Case Report

What is cheesier than a Whitmore's liver? An accidental diagnosis of melioidosis

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Received 21 September 2023; revised 4 November 2023; accepted 4 November 2023
doi:10.46475/asean-jr.v24i3.884

Abstract

Despite the endemicity of Melioidosis in India, there were no official reports of the same case in our area which can be attributed to a lack of awareness of its occurrence in this geographic region, varied manifestations and consequent misdiagnosis. We report a case of Melioidosis from Tirupati, Andhra Pradesh. A diabetic male presented with fever, jaundice, and breathlessness. Radiological investigations revealed abscesses in the liver and spleen with a swiss cheese or honey comb appearance on CECT abdomen. The patient rapidly succumbed to

THE ASEAN JOURNAL OF RADIOLOGY
ISSN 2672-9393

the illness even with appropriate antibiotics in view of delayed presentation. Pus aspirated from the patient isolated *Burkholderia* species which was later confirmed through molecular methods as *Burkhloderia pseudomallei.* Hence, it is advised to consider Melioidosis as a potential infection in this region, for a timely and appropriate management of the patient's conditions.

Keywords: *Burkhloderia pseudomallei,* Liver abscess, Melioidosis.

Introduction

"Melioidosis" (distemper of the horses) or "Pseudoglanders" (Glanders like) or "Whitmore's disease" (in honor of the pathologist who first documented) or the sinister name "Vietnam time bomb" (occurrence in USA soldiers returned from Vietnam war) is caused by *Burkholderia pseudomallei,* a Gram negative non-fermenting bacillus, also called the "Great Mimicker of diseases", because of its various manifestations ranging from fever of an unknown origin to sepsis, the most common being community acquiring pneumonia [1]. The disease is spread through inhalation, ingestion and inoculation with a surge in cases during the rainy season [2]. Melioidosis is endemic to the tropical belt of India, Pakistan, the Philippines, Malaysia, and other South Asian countries stretching to northern Australia and an approximate annual incidence of 52000 cases [3]. With the major risk factors for Melioidosis, namely, excessive alcohol consumption, cases of diabetes, chronic lung disease and chronic renal disease on the rise, it is safe to assume the burden of this disease would be escalating henceforth [4]. Not geographically reported from this particular area in Southern India, the microbiological suspicion lead to reconsideration of the patient's typical radiographic findings to be of hepatic Melioidosis by the radiologist.

Case Summary

A 42-year-old male patient who is a type – 2 diabetic, smoker and alcoholic was admitted in our hospital with complaints of fever with chills, cough, and breathlessness for 10 days. Prior to this, the patient was admitted in another hospital for one week due to yellowish discoloration of skin, passing yellow-colored stools, abdominal bloating, right sided abdominal pain, and nausea.

He was diagnosed with jaundice, multiple liver abscesses and splenic infarct with mild pleural effusion and was treated for those conditions. No further reports could be retrieved regarding the patient treatment regarding his previous hospitalization. He was transferred to our hospital for the further management in view of worsening patient condition.

The patient was febrile (101.4° F) and had icterus. Tenderness in right hypochondrium with hepatosplenomegaly was noted on palpation of the abdomen. On auscultation, diffuse crepitations were heard over the entire right lung. Other system examinations were normal.

Blood investigations

Blood culture and sensitivity was sterile after one week of aerobic incubation. Serum procalcitonin was >100 ng/mL.

Liver function test indicated impaired functioning with serum alkaline phosphatase – 158 IU/ml (90 to 120 IU/ml), serum alanine amino transferase (SGPT/ALT) – 42(10 to 40 IU/ml), serum aspartate amino transferase (SGOT/AST) – 85 (10 to 35 IU/ml). Serum bilirubin conjugated was 2.3 (0.1 to 0.3mg/dL) and serum bilirubin total was 4.4 (0.2 to 1.1 mg/dL).

Total leukocyte count was 11800 cells /mm^3 with neutrophilia – 86 % (50 – 70%) and lymphocytopenia – 7% (20-40%). The patient had anemia with hemoglobin - 6.4 mg/dL and red blood cells – 2.14 (4.5 – 6 million/ mm^3). Erythrocyte sedimentation rate was 110 mm/ first hour (0 to 9).

