Burkholderia pseudomallei, the etiological agent of melioidosis, also known as Whitmore’s disease takes its name after the discoverer, Alfred Whitmore. It is a Gram-negative bacillus displaying a safety pin appearance (bipolar staining) under the light microscope, resides in the soil, and spreads by inoculation, inhalation, and ingestion; therefore, agriculture, rainfall, and paddy fields are responsible for the transmission of the bacilli from the soil [1]. It was originally found to be endemic in North Australia and Southeast Asia [2]. The incidence was found to be 5.8 cases/100,000 native Australians. Although cases have been reported from several parts of India, only a few centers have successfully identified the bacterium [1].

Risk factors for contracting the disease includes diabetes mellitus, thalassemia, renal disease and chronic granulomatous diseases attributable to the neutrophil function defects. It is rightly named as the “Vietnamese time bomb” for its sporadic presentation after years of latency. Melioidosis, known as the great mimicker due to the lack of pathognomonic features, presents with fever, pneumonia, acute septicemia, and abscesses in various internal organs. Melioidosis continues to pose a threat to the clinicians despite not much drug resistance having been reported so far, probably due to the lack of specific symptoms and availability of rapid diagnostic test kits and a prolonged course of antibiotic treatment, wherein compliance to therapy becomes a challenge.

Melioidosis is considered to be a rural illness having a close association with soil and agriculture; however, we present a series of four cases in a tertiary care center of urban Chennai, the diagnosis and management of which depends on strong clinical suspicion and microbiological diagnosis.

CASE SERIES

Case 1

A young man aged 28 years working as a mechanical engineer with a history of episodic asthma for the past 10 years was admitted with a fever of 101°F, dry cough, and breathing difficulty for 1 week. The patient was febrile with tachycardia of 140 beats/min and bilateral wheeze on auscultation. Computed tomography (CT) chest revealed multiple discrete nodules with peripheral ground-glass opacity. Diagnostic bronchoscopy and lavage showed Gram-negative coccobacilli with bipolar staining resembling a safety pin appearance on Gram staining. Blood cultures sent simultaneously also grew a Gram-negative organism. Blood and bronchial cultures were positive for B. pseudomallei.

The patient was treated with I.V ceftazidime and cotrimoxazole. However, his respiratory status worsened over the next 48 h requiring mechanical ventilation and extracorporeal membrane oxygenation therapy (ECMO). By day 8, he gradually recovered and was weaned off ECMO and subsequently off the ventilator. He was discharged after 30 days of the hospital stay and advised to continue antibiotics at home. His follow-up CT chest after 2 months of illness showed complete clearance.

Case 2

A 55-year-old female with a history of episodic asthma for 25 years was admitted with a fever of 102°F, progressive breathlessness, cough, and chest discomfort of short duration. She was found to be febrile with tachycardia, tachypnea,
and bilateral wheeze on auscultation. Here also, the CT chest revealed multiple nodules with multifocal consolidation in both the lungs. Blood and respiratory samples were sent for microbiological examination. Although the Gram stain did not show the presence of any significant bacteria, the patient was started on the treatment for melioidosis with IV ceftazidime and oral cotrimoxazole based on the radiological examination and a strong clinical suspicion.

However, the next day, the culture plates showed growth of tiny colonies of a Gram-negative organism which was lactose non-fermenting with a pink rugose metallic sheen on MacConkey agar. Oxidase test performed was positive and it turned out to be *B. pseudomallei* on identification by VITEK 2 Compact. Blood cultures also flagged positive with the same bacteria. The patient recovered well after the initiation of therapy and was discharged after 18 days of hospitalization with the advice to continue treatment at home. Her CT chest showed complete clearance on follow-up.

**Case 3**

A 53-year-old male with a history of diabetes, systemic hypertension, and bronchial asthma for the 10 years was admitted with a short history of fever of 102°F and breathing difficulty for 3 days. He was febrile and severely hypoxic on admission with tachycardia and tachypnea. Chest X-ray and CT chest showed extensive bilateral consolidation with effusion. Based on this, a provisional diagnosis of fulminant pneumonia was made. Blood and respiratory samples were sent to the microbiology laboratory. In spite of the treatment, his hemodynamic status worsened and he developed acute respiratory distress syndrome with progressive organ failure which culminated in a cardiac arrest. After 24 h, his blood and respiratory samples showed the growth of *B. pseudomallei*.

