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Case report

Unresolved fever in methicillin-sensitive *Staphylococcus aureus* bacteremia: Insights from a case without an identifiable source

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ABSTRACT

Background: Methicillin-sensitive *Staphylococcus aureus* (MSSA) bacteremia is a serious infection that requires timely diagnosis and treatment to prevent complications. Persistent fever after clearing bacteremia is uncommon, especially with normal inflammatory markers and no clear source of infection. This presents a significant diagnostic and management challenge.

Case presentation: A 36-year-old man presented with a three-day history of intermittent fever and was diagnosed with MSSA bacteremia. Initial investigations revealed mild splenomegaly. Despite treatment with intravenous flucloxacillin and negative repeat blood cultures, the fever persisted, prompting further evaluation. Advanced imaging did not reveal the source of infection. After completing a 14-day course of flucloxacillin, the fever resolved, and the patient recovered completely.

Conclusion: This case highlights the challenges in managing MSSA with persistent fever and no clear source of infection. This emphasizes the importance of adhering to evidence-based therapy and thorough evaluations, even when clinical presentations deviate from the typical course.

Introduction

Methicillin-sensitive *Staphylococcus aureus* (MSSA) is a significant pathogen in both community and healthcare settings, causing infections ranging from mild skin infections to severe conditions, such as pneumonia and endocarditis. While MSSA infections are typically treatable with beta-lactam antibiotics [1], timely diagnosis is critical, especially in cases with atypical or predisposing factors, such as implants [2], to avoid complications. This case report describes the clinical course of persistent fever in a patient with MSSA bacteremia, highlighting the diagnostic challenges and importance of sustained treatment.

Case presentation

A 36-year-old male office worker presented with a 3-day history of intermittent fever accompanied by chills and rigor. Fever occurred every 4–5 h and subsided temporarily with paracetamol. He had no prior medical history of notes, prosthetic devices, or known addictions. He was not on regular medications and never had an immunocompromising illness. On admission, his vital signs included a temperature of 101.6 °F, a pulse rate of 104/min, a respiratory rate of 18/min, and a blood pressure of 140/90 mmHg. Oxygen saturation was 98 % in room air. Thorough physical examination, including cardiovascular, respiratory, abdominal, and neurological assessments, was unremarkable. There were no signs of lymphadenopathy, infective endocarditis, joint inflammation, or skin or soft tissue infections.

Given the seasonal prevalence of enteric fever, the patient was administered intravenous ceftriaxone after sending two-sets of blood culture (aerobic and anaerobic). The baseline investigations (Table 1) like dengue serology, malaria parasite on smear, liver and kidney functions, total and differential leucocyte counts, CRP, ESR were within normal limits, except for an abdominal ultrasound showing mild splenomegaly.

On Day 4, one-set of aerobic blood cultures identified MSSA growth. Ceftriaxone was discontinued and the patient was switched to intravenous flucloxacillin (2 g every 6 h). Despite targeted therapy, the

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Table 1
Lab parameters of the patient at admission.

Parameters	Values/results
Hemodynamic parameters	
Haemoglobin (g/dL)	13.1
Total Leucocyte count (/μL)	6200
Differential Count	
Neutrophils	56 %
Lymphocytes	37 %
Eosinophils	0.2 %
Platelets (μL)	188,000
Renal parameters	
Blood Urea (mg/dL)	30
Serum Creatinine (mg/dL)	0.9
Liver parameters	
Total Bilirubin (mg/dL)	0.7
ALT (IU/L)	22
AST (IU/L)	18
Alkaline Phosphatase (IU/L)	78
Inflammatory markers	
C-reactive protein (mg/L)	0.6
Erythrocyte sedimentation rate (mm/h)	12
Serology and histology	
Dengue NS-1 antigen	Negative
IgM serology	Negative
Malaria parasite smear	Negative

Abbreviations: AST-aspartate aminotransferase; ALT-alanine aminotransferase; IgM- Immunoglobulin M.

patient's high-grade fever persisted without a change in intensity or pattern. Repeat inflammatory markers (CRP and ESR) remained normal, and a transthoracic echocardiogram (TTE) showed no evidence of endocarditis.

Further investigations, including MRI of the spine and CT imaging of the chest and abdomen, were unremarkable, with no evidence of abscesses, osteomyelitis, or other localized infections. A repeat of blood cultures taken 48 h after initiation of flucloxacillin were negative indicative of clearance of bacteremia. An FDG-PET scan was performed to detect occult abscesses or valvular vegetation; however, no FDG-avid lesions were observed.