THE ASEAN JOURNAL OF RADIOLOGY
ISSN 2672-9393

Radiological investigations

A contrast enhanced CT scan (CECT) of the abdomen and chest was conducted in which multiple liver and splenic abscesses with massive hepatosplenomegaly were noted on the coronal plane (Figure 1). In Figure 2, a large focal lesion with multiple cystic areas and enhancing walls is seen giving a characteristic honeycomb appearance. It can be seen that some of the abscesses are coalescing to give a cavity in segments V, VII, VIII and IV. Similar lesions are also noted in the spleen. Chest X ray showed an elevated right dome of diaphragm with moderate right sided pleural effusion that was loculated. Figures 3 and 4 show the culture plate with growth of pale pink colonies with metallic sheen resembling *Burkholderia pseudomallei*, along with Gram stain (safety pin appearance).

Under the ultrasound guidance, aspiration of the abscess was implemented which was sent to Microbiology for Gram stain, culture and antimicrobial susceptibility testing. A pigtail catheter was inserted into the liver to drain the abscess. The patient was started on Inj. Piperacillin tazobactam 4.5 gm TID and Inj. metronidazole 500 mg TID along with a supportive therapy.

As soon as the sample was received, Gram stain was done, which revealed plenty of neutrophils with occasional Gram-negative bacilli whose peculiar morphology could not be ascertained. Aerobic culture was done on blood, MacConkey agar and nutrient agars. After 24 hours of incubation, it revealed pale non-lactose fermenting colonies on MacConkey which were slow oxidase positive. On Blood agar, the colonies were translucent and non-hemolytic which were wrinkled with prolonged incubation. No pigmentation was observed on any culture media, while Gram stain from the culture plate revealed typical Gram-negative bacilli with a notable safety pin appearance (Figure 4).

The patient continued to be tachypneic and an X-ray chest revealed haziness of the entire right lung. In view of worsening oxygen saturation levels, the patient was intubated the following day and antibiotics changed to meropenam 1.5 gm TID and tigecycline 50 mg OD, by which time the preliminary report was conveyed to

the treating surgeon. The fever was nonresponding despite the new regimen and the patient succumbed to the illness four days later due to sepsis and multiorgan dysfunctions.

The culture report of aspirated pus revealed *Burkholderia* species which was sensitive to cefoperazone-sulbactam, ceftazidime, chloramphenical, ciprofloxacin, cotrimoxazole, imipenem and meropenam. The isolate was resistant to amikacin, gentamicin, cefotaxime and netilmicin. The isolate was later sent to the Centre for Emerging and Tropical Diseases in Manipal, Karnataka for confirmation where, *Burkholderia pseudomallei* was confirmed by specific monoclonal antibody-based latex agglutination and type three secretion system (T3SS1) gene polymerase chain reaction (PCR).

