

# Melioidosis: A Fulminant Infection in a Patient with Uncontrolled Diabetes

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J Health Allied Sci <sup>NU</sup>;2021;11:50–53

## Abstract

Melioidosis is an endemic infection in Southeast Asia and Northern Australia commonly manifesting with pneumonia and localized skin infection. Though most exposures do not lead to severe illness, a fulminant infection can occur among patients with risk factors. A 59-year-old male presented with cough with expectoration and fever for 1 week. He had diabetes for 10 years with poorly controlled blood sugars. Contrast-enhanced computerized tomography (CECT) of thorax showed right upper lobe consolidation with diffuse ground-glass opacities in right upper lobe along with microabscesses in liver and spleen. Sputum culture and Xpert mycobacterium tuberculosis complex and resistance to rifampin (MTB/RIF) for tuberculosis were negative. Bronchoalveolar lavage culture grew *Burkholderia pseudomallei*. He was treated with initial intensive therapy with injection amoxicillin-clavulanic acid for 2 weeks and subsequently started on eradication therapy with tablet trimethoprim-sulfamethoxazole. Diagnosis of melioidosis should be considered in a patient of pneumonia with multiorgan involvement in an endemic area, especially with underlying risk factors.

## Keywords

- ▶ melioidosis
- ▶ *Burkholderia pseudomallei*
- ▶ microabscess

## Case History

A 59-year-old male patient, an electrician by occupation, with exposure to wet season soil and water during commutation for work, presented with a history of intermittent fever for 1 week. It was associated with cough along with whitish-yellow sputum. There was no history of shortness of breath or chest pain. The patient was hailing from Western coastal Karnataka, an endemic region for melioidosis and had no travel history outside the area. He had diabetes for 10 years and was on oral metformin 500 mg twice a day. His random blood sugar on admission was 323 mg/dL, and HbA1c was 12.7%. He had no other co-morbidities. He had a room air saturation of 97% on presentation. His chest X-ray showed illdefined nonhomogeneous consolidation in the right upper zone (▶**Fig. 1**). Sputum Gram stain showed numerous gram-positive cocci and gram-negative bacilli. Sputum culture yielded oropharyngeal flora. Sputum acid-fast bacillus (AFB) stain was negative. Blood culture did not show any organism. He was empirically started on intravenous amoxicillin-clavulanic acid 1.2 g thrice

a day, and insulin injections were given for blood sugar control. A CECT thorax was done, which showed right upper lobe consolidation with diffuse ground-glass opacities of the right upper lobe (▶**Fig. 2**). Multiple enlarged mediastinal lymph nodes were seen (▶**Fig. 3**) along with microabscesses in the liver and spleen. He underwent a bronchoscopy during which purulent secretions were seen coming from right upper lobe bronchus. Bronchoalveolar lavage was taken. AFB stain and Xpert MTB/RIF for tuberculosis were negative, and cytology showed numerous inflammatory cells. Culture of the bronchoalveolar lavage fluid in conventional blood culture medium grew *Burkholderia pseudomallei*. A sensitivity test was done using the Vitek-2 compact method, and the organism was found to be sensitive to amoxicillin/clavulanic acid, ceftazidime, imipenem, and trimethoprim/sulfamethoxazole. Since the patient was already receiving amoxicillin/clavulanic acid and was relieved of fever and cough by the time diagnosis was achieved, the same was continued for 2 weeks. He was started on eradication therapy with oral trimethoprim/

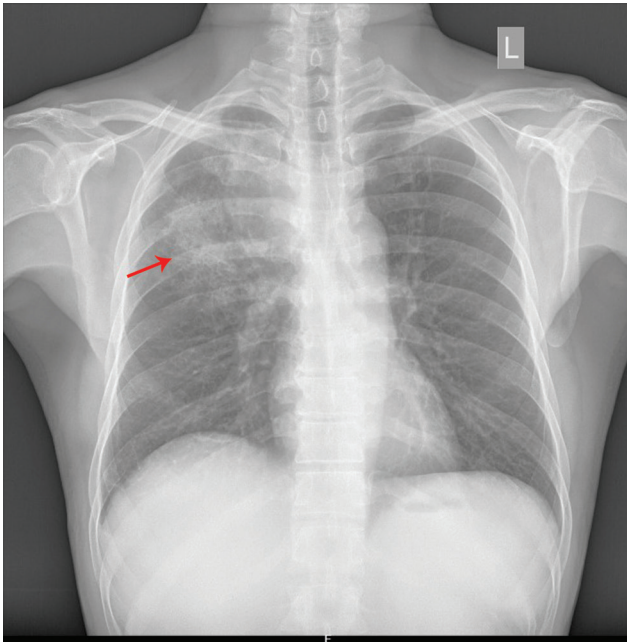
published online  
December 2, 2020

DOI <https://doi.org/10.1055/s-0040-1721232>  
ISSN 2582-4287.

