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BURKHOLDERIA PSEUDOMALLEI : THE RARELY SUSPECTED CULPRIT

Internal Medicine

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ABSTRACT

Introduction : We present the case of a 47-year-old gentleman with a medical history of Diabetes Mellitus,who was initially diagnosed with pneumonia later proved to be caused by Burkholderia pseudomallei which was treated with appropriate antibiotics.Within a few days,patient was readmitted with native valve infective endocarditis as a consequence of persistent bacteremia due to Burkholderia pseudomallei.However,patient was not complaint with the antibiotic course leading to its recurrence. Additionally,this pathogen does not respond to the usual broad-spectrum empirical antibiotics, highlighting the treatment challenges associated with infections from Burkholderia pseudomallei, which are relatively rare in India.1 Due to its unusual occurrence, it is not commonly considered as a primary causative organism in such cases. Furthermore, this organism exhibits intrinsic resistance to many commonly used antibiotics, complicating treatment efforts.2 Given these considerations, we emphasize the critical need to recognize Burkholderia pseudomallei as a potential pathogen in patients with diabetes or similar immunocompromised states. This awareness is particularly vital in instances where usual broad-spectrum empirical antibiotic therapies fail to produce the expected clinical improvement.We also stress on the fact to educate patients on completing the intravenous course of antibiotics needed to tackle this infection. Understanding the resistance patterns of this organism can guide more effective treatment strategies and ultimately enhance patient outcomes.

KEYWORDS

Burkholderia Pseudomallei, Pneumonia, Diabetes Mellitus,infective endocarditis

CASE HISTORY:

A 47-year-old male farmer from Uttar Pradesh, India, presented to the emergency department with a high-grade fever accompanied by chills and rigor lasting 15 days. He reported no diurnal temperature variation or rash but experienced a dry cough and generalized body aches for the past five days. The patient described profound weakness, rendering him unable to walk.

In addition, he complained of abdominal pain, primarily located in the right upper quadrant, radiating to the back, which was unrelated to food intake. His bowel and bladder habits remained normal. Upon examination, he exhibited labored breathing, bilateral basal crepitations in the lung fields, and tender hepatomegaly.

Initial Laboratory Investigations Revealed :

Serial Number	Investigation	Value	Interpretation
1	Gamma-Glutamyl Transferase	583 U/L	Elevated
2	alkaline phosphatase	544 U/L	Elevated
3	Aspartate aminotransferase	67.9 U/L	Elevated
4	Alanine aminotransferase	113 U/L	Elevated
5	Total Bilirubin	3.55 mg/dl	Elevated
6	Direct Bilirubin	2.65 mg/dl	Elevated
7	Serum Creatinine	0.74 mg/dl	Normal
8	Hemoglobin	11.1 gm/dl	Low
9	White blood cell count	7750 / microL	Normal

The clinical suspicion was raised for cholangitis versus enteric fever with superimposed pneumonia. The patient was subsequently admitted to the ward and initiated on empirical intravenous ceftriaxone and oral azithromycin.

On admission, an abdominal ultrasound revealed hepatomegaly and thickening of the gallbladder wall with increased pericholecystic echogenicity, as well as a suspicious periportal lymph node. A chest X-ray revealed bilateral pneumonia with syn - pneumonic effusion.

During his hospitalization, the patient experienced desaturation and was transferred to the ICU due to Type 1 respiratory failure. A GeneXpert test for Tuberculosis returned negative, and as the patient did not respond to the initial antibiotic regimen of intravenous ceftriaxone and oral azithromycin, the treatment was escalated to intravenous meropenem.

HRCT of chest was performed, showing multifocal peribronchovascular ground-glass opacities and consolidation in both lungs, predominantly in the superior and basal segments of both lower lobes.(Image 1a and 1b)

Thus a 2D echocardiogram was done to rule out Infective endocarditis which revealed incidental findings of hypertrophic cardiomyopathy without obstructive outflow tract and a left ventricle-to-aorta gradient of 20 mmHg, ejection fraction of 55%, with mild tricuspid regurgitation. The pulmonary artery systolic pressure (PASP) was elevated at 55 mmHg, indicating significant pulmonary artery hypertension.However,there was no vegetation seen suggestive of infective endocarditis. (1st admission)

In the abdomen, the CT scan demonstrated mild hepatosplenomegaly with fatty infiltration of the liver and pseudo-gallbladder wall edema.