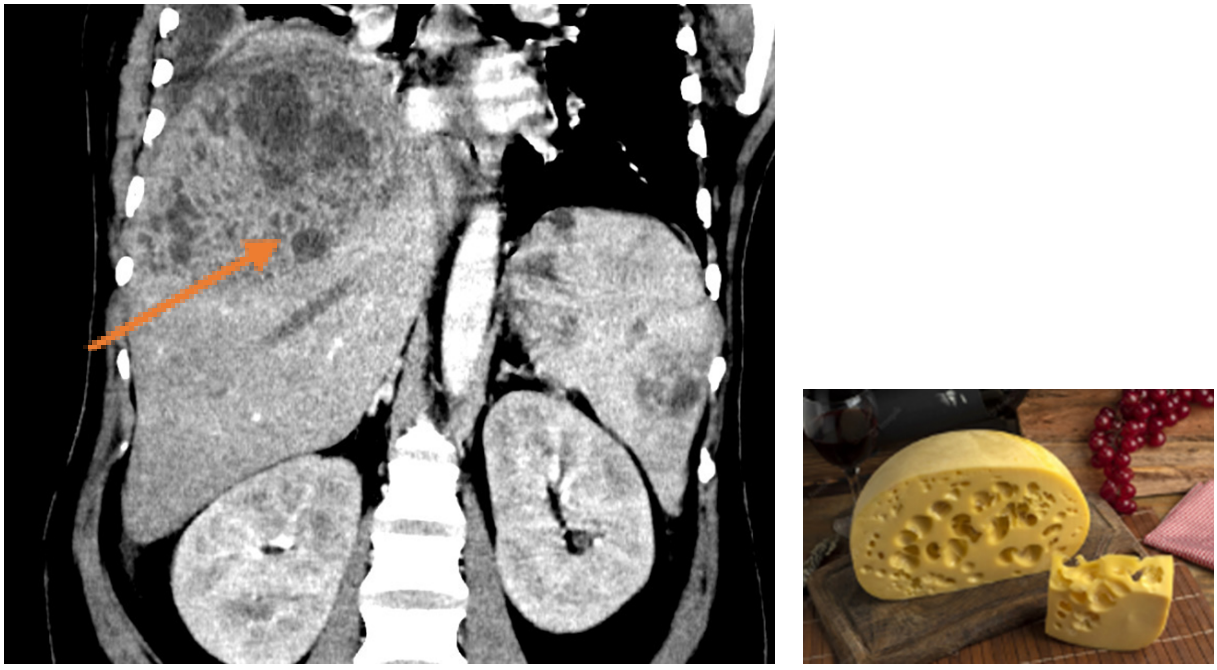

Figure 1. *Coronal abdominal CECT showing massive hepatomegaly and swiss cheese appearance of the liver abscess and similar findings in the spleen.*

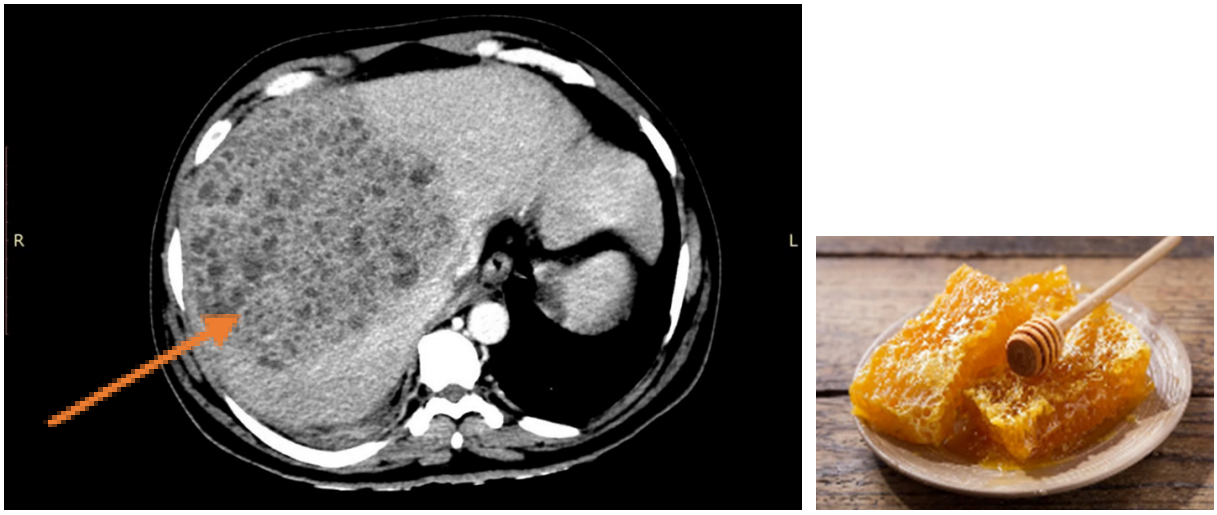

Figure 2. *Transverse abdominal CECT at the level of liver showing honeycomb appearance of the abscess.*

Figure 3. *MacConkey and Sheep blood agar plates showing growth of Burkholderia pseudomallei.*

