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Complications of MRSA Treatment: Linezolid-induced Myelosuppression Presenting with Pancytopenia

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Methicillin-resistant *Staphylococcus aureus* (MRSA) infections have grown to epidemic proportions in the United States. With the development of increasing drug resistance of MRSA to traditional antimicrobials, there has been a search for a more effective antibiotic treatment. Linezolid is one of the most effective oral medications used for outpatient treatment of MRSA infections. We present a case of pancytopenia after outpatient treatment with linezolid. Myelosuppression is a rare but serious side effect of linezolid of which emergency physicians need to be aware in order to provide early intervention.

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INTRODUCTION

Since their emergence onto the clinical scene in the 1960s, methicillin-resistant strains of *Staphylococcus aureus* (MRSA) have continued to plague clinicians. MRSA is no longer solely a nosocomial infection and has now become the most common cause of skin and soft tissue infections presenting in emergency departments (EDs).^{1,2} With the expanding resistance to multiple antibiotics, physicians are faced with the challenge of finding effective outpatient therapy. Linezolid is effective against multiple strains of MRSA and is available in an oral formulation for outpatient therapy.¹ We present a case of linezolid-induced myelosuppression. Myelosuppression is a rare yet significant side effect reported during post-marketing use of linezolid. ED physicians need to be aware of this serious side effect, which may place the patient at risk for further health-related complications as a result of cytopenias.

CASE REPORT

A 73-year-old female presents to the ED complaining of generalized weakness. The patient reported weight loss due to nausea, vomiting, and decreased appetite for two months. The patient had no known drug allergies and denied tobacco, alcohol, or illicit drug use. Review of systems included dyspnea on exertion and fatigability. Past medical history included a lumbar fracture due to a motor vehicle accident, requiring lumbar fusion. The patient later developed recurrent

osteomyelitis of the lumbar vertebrae. Repeated incision and drainage of the abscesses at her previous surgical site showed persistent MRSA-positive wound cultures. Subsequently, inpatient treatment with intravenous vancomycin for MRSA osteomyelitis of the lumbar spine was instituted. The patient had been discharged on oral linezolid for continued outpatient treatment for MRSA at a dose of 600 mg twice a day for six weeks, with Zofran as needed for nausea and vomiting.

On this visit, the patient was in no acute distress and nontoxic appearing. Her mucous membranes were pale, with no gingival bleeding; the fundoscopic eye exam was normal. The lungs were bilaterally clear to auscultation; the heart had a regular rate and rhythm with no murmurs, gallops or rubs. Abdominal exam was soft, non-tender, non-distended with normoactive bowel sounds. A rectal exam revealed normal tone, brown stool was hemoccult negative. Extremities exhibited full range of motion and intact neurovascularization; the skin was without rashes and petechiae; pulses were full throughout. Exam of the back demonstrated a healed incision in the lumbar region, correlating with the previous surgeries; no erythema, tenderness, warmth, rashes, lesions, open wounds, or fluctuance were noted. Cranial nerves II-XII were intact; motor and sensory exams, reflexes, and gait were normal with no focal neurologic signs.

ED laboratory tests included a complete metabolic panel, complete blood count, urinary analysis, lipase level, cardiac

enzymes, partial thromboplastin time, prothrombin time and INR, and reticulocyte count. All labs were within normal limits, except the CBC, which reported a white blood cell count of 2,100 with a normal differential, hemoglobin of 4.2, platelet count of 64,000, with normal red blood cell indices and normal peripheral smear. EKG and chest x-ray were normal. Inpatient TIBC, iron and transferrin levels, and high reticulocyte values were consistent with iron deficiency and active bone marrow response.

The patient was admitted for treatment of linezolid-induced myelosuppression. She received IV fluids and was transfused with packed red blood cells due to symptomatic anemia. Treatment with linezolid was discontinued, and the patient was restarted on IV-administered vancomycin. Her hospitalization was uneventful, and the patient's cell counts returned to baseline, without the need for a bone marrow biopsy. A peripherally inserted central catheter line was placed and the patient was discharged home to continue outpatient IV therapy with vancomycin for her persistent MRSA osteomyelitis.

DISCUSSION

MRSA infections present most commonly as skin or soft tissue infections, in the form of cellulitis, furuncles or abscess, as well as more serious infections, such as pneumonia and sepsis. MRSA infections have historically occurred more frequently in hospitalized patients with compromised immune systems. More recently, community-acquired MRSA infections are of epidemic proportions in previously low-risk groups in the United States.^{3,4} The genetic element that confers methicillin resistance continues to evolve, creating multi-drug resistant strains. Without a definitive marker for identifying MRSA strains, outpatient treatment continues to challenge the medical community.^{1,5}

Historically, MRSA has been treated successfully with outpatient oral sulfonamides, clindamycin, rifampin, doxycycline, or a combination of these agents.⁵ With the development of increasing drug resistance of MRSA to these traditional antimicrobials, there has been a search for more effective antibiotics. One recent study demonstrated that vancomycin, linezolid, and quinupristin-dalfopristin were the most effective antibiotics against multiple strains of MRSA.¹ The parenteral administration of vancomycin and quinupristin-dalfopristin has limited their use in the outpatient setting; however, the availability of an oral formulation of linezolid has led to its increasing utilization.

Linezolid is an oxazolidinone antibiotic indicated for the treatment of Gram-positive bacterial infections, including bacterial pneumonia, skin and soft tissue infections, and vancomycin-resistant enterococcal infections. The most common adverse effects include diarrhea, nausea, and headache; less common side effects include hypertension, lactic acidosis, and elevated liver enzymes. Among the most

severe adverse effects, seen with prolonged courses of therapy, include irreversible peripheral neuropathy, optic neuropathy, and reversible myelosuppression.⁸

Oral linezolid is now being prescribed more frequently for outpatient treatment of MRSA due to the increase in multi-drug resistant microbes. In the literature, five cases of linezolid-induced myelosuppression have been reported.^{6,7} Of these cases, four reported anemia and thrombocytopenia and only one case reported pancytopenia. In this case, pancytopenia developed after only six weeks of therapy, whereas the other case reported pancytopenia developing after five months of treatment with linezolid. In addition to our patient, three of the five reported cases had their myelosuppression reversed after discontinuation of linezolid.⁷ Per the manufacturer's recommendation, patients on linezolid therapy for longer than two weeks should be monitored regularly in order to identify myelosuppression.

Emergency physicians need to be aware of this rare and serious side effect of linezolid-induced myelosuppression.

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