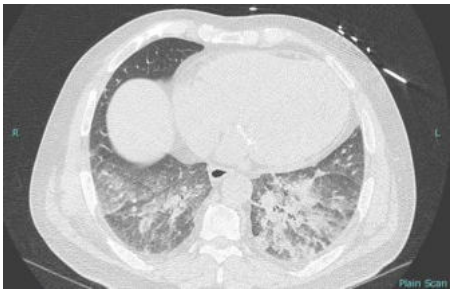


Image 1a

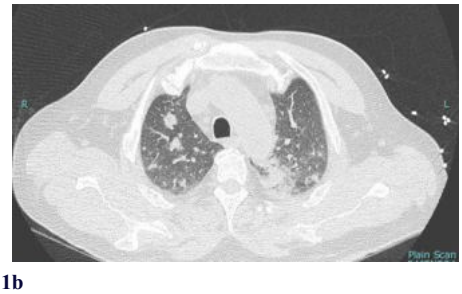


Image 1b

Blood cultures subsequently confirmed the presence of Burkholderia pseudomallei. The patient demonstrated a positive response to intravenous meropenem, and based on sensitivity reports, the treatment was switched to intravenous ceftazidime. With improvements in oxygen saturation, blood counts, and liver function tests, the patient was successfully transferred out of the ICU. Eventhough,the patient was improving,he decided to take discharge without completing the advised course of intravenous ceftazidime. During discahrge, his clinical condition had improved significantly. His total bilirubin was 2 with direct bilirubin of 0.7.ALT was 67 and

AST was 68 the patient was afebrile and asymptomatic and was prescribed oral cotrimoxazole for a six-month course.

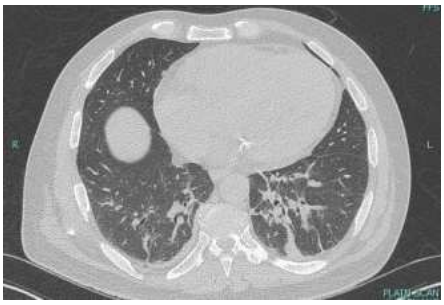
After 4 days of discharge, He revisited the accident and emergency department of our hospital. He was tachypnic with increased work of breathing and complained of right leg pain. Routine investigations revealed :

Serial number	Investigation	Value	Interpretation
1	Gamma-Glutamyl Transferase	266 U/L	Elevated
2	alkaline phosphatase	420 U/L	Elevated
3	Aspartate aminotransferase	68 U/L	Elevated
4	Alanine aminotransferase	67 U/L	Elevated
5	Total Bilirubin	7.9 mg/dl	Elevated
6	Direct Bilirubin	7.1 mg/dl	Elevated
7	Serum Creatinine	0.6 mg/dl	normal
8	Hemoglobin	9 mg/dl	Low
9	White blood cell count	12663 / microL	Elevated
10	Serum Sodium	121 mmol/L	low

He had new onset cholestasis most likely due to sepsis. Lower limb doppler was done which ruled out Deep vein thrombosis.Computed Tomography pulmonary angiography was done which ruled out pulmonary embolism but revealed that there was interim regression in multifocal peribronchovascular ground glass opacities, consolidation in both lungs predominantly in the superior and basal segments of both lower lobes.

Patient was restarted on Intravenous ceftazidime Previously seen multiple small variable sized well-defined angiocentric nodules shows interval regression in size, with few showing cavitation within.Blood culture was sent which was again positive for burkholderia pseudomallei which was sensitive for ceftazidime which was thus continued

A repeat CT abdomen which ruled out biliary tree pathology and revealed hepatosplenomegaly with Liver shows altered lobe anatomy with prominence of caudate lobe.



(Image 2)

Even though his lung consolidation had improved (Image 2),his clinical condition during the course of the hospitalisation had worsened. The next day of admission the patient became hemodynamically unstable requiring inotropic support. ECG was suggestive of Atrial fibrillation.Thus 4 Direct current cardioversions of 200 joules were given to revert the patient back to sinus rhythm

A repeat 2D echo was done which revealed Ejection fraction of 50-55%,moderate pulmonary hypertension.no regional wall abnormality and hypertrophic obstructive cardiomyopathy and a mobile echogenic structure on aortic valve suggestive of infective endocarditis.Patient was offered transesophageal echocardiography to further delineate the lesion but refused to do so.