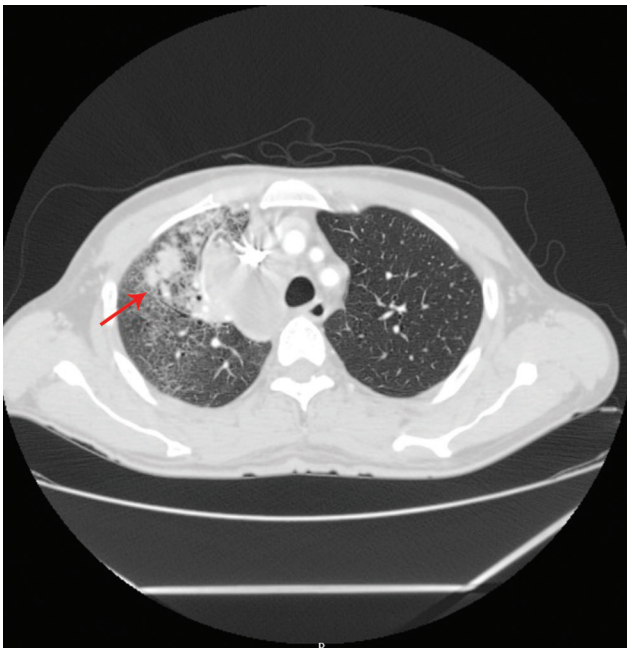
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**Fig. 1** Chest X-ray showing illdefined nonhomogenous consolidation in right upper zone.

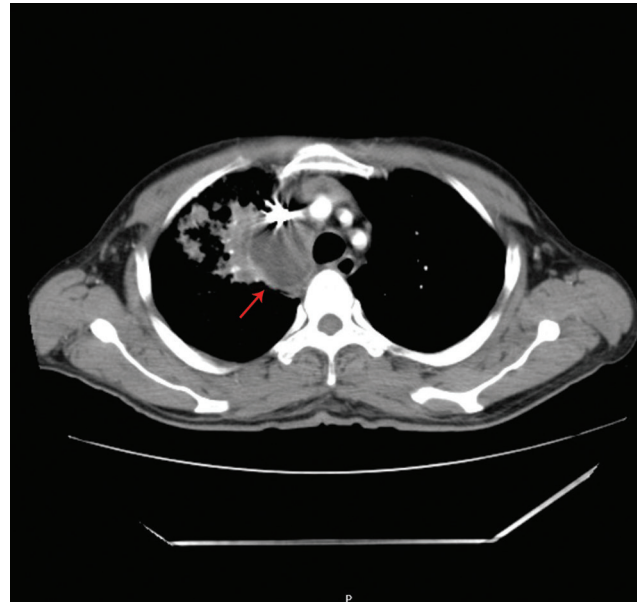


**Fig. 2** CECT thorax (lung window) showing right upper lobe consolidation with diffuse ground glass opacities of the right upper lobe. CECT, contrast-enhanced computerized tomography.

sulfamethoxazole (800/160 mg) two tablets twice a day with a plan to continue for 3 to 6 months. The patient was asymptomatic on follow-up at week 4.

## Discussion

Most studies indicate an increased risk of infection among people with diabetes compared with the general population.<sup>1,2</sup> Risk of infection increases with poor



**Fig. 3** CECT thorax (mediastinal window) showing multiple enlarged mediastinal lymph nodes. CECT, contrast-enhanced computerized tomography.

glycemic control. There are various host-related factors which predispose diabetic patients to infection, including hyperglycemia-related impairment of immune response, autonomic neuropathy, sensory neuropathy, vascular insufficiency, and skin and mucosal colonization with pathogens. Diabetics with hyperglycemia have depression of immune functions such as neutrophil chemotaxis, phagocytosis, intracellular bactericidal activity, opsonization, and cell-mediated immunity.<sup>3,4</sup> Hence such patients are at risk for severe infections.

Awareness of the epidemiology of infection in the local community provides useful clues for diagnosis. Early diagnosis of the pathogen and appropriate treatment is the key to treatment success. Routine chest radiography and sputum sampling may fail to give an etiological diagnosis in many patients. It is necessary to pursue a microbiological diagnosis aggressively in diabetic patients with lung infiltrates. It helps in early directed therapy, simultaneously avoiding overly broad antimicrobial treatment.

