Persistent MRSA Bacteremia - A Diagnostic Conundrum

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Abstract

Multiple studies have demonstrated that the incidence of Methicillin Resistant Staphylococcus Aureus (MRSA) bacteremia is increasing. Timely treatment of MRSA bacteremia is important because it is associated with a 30-day all-cause mortality rate of up to 20%. We present an interesting case report of a patient with primary MRSA bacteremia without a clear identifiable source despite an extensive workup. Our patient was a 40-year old female with a past medical history significant for obesity and chronic smoking, who presented with a 10-day history of worsening acute back pain associated with intermittent episodes of subjective fever, nausea and vomiting. With the initiation of antibiotics, the patient experienced improvement in her initial symptoms, yet blood cultures remained positive for 9 days. Collaboration between the infectious disease and internal medicine teams was crucial for management of our patient.

Introduction

With the rise of Intravenous (IV) drug abuse among the adult population, bacteremia and septic emboli are common complications. Risk factors for bacteremia include diabetes mellitus, hemodialysis dependence, HIV infection, malignancy and trauma [1]. Staphylococcus aureus (S. aureus) is a common pathogen associated with bacteremia, both in the setting of community acquired and healthcare associated infections. Multiple studies have demonstrated that the incidence of Methicillin Resistant Staphylococcus Aureus (MRSA) bacteremia is increasing [2-4]. Timely treatment of MRSA bacteremia is important because it is associated with a 30-day all-cause mortality rate of up to 20% [2].

Persistent bacteremia, defined by the presence of a positive culture despite 7 days of treatment, poses significant clinical challenges; including an extended hospital stay and adverse effects from the use of broad-spectrum antibiotics. Several studies have shown that persistent bacteremia is associated with significantly higher mortality rates when compared to non-persistent controls [2,3].

We present an interesting case report of an adult female patient with primary persistent MRSA bacteremia without a clear identifiable source despite an extensive workup.

Case Report

History and Physical

A 40-year old female with past medical history significant for obesity and chronic smoking was brought in by her family to our hospital with a 10-day history of worsening acute back pain associated with intermittent episodes of subjective fever, nausea and vomiting. The back pain was described as a constant, dull aching pain that radiated along her the entirety of her spine without any specific aggravating or relieving factors. She denied saddle paresthesia, urinary retention, bowel incontinence, or lower extremity weakness. Review of systems was positive for loss of appetite from nausea and several episodes of vomiting, and negative for urinary retention, bowel incontinence, or lower extremity weakness. Review of systems was positive for loss of appetite from nausea and several episodes of vomiting, and negative for urinary retention, bowel incontinence, or lower extremity weakness.

On admission, she was noted to have a temperature of 98.5ºF, heart rate 86, respiratory rate 17, blood pressure 134/81, and pulse oximetry 97% on room air. The patient was not toxic appearing. Positive physical exam findings included tenderness to palpation of the lumbar spine and a systolic murmur at the left lower sternal border. No Costovertebral Angle (CVA) tenderness was noted. No abrasions, track marks, or open wounds were noted anywhere on the body.

Laboratory workup revealed White Blood Cell (WBC) count of 14.9 K/cmm, blood urea nitrogen of 17, and creatinine of 0.98. Blood cultures from two sites grew MRSA. Urine drug screen was positive after receiving IV morphine for pain. Urinalysis revealed cloudy urine with 500 mg/dL glucose, 40 mg/dL ketones, 100 mg/dL protein, negative for nitrates, trace leukocyte esterase present. With 5-10 WBC, 3-5 RBC, and 1+ bacteria. Urine culture was contaminated with normal flora. The patient was noted to have a Hemoglobin A1c of 11.6, consistent with a new diagnosis of diabetes mellitus.

Initial imaging included a Magnetic Resonance Imaging (MRI) of the cervical and thoracolumbar spine that did not show any evidence of osteomyelitis, discitis, or epidural abscess. Transsthoracic echocardiogram was negative for infective endocarditis. Computed Tomography (CT) of the abdomen and pelvis with contrast showed 1) Multiple areas of abnormal enhancement in the left kidney with small areas of low attenuation most consistent with acute pyelonephritis with a small area of low-attenuation that may represent developing abscesses. 2) Cavitary nodules in the lung bases, concerning for septic emboli (Figure 1). Despite the CT abdomen findings, the patient did not have any symptoms of a urinary tract infection. The infectious disease team was consulted, and the patient was started on IV vancomycin for MRSA bacteremia.