By Day 9, the fever had subsided in both intensity and frequency, and chills were absent. Inflammatory marker levels and leukocyte counts remained normal throughout the hospital stay. On Day 10, the patient was discharged with oral flucloxacillin (500 mg QID). His fever resolved completely five days after discharge. Flucloxacillin was administered for 14 days after the negative blood culture. He was followed up 10 days after discharge on completing flucloxacillin therapy and then 1 month later. He achieved full recovery without complications or symptom recurrence.

Discussion

The annual incidence of *S. aureus* bacteremia (SAB) ranges from 9.3 to 65 cases per 100,000 person-years, depending on the region and population [3]. The prevalence of community-acquired MRSA ranges from 16.5 % to 23.5 % [4], but that of MSSA bacteremia in India is not readily available. Patients with community-acquired SAB include patients who inject drugs and patients with a clinically inapparent source of bacteremia (such as vertebral osteomyelitis or epidural abscess). Patients with the onset of SAB acquired in the community are likely to present with complicated infection. In one study, more than 40 % of patients with community-acquired SAB had a metastatic infection, including infective endocarditis (IE) [5]; another study noted as many as 90 per cent of patients with community-acquired SAB had one or more complications [6].

Managing MSSA bacteremia becomes particularly challenging when the source of infection is unclear, and the patient presents with persistent fever despite culture clearance. This case of a 36-year-old male with MSSA bacteremia and normal inflammatory marker levels highlights these difficulties.

Persistent fever in bacteremia typically suggests an ongoing infection, such as hidden abscesses or endovascular involvement. These are common in conditions like infective endocarditis [7]. Despite appropriate antibiotic therapy and resolution of bacteremia, the fever persisted in this patient, prompting extensive investigation. Imaging studies, including CT, MRI, and FDG-PET, failed to identify the source of the infection. PET scans, which are particularly useful for detecting occult infections [8], were unremarkable, adding to the complexity of the case. The possibility of a viral co-infection is unlikely due to the prolonged duration of the fever. Also, non-infectious causes of fever were considered less likely in the setting of normal inflammatory markers and the fever being associated with chills.

Another unusual aspect was the patient's consistently normal levels of inflammatory markers, including CRP, ESR, and WBC counts. These markers typically increase in systemic infections and can guide clinical decision-making [9]. Elevated CRP levels are often linked to deeper infections and worse outcomes in *Staphylococcus aureus* bacteremia [10]. However, in rare cases, such as this one, normal inflammatory markers do not always correspond with infections or bacteremia, adding another layer of diagnostic uncertainty [11].

Achieving culture conversion typically signifies an effective treatment; however, in some cases, patients may not exhibit a corresponding clinical response [12]. The persistence of fever after bacteremia clearance raises the possibility of unresolved infections, drug fever, or non-infectious causes. However, with negative imaging and microbiological clearance, there was no justification for changing antibiotic therapy. The Infectious Diseases Society of America (IDSA) guidelines emphasize the importance of reassessing the source and treatment in cases of persistent bacteremia [13]. In this case, given the negative cultures and absence of new findings, the decision to continue flucloxacillin treatment was both evidence-based and clinically appropriate.

Determining the duration of antibiotic therapy is another important point of consideration. Persistent fever typically argues against classifying a case as uncomplicated bacteremia. However, in the absence of a detectable source of infection, a 14-day course of flucloxacillin post-negative blood cultures was deemed sufficient. This decision aligns with the standard guidelines for uncomplicated MSSA bacteremia [14], even though the clinical presentation was atypical.

Conclusion

This case highlights the unique challenges in diagnosing and managing MSSA bacteremia when persistent fever occurs despite normal inflammatory markers and negative repeat blood cultures. This emphasizes the importance of adhering to evidence-based antibiotic therapy even when the clinical presentation is atypical. Persistent fever can be concerning, but as this case shows, it does not necessarily warrant premature changes in treatment if the bacteremia has cleared. No other source of infection was identified.

Ultimately, this case underscores the value of thoughtful clinical judgment, thorough diagnostic workups, and adherence to the established guidelines. Balancing persistence and caution in such complex scenarios are key to achieving optimal patient outcomes.

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Ethical approval

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Consent

Consent obtained.

CRediT author statements

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A written consent was obtained from the patient.

CRediT authorship contribution statement

Topiwala Moiz: Writing – review & editing, Writing – original draft, Investigation, Conceptualization. **Yadav Sanjay:** Writing – review & editing, Writing – original draft, Investigation. **Verma Deependra:** Writing – review & editing, Writing – original draft, Investigation. **Medisetty Mahender:** Writing – review & editing, Writing – original draft, Investigation.

Declaration of Interest statement

None of the authors have anything to disclose.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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