Antibiotics were escalated to intravenous Meropenem and cotrimoxazole was restarted.Although patient was febrile for 14 days after admission, his clinical condition improved with the current regimen.in this admission he received , 14 days of intravenous meropenem and he was discharged in hemodynamically stable condition being afebrile for 2 days

DISCUSSION:

Melioidosis, caused by Burkholderia pseudomallei, is a serious and potentially fatal infection. In non-endemic regions, healthcare providers may not readily suspect this pathogen, leading to delays in diagnosis and treatment. B. pseudomallei is a gram-negative bacterium commonly found in stagnant water and soil.[3] The well-documented risk factors for melioidosis include diabetes mellitus, chronic alcohol use, chronic kidney disease, and lung conditions such as chronic obstructive pulmonary disease (COPD) and lung involvement in cystic fibrosis.[4,5] The incidence of infection tends to rise during the monsoon season, primarily due to exposure to contaminated water or wet soils.

In this case, the patient had poorly controlled diabetes mellitus as the sole immunocompromising factor, with no prior history of multiple infections or known lung or kidney disease. It is likely that he was exposed to B. pseudomallei through his occupation as a farmer, which increases the risk of contact with contaminated soil.

Thrombocytopenia is a recognized hematological manifestation of B. pseudomallei infections and serves as a prognostic indicator for inpatient mortality.[6] In our patient's case, the platelet count upon admission was 273 per microliter, which later decreased to 149 per microliter before gradually improving.

Hyponatremia is observed in 84.1% of patients hospitalized with melioidosis. Factors such as advanced age and acute kidney injury (AKI) are linked to an increased risk of developing hyponatremia. Additionally, severe hyponatremia serves as an independent predictor of higher in-hospital mortality, the necessity for mechanical ventilation, and prolonged ICU admission.[7]

The sensitivity of transthoracic echocardiography(TTE) to diagnose infective endocarditis ranges from 40 to 63%. Where as for transesophageal echocardiography(TEE) it is 90-100%,[8] Native valve endocarditis with Burkholderia pseudomalle is rare (1%) [9].Thus,TEE may not be indicated in all cases of sepsis burkholderia pseudomalle, but should be considered if infective endocarditis is strongly suspected with negative TTE or if patient condition does not improve or worsens with appropriate antibiotics.

Barman et al. documented a case in which melioidosis went undiagnosed for two months, underscoring the diagnostic challenges posed by this condition, particularly given its similarity to other infections, especially tuberculosis.[10]

A randomized trial has demonstrated that ceftazidime significantly reduces mortality rates—by approximately 50%—for severe melioidosis compared to standard treatments. Carbapenems exhibit the lowest minimum inhibitory concentration (MIC) against B. pseudomallei and are equally effective as ceftazidime. Following the initial intensive treatment phase, it is recommended to initiate eradication therapy with cotrimoxazole, continuing for a minimum of three months. [3]

However, in our case,patients pneumonia responded to ceftazidime but in later admission, sepsis and infective endocarditis did not respond to intravenous ceftazidime but did to Intravenous meropenem. Patients suffering from septicemic melioidosis often face high mortality rates.[11]

In this instance, during the patient's initial admission, there was no clinical response to empirically administered intravenous ceftriaxone and oral azithromycin. The patient's acute desaturation, along with a negative GeneXpert result for tuberculosis, led to the escalation of antibiotic therapy to meropenem, and later ceftazidime which ultimately proved effective for lung consolidation. This case emphasizes the importance of considering Burkholderia pseudomallei as a potential cause of pneumonia that may be resistant to broad-spectrum antibiotics, especially in immunocompromised individuals working in agricultural environments.Also,one should consider invasive investigations such as TEE in scenarios of high suspicion of infective endocarditis in rare causes such as Burkholderia pseudomallei.

During the second hospitalization, although there was some improvement in lung consolidation, the patient's infective endocarditis worsened, and the condition did not respond to single-agent intravenous ceftazidime. This highlights the necessity of using combination antibiotic therapy—in this case, intravenous meropenem and oral cotrimoxazole—when treating more resistant infections, such as infective endocarditis.

CONCLUSION:

This case serves as a reminder of the importance of maintaining a high index of suspicion for melioidosis in patients, particularly those who do not respond to standard treatments. It also underscores the need to consider Burkholderia pseudomallei as a potential cause of infective endocarditis, especially in patients with treatment failure or relapse. To better manage this emerging infectious disease, it is essential to raise clinician awareness through focused training, workshops, and conferences.It is also crucial to generate patient awarness and compliance for the long duration of intravenous antibiotics wherever necessary. Additionally, enhancing the capabilities of microbiological testing laboratories is crucial for enabling early detection and timely intervention, ultimately improving patient outcomes.

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