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Pancytopenia Associated with Linezolid Therapy in a Hemodialysis Patient

Hemodiyaliz Hastasında Linezolid İlişkili Pansitopeni

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ABSTRACT

Linezolid is a drug used frequently for the treatment of infections due to resistant gram-positive bacteria including methicillin-resistant Stapylococcus aereus (MRSA), penicillin-resistant pneumococcus and vancomycin-resistant enterococcus. However, reversible bone marrow suppression has been reported in cases treated with linezolid in high doses for 2 weeks. Here we reported the development linezolid-associated pancytopenia in a hemodialysis patient with catheter infection. This patient was treated with linezolid for blood stream MRSA infection. Fever and other symptoms regressed at the beginning but fever and pancytopenia developed on the 10th day of linezolid therapy. After excluding other causes of pancytopenia, linezolid treatment was changed to a combination of meropenem and daptomycin. The pancytopenia regressed in a 6 day and did not recur during the 13-month follow-up.

KEY WORDS: Myelosupression, Linezolid, MRSA, Bloodstream infection

ÖZ

Linezolid, metisilin dirençli stafilokokus aureus (MRSA), penisilin dirençli pnömokokus ve vankomisin dirençli enterokokus gibi dirençli gram pozitif bakterilere bağlı gelişen enfeksiyonların tedavisinde sıklıkla kullanılır. Ancak 2 hafta boyunca yüksek doz linezolid ile tedavi edilen hastalarda, linezolid tedavisine sekonder geri dönüşümlü kemik iliği baskılanması nadiren bildirilmiştir. Burada, kan kültüründe MRSA üremesi olan ve linezolid tedavisi sırasında ateş ve pansitopeni gelişen hemodiyaliz hastası sunulmuştur. Linezolid tedavisi ile ateş ve enfeksiyon iyi kontrol altında iken, tedavinin 10. gününde yeniden ateş ve pansitopeni gelişti. Diğer nedenler dışlandıktan sonra pansitopeni linezolid ilişkili olabileceği düşünüldü ve linezolid yerine meropenem -daptomycin kombinasyonu başlandı. Linezolid kesildikten kısa süre sonra pansitopeni geriledi ve 13 aylık takipte pansitopeni yeniden gözlenmedi.

ANAHTAR SÖZCÜKLER: Kemik iliği baskılanması, Linezolid, MRSA, Kan akımı enfeksiyonu

INTRODUCTION

Linezolid is the first member of the oxazolidinone group that inhibits protein synthesis by binding to the bacterial 23S rRNA of the 50S ribosomal subunit and prevents protein translation. Dose adjustment is not necessary in patients with renal and/or hepatic failure. This drug is effective in the treatment of vancomycin-resistant enterococcus, methicillin-resistant staphylococcus and penicillin-resistant pneumococcus (1).

CASE REPORT

A 22-year-old woman undergoing hemodialysis 3 times a week was admitted to our unit due to fever and MRSA-positive blood stream infection. She had been on hemodialysis via jugular venous catheter in the last year due to chronic renal failure of unknown etiology. The fever persisted despite replacing the jugular venous catheter for the possible catheter infection and intravenous vancomycin treatment. Linezolid was started on the 7th day of

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hospitalization. Fever and high levels of C reactive protein (CRP) and procalcitonin regressed on the 3rd day of linezolid therapy. Pancytopenia and fever (39°C) developed on the 10th day of Linezolid treatment. After excluding other possible reasons of pancytopenia, Linezolid was discontinued. Blood cultures were repeated. Atypical lymphocytes were detected in the peripheral blood smear and bone marrow aspiration and bone marrow biopsy was found to be normocellular (Figure 1). The meropenem and daptomycin combination was initiated. The pancytopenia improved and fever disappeared 6 days after Linezolid cessation. During the 13-month follow-up period, she was asymptomatic and there was no evidence of atypical lymphocytes and/or peripheral cytopenia. Table I shows the peripheral blood tests during clinical follow up.

DISCUSSION

Central venous catheters, which are frequently used in hemodialysis patients, are the most common causes of nosocomial septicemias in hemodialysis units. Catheter-associated bacteremia can cause endocarditis, osteomyelitis and abscess formation in various parts of the body and also increase mortality in this population. Infections are the most common reason for catheter loss (2). Gram-positive bacteria, and especially Staphylococcus species, are the most common cause of bloodstream infections in these cases. Staphylococcus epidermidis is the most common pathogen in exit site infections and catheter colonization (60-75%) while Staphylococcus aureus is most common pathogen in bacteremia cases (42-56%). The most common microorganisms in blood stream infection are coagulase-negative staphylococci and Staphylococcus aureus, and less commonly enterococci, Pseudomonas aeruginosa, acinetobacter, enterobacter, klebsiella, Candida species and corynebacterium JK. Linezolid is an effective treatment in cases with resistant microorganisms including MRSA and Vancomycin-resistant enterococus (VRE) (1). Linezolid is generally tolerated well but side effects are seen in one third of the cases and these are not related to the drug dose. The side effects are nausea (5.4%), diarrhea (5.2%), color change in tongue (2.5%), oral candidiasis (2.3%), headache (2.4%), thrombocytopenia (2.4%), reversible myelopathy, optic and peripheral neuropathy and bradycardia. However bone marrow suppression is an important problem in cases treated with