**Case 4**

A 70-year-old male with diabetes for 30 years presented with a short history of fever of 101°F, cough, and breathing difficulty for 4–5 days. His CT chest showed multifocal consolidation with cavitation in both the lungs. The patient developed worsening of hemodynamic status requiring mechanical ventilation, however, he could not be revived. Blood culture showed the growth of *B. pseudomallei* after 24 h of incubation.

**DISCUSSION**

Melioidosis, an infectious disease can present as acute localized, pulmonary, acute septicemic or chronic suppurative infection, particularly after years of latent infection ranging from 2 to several years. The disease is known to occur in patients with comorbid conditions, especially diabetic; however, stress, immune status, and environmental factors could also be responsible for provoking reactivation of the latent pathogen [3]. Recovery of *B. pseudomallei* from any clinical sample be it blood, urine, sputum, or pus, is considered significant. They slowly grow on standard laboratory media usually after 24–48 h and appear as dry wrinkled colonies (Fig. 1), morphologically similar to *Pseudomonas stutzeri* or aerobic spore-forming bacilli which may be easily dismissed as a laboratory contaminant in non-endemic regions.

With a high risk of aerosol transmission during laboratory bench work, it is advisable to use biosafety hood and not to sniff the culture plates or process the cultures further, once *B. pseudomallei* is suspected. Demonstration of Gram-negative bipolar stained bacilli (Fig. 2), with dry wrinkled, oxidase-positive colonies that are resistant to gentamicin and colistin and susceptible to amoxicillin-clavulanate, is useful for the confirmation of the isolate as *B. pseudomallei* [4].

All the four isolates were susceptible to ceftazidime, cotrimoxazole, doxycycline, and meropenem. The first two patients in our study did not have any associated comorbidities other than episodic asthma, whereas the third and the fourth were diabetics which could be the reason for the rapid progression of the disease, despite treatment being initiated immediately on clinical suspicion without waiting for laboratory confirmation. In a study conducted by Alsaif *et al.*, it was noted that the lung was most commonly affected in melioidosis with pneumonia as the most common presentation both clinically and radiologically. This was very much similar to our patients as they classically presented with diffuse nodular infiltration and pneumonic consolidation on CT [5] (Fig. 3). The presentation and CT chest picture raised suspicion of pneumonia and septicemic plague which were the differential diagnosis in the cases.
Spread from the lungs or skin gives rise to septicemic forms of melioidosis which was proved by the blood culture positivity of the bacilli in these four patients. It was found that the time to blood culture positivity is directly proportional to the bacterial load and correlation with mortality as 73.7% of the patients with blood cultures positive within 24 h died compared to 41% of those with time to positivity over 24 h [6]. The ideal time for positive blood cultures range was 22–24 h on average for all the four patients in our study. In the first two cases, bacteremia cleared within 5 days of initial positivity.

Treatment is long drawn which consists of an intensive phase of 2 weeks of IV ceftazidime 50 mg/kg 8th h/imipenem/meropenem 25 mg/kg 8th hourly followed by oral cotrimoxazole 8 mg/kg/day for 3 months as maintenance dosing [7]. In spite of timely intervention, the management of melioidosis remains a challenge due to the severe complications associated with septicemia and the high mortality rates. A review by Mukhopadhyay et al. mentions the isolation of the Whitmore’s bacilli from the environment in Tamil Nadu and Kerala which makes India an endemic region for this mysterious bug though the extent of distribution in the country remains unknown [1].

Patients traveling to endemic areas must follow proper hygienic measures such as the use of safe water for ingestion and waterproof boots to protect from inoculation [8]. It is worthy to note that the patients described here were reportedly residents from the same area in Chennai and had no significant exposure to soil or agriculture. The burden of this neglected killer disease is predicted to be high in India due to the exploding population, high prevalence of diabetes mellitus, lack of diagnostic services, and awareness among health-care providers. A high index of suspicion among clinicians and microbiologists will pave the way for early diagnosis and therapy [9].

CONCLUSION

Melioidosis is a possible emerging disease even in an urban metropolitan city like Chennai, South India. The burden of disease is considerably high in India though statistical evidence is lacking because it is currently not a notifiable disease here. The diagnosis and management depends on the combined expertise of the clinician and microbiologist without which the patient may be inappropriately treated for tuberculosis. As it is known for its association with rainfall and paddy fields, appropriate training of laboratory staff and health-care professionals in the rural regions will bring out the true burden of the disease which will help devise prevention and control policies.

REFERENCES


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