Sputum samples should be sent for staining and culture whenever possible. Sometimes, induced sputum specimens may be required and most useful for diagnosing mycobacterial infections and pneumocystis pneumonia.<sup>5</sup> In many cases, bronchoscopy and bronchoalveolar lavage are necessary to obtain adequate specimens.<sup>6</sup> The sensitivity of bronchoalveolar lavage (BAL) is improved by early over late sampling and is reduced by ongoing or prior antimicrobial treatment.<sup>7,8</sup> BAL samples should be sent for microbiological studies (Gram stain/culture, AFB, Xpert MTB/RIF, KOH mount/fungal culture) to improve sensitivity.

*B. pseudomallei* is a facultative intracellular gram-negative bacterium responsible for causing melioidosis.<sup>9</sup> It is a saprophyte distributed widely in soil and freshwater in endemic regions.<sup>10</sup> Infection is localized mainly to Southeast Asia and

Northern Australia.<sup>11</sup> Southern and Eastern states of India are considered endemic regions for melioidosis.<sup>12</sup> The predominant mode of transmission is percutaneous inoculation from wet season soil or contaminated water. Other ways of transmission like inhalation, aspiration, and ingestion can also occur.<sup>13</sup>

Most exposures to *B. pseudomallei* do not result in illness in healthy individuals. Fulminant disease and fatalities can occur in those with defined risk factors. Most common risk factors for melioidosis are uncontrolled diabetes, alcoholism, chronic kidney disease, and chronic lung disease.<sup>14</sup>

Majority of endemic melioidosis occur during monsoon season.<sup>14</sup> Index patient also presented in August during the peak of Southwest monsoon season in Western coastal Karnataka. This is attributed to increased exposure to soil and freshwater at work during the season.

Though most infections with *B. pseudomallei* result in non-severe illness, immunocompromised hosts can have severe manifestations.<sup>15,16</sup> Most common involvement are pneumonia and localized skin infections. Over half of patients of melioidosis can have bacteremia which can disseminate the organism to virtually any organ.<sup>15</sup> Though it can affect people of any age; adults are commonly affected. Pneumonia is the most common manifestation in adults, whereas pneumonia and bacteremia are infrequently seen in children.<sup>17</sup>

An acute presentation with pneumonia may consist of high fever with chills and rigors, cough, sputum, and respiratory distress with or without shock.<sup>18</sup> Chronic presentation may also be seen consisting of cough, purulent sputum production, hemoptysis, and night sweats closely resembling tuberculosis. Co-infection of melioidosis with tuberculosis has been reported previously.<sup>19</sup> Presentation of melioidosis with mediastinal masses is described in literature.<sup>15</sup> Our patient had necrotic mediastinal lymph nodes, raising further suspicion for tuberculosis. Investigations for tuberculosis were negative. Abscesses in internal organs like liver, spleen, kidney, and prostate are well recognized and should raise suspicion for melioidosis in endemic areas.<sup>20</sup>

Gram stain of sputum and abscess pus may reveal gram-negative bacilli of *B. pseudomallei* with characteristic bipolar staining with a "safety pin" appearance. However, culture is the mainstay of diagnosis.<sup>21</sup> If initial sputum work-up is nondiagnostic, more invasive procedures like bronchoalveolar lavage may be required for the diagnosis.

Resistance to various antibiotics is well known, and treatment should be guided by culture sensitivity reports.<sup>22</sup> Treatment should consist of an initial intensive phase with intravenous antibiotics for at least 2 weeks, followed by eradication therapy with oral antibiotics. Eradication therapy should be continued for at least 3 months as it helps in reducing the rate of relapse.<sup>23</sup> Ceftazidime is the mainstay of intensive phase treatment, with carbapenems reserved for severe infections or treatment failures. Amoxicillin/clavulanic acid is used as second-line therapy. Trimethoprim/sulfamethoxazole (co-trimoxazole) is preferred for the eradication phase.<sup>24</sup> However, treatment for individual patients should be adjusted according to clinical manifestations and response to treatment. Since index patient was already receiving

amoxicillin/clavulanic acid when diagnosis was made and his symptoms had resolved and organism was found sensitive to amoxicillin/clavulanic acid, same was continued for intensive phase treatment. These patients require a close follow-up to observe for any relapse.

## Conclusion

Melioidosis should be considered in the differentials when an immunocompromised patient presents with pneumonia and multisystem involvement. Microabscesses in internal organs are common. Infections are common among adults and in monsoon season in endemic areas. Culture is the mainstay of diagnosis. Appropriate samples should be sent for culture and may require invasive procedures like bronchoscopy for obtaining appropriate clinical samples if initial testing is nondiagnostic. Treatment consists of an initial intensive phase with intravenous antibiotics followed by prolonged eradication therapy with oral antibiotics as relapse is common.

## Conflict of Interest

None declared.

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