Table I: The levels of hemoglobin (Hb), hematocrit (hct), white blood cell (WBC) platelets (plt) and C reactive protein (CRP) during and post linezolid (LNZ) therapy.

	LNZ Day 1	LNZ Day 10	Post LNZ Day 2	Post LNZ Day 4	Post LNZ Day 6	Post LNZ Month 13
WBC (1000/qL)	4.95	0.46	0.33	2.99	7.03	7.72
Ne %	3.16	0.02	0.01	0.4	3.4	3.98
Hb (g/dL)/Hct%	8/24.7	8.2/24.8	6.6/21.1	9.7/30.9	9.1/28.7	8.8/28.8
Plt (1000/ql)	173	104	65	120	285	189
CRP (0-0.8 /dL)	0.617	10.8	2.46		0.694	

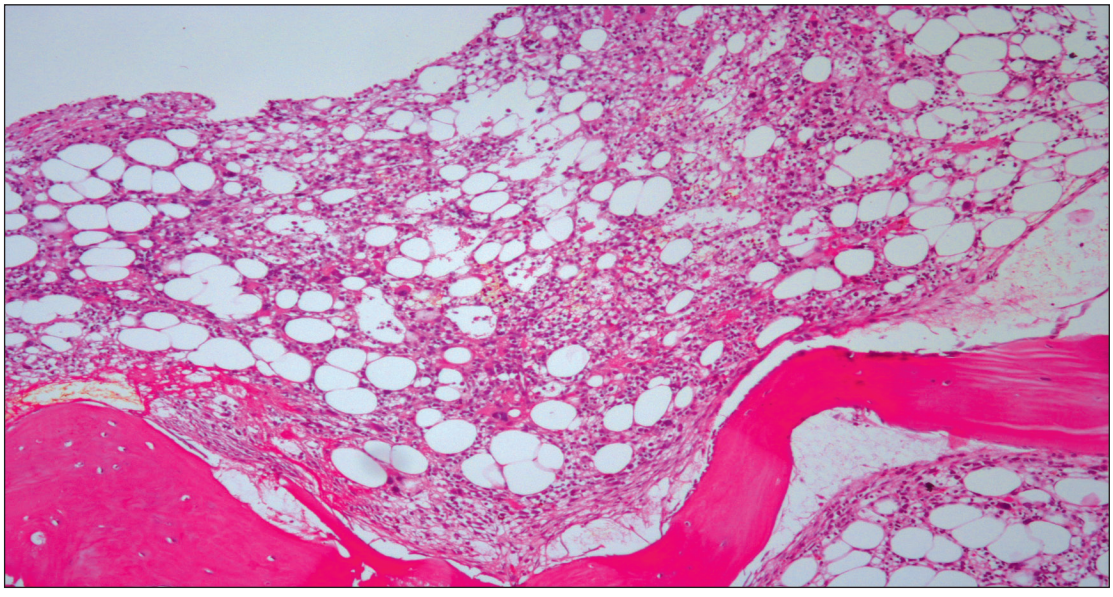

Figure 1: *Bone marrow examination results were normal (HEx40).*

linezolid more than a few weeks and requires the cessation of treatment (3,4). Pancytopenia has also been reported during linezolid therapy in pediatric patients with VRE infection (5). Pancytopenia, lactic acidosis and elevated liver enzyme tests related to linezolid treatment have been reported in a patient with empyema (6,7). Pancytopenia during linezolid treatment is important and life-threatening problems may occur if a clinician is not aware of this problem. However, other possibilities should be considered. In our patient, pancytopenia and fever developed in the second week of linezolid treatment and leucocytes mimicking blasts and atypical cells in the peripheral blood smear were detected during pancytopenia at the first evaluation. However, bone marrow aspiration and biopsy were reported as normocellular and atypical cells were not found on repeated peripheral blood smears. The mechanism of bone marrow suppression related to Linezolid is not completely understood. Generally, pancytopenia is reversible and recovery occurs after discontinuing the drug, as in our patient.

In conclusion, it should be remembered that pancytopenia can develop during linezolid treatment and negatively affects the clinical outcome. Early diagnosis is only possible by frequently monitoring the complete blood cell count and can be reversible after early discontinuation of the drug as in our case.

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