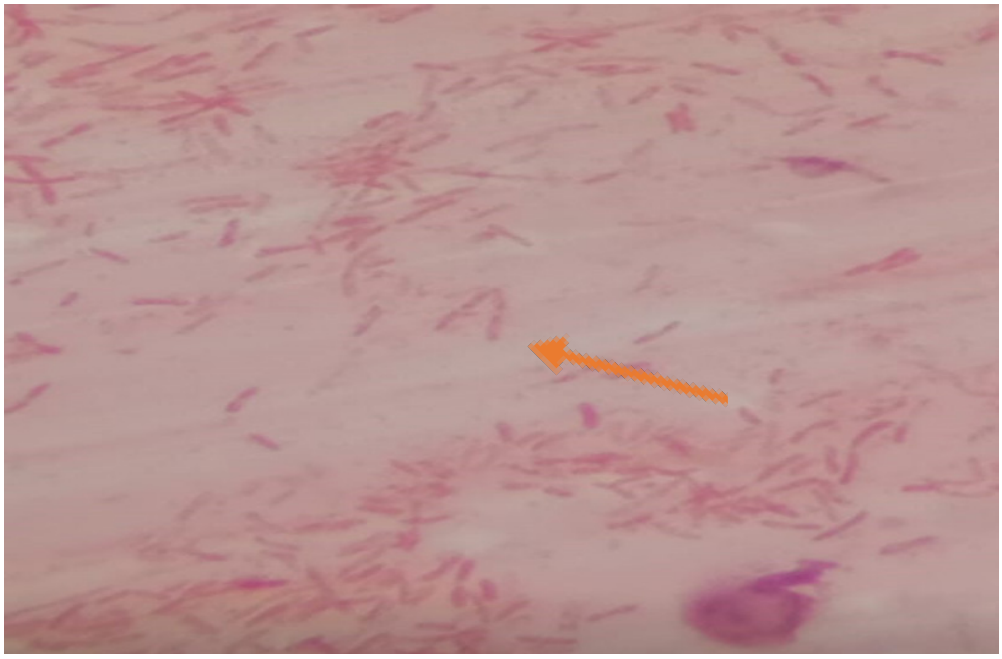

Figure 4. *Gram stain showing safety pin appearance of Burkholderia pseudomallei.*

Discussion

Burkholderia pseudomallei, an environmental saprophyte causing Melioidosis, has been classified as an agent of bioterrorism by the Centre for Disease Control (CDC) in nature of its easy transmissibility and high fatality (6). Paddy cultivating countries are known for their endemicity of Melioidosis, regardless of which, it is grossly under reported for diverse reasons. A lack of awareness of the Melioidosis burden in this geographic area due to under reporting resulted in an almost missed diagnosis despite typical radiographic features. While blood cultures may not be always positive, the culture of samples onto blood and MacConkey agars from specific site may be helpful. Colonies are 1-2 mm in diameter with a wrinkled surface and no haemolyis on Blood agar while on MacConkey colonies are pale, with a pinkish metallic sheen and oxidase positive. Unless looked with suspicion, these features can be easily misinterpreted as Pseudomonas or aerobic spore bearers. Automated tools like MALDI -TOF or VITEK 2 may not be definitive in

identification of the organism as it happened with the current isolate. Amoxycillin clavulanate sensitivity and polymyxin resistance are more clues towards *Burkholderia pseudomallei.*

Most cases presented in the critical stages of illness with multiple internal organ abscesses, pneumonia and sepsis [7]. The chronic disease occurs because of the organism's ability to survive inside macrophages, and can mimic granulomatous diseases [8]. Early diagnosis and prompt administration of antibiotics can cut down the mortality rate drastically [7]. This is possible with a radiological diagnosis like CT or ultrasonography as microbiology can take more than 24 hours for the earliest definitive diagnosis. The revealing features of Melioidosis on CECT would be a thick-walled abscess with cavitation akin to Swiss cheese or honeycomb pattern, typically seen in the internal organs like lungs, liver and spleen [9,10]. Cluster sign can be used to describe the multiple small abscesses coalescing to form a single large abscess especially in liver [9]. The definitive diagnosis remains to be culture and confirmation with PCR.

The rate of recurrence can be 25% and is often fatal even in people who have been treated for Melioidosis [11]. Hence, the treatment is done in two phases:

1. Intensive phase (for sepsis) - Ceftazidime (2gm, TID) is the drug of choice for 10-14 days. Meropenem (1g, TID) in case of worsening condition, for >four weeks,

2. Eradication phase (prevent relapse) - Cotrimoxazole (800/160mg, BD) for three to six months. Amoxiclav in case of resistance or allergy to cotrimoxazole.

Despite invitro susceptibility, a clinical failure can occur for various reasons like overwhelming sepsis or biofilm production [5]. This calls for newer, quicker diagnostic methods and an increase in awareness of the burden, presentation and management of Melioidosis.

Conclusion

Melioidosis may escape diagnosis due to a lack of awareness of its occurrence. *Burkholderia* should be considered in case of Gram-negative bacteria which is non-fermentative, amoxicillin-clavulanate sensitive and polymyxin resistant. Prompt treatment with ceftazidime or meropenem can reduce mortality.

Conflicts of interest

None

Funding

None

Acknowlegments

Vandana K E (Professor and HOD, KMC Manipal), Dr. Gurlal Singh (M. Ch 1st year SGE, SVIMS), and Dr. M Harsha Choudhary (DM ID, KMC Manipal).

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