

CASE REPORT

A Difficult Decision in an Acute Myeloid Leukemia Patient with Methicillin Resistant *Staphylococcus Aureus*-Associated Spondylodiscitis: Hematopoietic Stem Cell Transplantation

Metisiline Dirençli Staphylococcus Aureus Spondilodiskiti Olan Akut Miyeloid Lösemili Hastada Zor Karar: Hematopoetik Kök Hücre Nakli

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Abstract

Blood stream infections cause high morbidity and mortality in patients with hematological malignancies. Methicillin-resistant *Staphylococcus aureus* (MRSA) is a multidrug resistant bacteria and produces biofilm, causing catheter-related bloodstream infections. MRSA bacteremia can lead to metastatic infections, including pyogenic spondylodiscitis. Treatment requires a long period of up to 12 weeks. In patients with hematologic malignancies, it may be necessary to start bone marrow transplantation as soon as possible. Here, we present the difficult decision of a patient who was receiving chemotherapy for relapsed acute myeloid leukemia and required hematopoietic stem cell transplantation but was diagnosed with MRSA spondylodiscitis.

Keywords: Methicillin-resistant *Staphylococcus aureus*; Catheter-related bloodstream infections; Pyogenic spondylodiscitis; Hematopoietic stem cell transplantation

Patients with hematological malignancies (HM) are at high risk for infection with resistant microorganisms due to the long duration of chemotherapy, neutropenia, hospitalization, and increased invasive procedures.^[1] Central venous catheters constitute an invasive procedure frequently used in hematology patients for fluid infusions, blood product transfusions, drug-chemotherapy applications, or hemodialysis.^[2]

Bloodstream infections are common in neutropenic patients and are usually associated with mucosal injury or central venous catheter.^[3] Catheter-related bloodstream infections (CRBSI) are the most important infectious complications in HM patients.^[4] CRBSI contributes to prolonged hospitalizations, is challenging to treat due to resistant strains, and is associated with

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significant morbidity and increased healthcare costs.^[5] Although the epidemiology varies by region and time, gram positive bacteria are more frequently identified as causative agents in blood stream infections (BSI).^[6] Bacteremia is one of the severe complications in methicillin-resistant *Staphylococcus aureus* (MRSA) infections and is associated with a 15-60% mortality rate. In addition, metastatic events are also amongst those that increase morbidity in MRSA infections. MRSA causes complicated infections in HM patients owing to antibiotic resistance and biofilm layers.^[7] In addition to the treatment of infection in patients with HM, the continuation of chemotherapy and transplantation poses yet another crucial problem.

Here, we present a complex case of MRSA bacteremia and spondylodiscitis in a patient undergoing chemotherapy for relapsed acute myeloid leukemia (AML) and in preparation for transplantation. The complex process of managing immunosuppressive drugs and allogeneic hematopoietic stem cell transplantation (HSCT) simultaneously with treating spondylodiscitis, observing the successful outcome despite the bacterial infection, underscores our confidence in the effectiveness of our treatment strategy in such challenging cases. The patient's recovery, despite the formidable challenges posed by AML, MRSA, and the need for HSCT, stands as a testament to the effectiveness of the treatment strategy.

Case Report

A fifty-three-year-old male patient received remission induction and consolidation chemotherapies with the diagnosis of AML (M4). In remission, blast infiltration in the bone marrow was observed one year after the initial diagnosis. Chemotherapy was re-started with the diagnosis of relapse. Hematopoietic stem cell transplantation was planned for the patient, who was in remission after the Fludarabine, cytarabine, idarubicin, G-CSF (FLAG-IDA) chemotherapy protocol. Meanwhile, the patient was evaluated with complaints of fever and chills. On physical examination, the general condition was fair, conscious, cooperative, and oriented. Fever: 38.9 °C, pulse: 160/min, respiratory rate: 23/min, blood pressure: 110/60 mmHg was measured. There was redness approximately 1 cm in diameter around the suitable jugular catheter. In the patient's biochemical examinations, liver and kidney function tests were routine; C reactive protein was 91 mg/L (reference range 0-5 mg/L), leukocyte count ($10^3/\mu\text{l}$): 0.04, neutrophil count ($10^3/\mu\text{l}$): 0.01 Hgb: 6.9 g/dL, platelet ($10^3/\mu\text{l}$):

Table 1. Antimicrobial susceptibility test of *Staphylococcus aureus*

Antibiotics	Susceptible	Resistant	MIC
Benzylpenicillin		+	≥ 0.5
Clindamycin		+	≥ 4
Erythromycin		+	≥ 8
Linezolid	+		2
Levofloxacin		+	4
Methicillin		+	
Trimethoprim/sulfamethoxazole	+		≤ 10
Vancomycin	+		1

MIC: Minimum inhibitor concentration.