Figure 1: CT abdomen and pelvis with contrast on hospital day 1 showed multiple areas of abnormal enhancement in the left kidney with small areas of low attenuation most consistent with acute pyelonephritis with a small area of low-attenuation that may represent developing abscesses (red arrow).

Hospital Course

With initiation of IV vancomycin, patient experienced improvement with her nausea, vomiting and back pain. However, she continued to spike a fever and blood cultures remained positive for 72 hours following the initiation of antibiotics. Due to difficulties reaching therapeutic levels, vancomycin was switched to IV daptomycin and IV sulfamethoxazole-trimethoprim (SMX-TMP) on hospital day 5. SMX-TMP was added for its good soft tissue and gentiunopercy penetration and MRSA coverage. On hospital day 6 the patient began experiencing left flank pain. A retroperitoneal ultrasound was performed to explore the possibility of a renal abscess. The ultrasound showed normal cortical echogenicity in both kidneys. No renal abscesses were visualized. Due to worsening left flank pain on hospital...
<table>
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<tr>
<th>Hospital Day</th>
<th>Pertinent Procedures/ Imaging</th>
<th>Results</th>
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<th>Other comments</th>
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<tr>
<td>1 (day of admission)</td>
<td>Total spine MRI, Trans-thoracic echocardiogram, CT abdomen with contrast, CT chest with contrast</td>
<td>Total spine MRI negative, Trans-thoracic echocardiogram negative, CT abdomen with contrast showed areas in the left kidney suggestive of acute pyelonephritis and multiple areas concerning for possible abscesses (Figure 1), CT chest with contrast showed septic pulmonary emboli</td>
<td>Blood culture x2, urine culture, urine drug screen</td>
<td>Chief complaint is back pain. Rated pain as 8/10. Patient with maximum temperature of 103.2°F</td>
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<tr>
<td>2</td>
<td>Blood culture x2, respiratory viral panel, HIV antibody test, Hepatitis antibody panel, Vancomycin levels x2</td>
<td>Blood cultures positive for MRSA, respiratory viral panel negative, HIV non-reactive, Hepatitis B antigen negative, Hepatitis B Core IgM negative, hepatitis C antibody negative, Hepatitis A IgM negative, Vancomycin levels 8.3 ug/ml and 11.1 ug/ml</td>
<td>Rated pain as 4/10. Patient with maximum temperature of 102.8°F</td>
<td></td>
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<td>3</td>
<td>Transesophageal echocardiogram negative</td>
<td>Blood culture x2, Vancomycin level</td>
<td>Blood cultures positive for MRSA, Vancomycin level 14.3 ug/ml</td>
<td>Denies back pain. Patient with maximum temperature of 102.3°F</td>
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<td>4</td>
<td>Blood culture x2, Vancomycin level</td>
<td>Blood cultures positive for MRSA, Vancomycin level 17.6</td>
<td>Denies back pain. Patient with maximum temperature of 102.3°F</td>
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<td>5</td>
<td>Blood culture x2</td>
<td>Blood cultures positive for MRSA</td>
<td>Denies back pain. Patient with maximum temperature of 102.0°F</td>
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<td>Retroperitoneal ultrasound</td>
<td>Ultrasound showed normal cortical echogenicity in both kidneys. No renal abscesses were visualized.</td>
<td>Blood culture x2</td>
<td>Blood cultures positive for MRSA</td>
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<td>7</td>
<td>CT abdomen with contrast</td>
<td>Imaging revealed heterogeneous enhancement of both kidneys, suggestive of bilateral pyelonephritis. One of the previously noted potential abscesses had increased in size (Figure 2).</td>
<td>Blood culture x2</td>
<td>Blood cultures positive for MRSA</td>
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<td>8</td>
<td>Blood culture x2</td>
<td>Blood cultures positive for MRSA</td>
<td>Continued left flank pain.</td>
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<td>9</td>
<td>FNA of left kidney</td>
<td>Blood culture x2, FNA aspirate</td>
<td>Blood cultures were negative for bacterial growth. The FNA aspirate was cultured and grew MRSA, but acid fast bacilli testing, acid-fast, and anaerobic bacteria cultures were negative.</td>
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<td>10</td>
<td>Blood culture x2</td>
<td>Blood cultures were negative for bacterial growth</td>
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<td>11</td>
<td>Blood culture x2</td>
<td>Blood cultures were negative for bacterial growth</td>
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<td>12</td>
<td>Blood culture x2</td>
<td>Blood cultures were negative for bacterial growth</td>
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MRI: Magnetic Resonance Imaging; MRSA: Methicillin Resistant Staphylococcus Aureus; CT: Computed Tomography; FNA: Fine Needle Aspiration
day 7, a repeat CT of the abdomen with contrast was performed which revealed: 1) Overall a mildly worsened appearance of the left kidney consistent with pyelonephritis and renal and pararenal abscesses. 2) Suspected right-sided pyelonephritis. 3) New small bilateral al pleural effusions and persistent suspected right lower lobe septic emboli. One of the previously noted hypodense collections within the left kidney had increased in size (Figure 2). Due to continued blood cultures with growth of MRSA, IV Cefaroline was added to the antibiotic regimen on hospital day 8 for a synergistic effect with the current antibiotic regimen.

