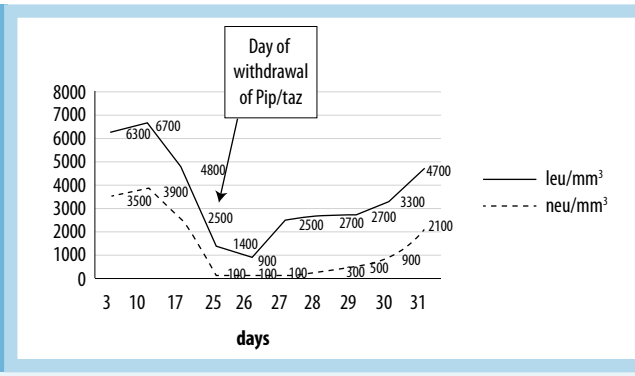


Figure 1.

The courses of leukocyte and neutrophil counts.

preceding signs of neutropenia[3]. Two days before the onset of neutropenia, the patient complained of fever and periumbilical pain, and although the periumbilical pain resolved, the patient's fever persisted for two more days. Moreover, neutropenia appeared after the patient had received a mean of 26.8 days of therapy and a mean cumulative dose of 330.3 g of piperacillin[3]. Another report suggests that patients on a high cumulative dose of PT must be cautious of neutropenia[5]. In our patient, neutropenia occurred with a cumulative dose of 328.5 g PT on the 25th day. She had been receiving teicoplanin as well for 15 days when the neutropenia was discovered. To our knowledge, a case of leukopenia with neutropenia (WBCs 2000/mm^3, neutrophils 46%) associated with teicoplanin was reported after 20 days of teicoplanin administration. Furthermore, after teicoplanin was discontinued, WBCs and neutrophil counts normalized[6]. In another study, 95% of cases showed a recovery period of one to seven days after the withdrawal of beta-lactams[1]. Comparatively, neutrophil counts of our patient decreased to 100/mm^3. However, neutropenia promptly reversed after discontinuation of PT, and teicoplanin was continued. After six days, neutrophil counts had completely recovered.

In conclusion, because the true incidence of adverse effects is unknown, patients receiving prolonged PT treatment should be carefully followed for neutropenia. Moreover, the fever could be an early sign requiring precise evaluation of PT-induced neutropenia.

REFERENCES

1. *Neftel KA, Hauser SP, Muller MR. Inhibition of granulopoiesis in vivo and in vitro by beta-lactam antibiotics. J Infect Dis 1985; 152: 90-8.*
2. *Scheetz MH, McKoy JM, Parada JP, Djulbegovic B, Raisch DW, Yarnold PR, Zagory J, Trifilio S, Jakiche R, Palella F, Kahn A, Chandler K, Bennett CL. Systematic review of piperacillin-induced neutropenia. Drug Saf 2007; 30: 295-306.*
3. *Peralta FG, Sanchez MB, Roiz MP, Pena MA, Tejero MA, Arjona R. Incidence of neutropenia during treatment of bone-related infections with piperacillin/tazobactam. Clin Infect Dis 2003; 37: 1568-72.*
4. *Ekmekci A, Yakar F, Tufan F, Demirturk M, Cagatay A. Piperasilin/Tazobaktama bağlı kemik iliği baskılanması ile seyreden bir olgu sunumu. Nobel Med 2007; 4: 28-30.*
5. *Ruiz-Irastorza G, Barreiro G, Aguirre C. Reversible bone marrow depression by high-dose piperacillin/tazobactam. Br J Haematol 1996; 95: 611-2.*
6. *Del Favero A, Patoia L, Bucaneve G, Biscarini L, Menichetti F. Leukopenia with neutropenia associated with teicoplanin therapy. Ann Pharmacother 2007; 41: 891-4.*

Yazışma Adresi /Address for Correspondence

Yrd. Doç. Dr. Hayati DEMİRASLAN

Erciyes Üniversitesi Tıp Fakültesi

Enfeksiyon Hastalıkları ve

Klinik Mikrobiyoloji Anabilim Dalı

Kayseri-Türkiye

E-posta: tigin68@hotmail.com