30.000. Methicillin-resistant *Staphylococcus aureus* was isolated in the catheter, and a peripheral blood culture was taken. The antibiotic susceptibility test is presented in Table 1. Vancomycin treatment (2 g/day) was initiated for catheter-related bloodstream infections. The central catheter was removed, and thrombosis was observed in the right jugular vein. On the 7th day of vancomycin treatment, the patient complained of pain in his back. The magnetic resonance imaging observed heterogeneous contrast enhancement in the T6-12 vertebra corpus bone marrow. It was found to be compatible with pyogenic spondylodiscitis (Fig. 1). A biopsy could not be performed because the thrombocyte level was $< 10,000/\text{mm}^3$ and the patient did not give consent for the invasive procedure. The patient was considered as having MRSA spondylodiscitis. On the 11th day of treatment, since the vancomycin-related nephrotoxicity, the treatment was changed to daptomycin (500 mg/day) according to IDSA guidelines.^[8] On the 17th day of treatment, there was no growth in control blood cultures. A council was held with the department of Infectious Disease and Clinical Microbiology and Hematology. Since the patient had a high risk of relapse, it was decided to perform allogeneic HSCT under antibiotics. Rifampicin (600 mg/day, PO) was thereupon added to the antibiotic treatment. Unrelated allogeneic HSCT was performed on the 28th day of daptomycin treatment. Daptomycin and rifampicin treatment were extended to 12 weeks. The patient underwent a follow-up MRI the third month after treatment, and no lesion was detected. The patient was discharged with complete recovery. No blast was spotted in the bone marrow aspirate in the first year of post-transplant control, the patient was found to be in remission. Moreover, no lesion was detected on control vertebral MR imaging after a-year of spondylodiscitis treatment (Fig. 2).



Figure 1. Spondylodiscitis in thoracic vertebrae.



Figure 2. Vertebrae after treatment.

Discussion

Infections are life-threatening complications in the treatment of HM. It may be necessary to continue cancer treatment with antibiotic therapy.^[1] Here, we report a case of MRSA-associated CRBSI and spondylodiscitis in a patient with relapsed AML who was scheduled for allogeneic HSCT transplantation. This very case, with its unique challenges and successful outcomes, underpins the need for effective treatment strategies in managing such complex infections.

Bacterial infections are common complications in patients with HM. Invasive procedures, immunosuppression, and neutropenia are risk factors.^[1] Prophylactic antibiotic use and prolonged hospitalization also cause infections with resistant bacteria.^[3] MRSA infections have high mortality and morbidity. Due to resistance, antibiotic treatment is rather complex. Catheter-associated bacteremia, in particular, causes metastatic complications and leads to infections that are difficult to treat.^[7,9]

Spondylodiscitis is a difficult-to-treat bone infection. Pathogenic organisms reach the spine either hematogenous via arteries or veins or by direct transmission during surgical procedures.^[10] Catheter-associated, hospital-acquired MRSA infection is an essential cause of spondylodiscitis. Microbiological sampling is required to diagnose spondylodiscitis if there is clinical suspicion and no growth in blood cultures. However, since MRSA grew in our patient's blood samples, we accepted it as the causative agent. Further, it was not appropriate to perform a biopsy on account of the co-morbid condition. Conservative and antibiotic treatments are recommended in the treatment

of spondylodiscitis. Suspicious diagnosis, non-response to treatment, persistent pain, progressive neurological deficit, progressive spinal deformity are among the indications for surgery.^[8] Our patient did not have any of these, but the Council did not agree that the current immunosuppressive condition required surgery. The duration of antimicrobial treatment is controversial though. There exist various treatment duration recommendations, primarily based on observational studies and expert opinion, ranging from four to six weeks to three months. Considering the patient's immunosuppressive status, we extended his treatment parenterally for 12 weeks. We discontinued antimicrobial therapy after witnessing the radiological healing of the bone lesion and assuring no growth in blood culture.

Conclusion

There are a fair number of risk factors for severe infections in patients with HM. CRBSI may result in more severe complications and become more challenging to treat. Treatment of bone-vertebra infections is most often a long-term process and gets complicated in HM patients. Considering all these, compliance with infection control measures is deemed lifesaving in HM patients.

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