Subsequently a Fine Needle Aspiration (FNA) of left kidney parenchyma was performed on hospital day 9. The histopathology report of the FNA showed multiple small fragments of fibrous tissue and detached fibrinopurulent debris with marked chronic inflammation in the background of acute inflammation. The report suggested that the fibrinopurulent debris may represent abscess formation. The aspirated tissue was cultured and grew MRSA. Acid fast bacilli testing, anerobic bacteria cultures, and acid-fast cultures were negative. On hospital day 10, blood cultures finally came back negative, following which, cefaroline and SMX-TMP were discontinued. The patient was discharged on hospital day 13 with a peripherally inserted central catheter and was instructed to continue daily IV infusions of daptomycin for six weeks at a local infusion clinic near her home. The treatment plan was arranged in coordination with a physician at the infusion clinic. After discharge from the hospital the patient was lost to follow-up. She did not show up to her scheduled follow up appointment with the infectious disease specialist that managed her case in the hospital. She was unreachable at the phone number listed in her chart despite attempts to call her. It is unknown if she completed the antibiotic regimen on hospital day 8 for a synergistic effect with the current antibiotic regimen.

For a more detailed account of the patient’s hospital course please refer to Table 1.

Discussion

MRSA bacteremia is a serious infection and needs to be treated aggressively, even in relatively healthy individuals. Common identifiable sources of MRSA bacteremia include Intravascular (IV) catheters, soft tissue including surgical wounds, and endovascular sites other than IV catheters [1,5]. Less common sources include the lower respiratory tract, urinary tract, intra-abdominal organs, bone and joints [5]. The primary source of the bacteremia remains unknown in our patient after eliminating the most common causes of infection with a thorough workup. Previous studies have shown that 45-85% of community-associated S. aureus bacteremia patients have no apparent primary source [4].

An interesting aspect of our case is that although the initial CT imaging of the abdomen revealed multiple areas of abnormal enhancement in the left kidney with small areas of low attenuation consistent with acute pyelonephritis (Figure 1), the patient did not have symptoms of a urinary tract infection, nor CVA tenderness on admission. A renal ultrasound was also normal, so the kidney was not thought to be the source of infection. After the second CT abdomen and FNA of the left kidney, there was concern for abscess formation within the kidney. But we were unable to confirm this as the primary source of the patient’s MRSA bacteremia. We believe that the renal abscess was a complication of the patient’s persistent bacteremia, not the source of the bacteremia.

The patient was initially started on IV vancomycin, as this is widely accepted as the empiric treatment for MRSA bacteremia [4]. Yet, there were some limitations to consider with vancomycin. With a Body Mass Index (BMI) of 37, our patient required a higher concentration of antibiotics to reach a therapeutic level compared to a patient with a normal BMI. This influenced our decision to alter the antibiotic regimen, because we did not want renal toxicity to occur with increasing amounts of vancomycin required to reach therapeutic levels.

Additionally, some studies suggest that the development of persistent bacteremia infections may be due to the absence of MRSA isolates with reduced susceptibility to vancomycin [3]. Minimum Inhibitory Concentration (MIC) values approaching 2 mcg/mL are considered to be borderline susceptible [2]. Our patient’s vancomycin MIC value was 2 mcg/mL. Guidelines vary, but some suggest switching vancomycin to daptomycin if there is a poor response to initial therapy in cases of MIC ≥2 mcg/mL [6]. This also influenced our decision to replace the patient’s IV vancomycin with IV daptomycin.

Our case report serves as an important reminder that patients with MRSA bacteremia may not always have an identifiable source, but a thorough history and physical exam with appropriate work up is necessary to reveal a source for the bacteremia, if present. Collaboration between the infectious disease and internal medicine teams is crucial for management of patients with persistent bacteremia.

References