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Case Report

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Melioidosis- Report of Two Cases

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ABSTRACT

Melioidosis which is caused by burkholderia pseudomallei occurs predominantly in Southeast Asia. Cases are now being reported from india as well. It can present with varying clinical manifestations like pneumonia, septicemia, arthritis, abscess etc. Neurologic meliodiosis, though rare can occur in upto 3-4% cases. Here we present two cases of melioidosis from Indian subcontinent, one involving central nervous system causing cerebral abscess and second one involving multiple splenic and liver abscess with bacteremia. First patient with cerebral abscess was managed with surgical debridement with antibiotics and discharged in a stable condition after 15 days while the bacteremic patient developed septic shock with mutiorgan failure and succumbed to death after 12 days of treatment.

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Introduction

Burkholderia pseudomallei are a gram-negative, facultative organism causing the disease melioidosis. Melioidosis is contracted by inoculated soil and water through wounds or inhalation [1]. Though the disease is endemic to areas of Southeast Asia and Australia, there is also increasing cases in Indian subcontinent [2]. Melioidosis has a wide range of clinical presentations, including pulmonary and genitourinary infection, bone and soft tissue infection, severe sepsis, and neurologic Complications. Though neurologic melioidosis comprises 4% of all cases of melioidosis, it has a mortality rate of approximately 25% and survivors have significant morbidity [3]. Fifty-five percent of the cases were bacteremia upon presentation, and about one fifth of all patients developed septic shock, with a fatality rate of 50% [4].

Case Report

Case 1

A 55 year old diabetic presented to our hospital with complaint of fever for 2 weeks and abdominal pain since last 5 days. On evaluation, found to have multiple splenic abscess and urosepsis. On day2 of admission, patient developed shortness of breath and hypotension, for which we have to put on mechanical ventilation and started inotropes. Empirical antibiotics piperacillin tazobactam and teicoplanin was initiated. Gradually due to worsening renal function, patient required two episodes of hemodialysis. Subsequently, the blood culture showed burkholderia pseudo mallei, for which antibiotics were escalated to meropenem. Endotracheal and urine culture were sterile. Gradually patient showed signs of improvement in terms of weaning of inotrope and weaned from ventilator. Gradually renal parameters improved and there was no requirement of hemodialysis. Patient was extubated on day 7 after mechanical ventilation. Day 9 of admission, patient again became drowsy, there was worsening liver function (Cholestatic jaundice). Repeat CT abdomen – showing resolving splenic abscess. Patient was reintubated after 4 days due to worsening sensorium [septic/metabolic encephalopathy], CT brain was done which was normal, repeat blood culture was - sterile, Enotracheal culture showed growth of klebsiella pneumonia, which was sensitive to meropenem and colistin. Hence we have started intravenous colistin along with meropenem as the patient was deteriorating. Gradually patient developed worsening liver function, acute kidney injury, septic shock, lactic acidosis. Patient succumbed to death after 12 days of hospitalization.

Case 2

33 year old known diabetic since last 5 years on oralhypoglycemic agent presented to our hospital with complain of fever for 10 days and headache since last 7 days. On examination, found to have painful firm swelling (2x 3 cm) in the left temporal region of scalp. MRI brain done which showed osteomyelitis parietal bone with subgaleal empyema. Surgical consultation with debridement of scalp abscess involving trans osseous and trans dermal extension was done. Patient was empirically started injection piperacillin tazobactam, metrogyl and vancomycin. Fever was subsided, but patient continued to complain headache. Subsequent pus culture

on third post-operative day showed Burkholderia pseudo mallei, which was sensitive to meropenem and ceftazidime. Antibiotics were escalated to meropenem. Patient was better and discharged to ward on post-operative day 11 with intravenous meropenem for 6 weeks. Then patient was started on maintenance therapy with oral trimethoprim- sulfamethoxazole for 6 months. Patient was being followed up and in a stable condition after maintenance phase.

Discussion

Melioidosis is an infectious disease, caused by a gram negative obligatory aerobic non-spore forming bacillus, Burkholderia pseudomallei. It can cause a variety of clinical presentations, including asymptomatic infection, localized skin ulcers, abscesses, chronic pneumonia and fulminant septic shock. Melioidosis is endemic in northern Australia, Papua New Guinea, Southeast Asia, in most of the Indian subcontinent, and in southern China, Hong Kong, and Taiwan, and it is considered "highly endemic" in northeast Thailand, northern Australia, Singapore, and in parts of Malaysi [5]. Humans are typically infected via percutaneous inoculation, inhalation, and ingestion [6]. The incubation period varies between 1 and 21 days with a mean of 9 days [7]. Intracellular survival and cell-to-cell spread may have contributed to the organism's ability to evade the immune response, causing a persistent infection [8].

Melioidosis can present as Pneumonia the most common clinical manifestation (51%, 278 cases), followed by genitourinary infection (14%), skin infection (13%), bacteremia without evident focus (11%), septic arthritis or osteomyelitis (4%), and neurological melioidosis (meningoencephalitis, myelitis, and cerebral abscesses (3%) [9]. Monton et al reported a case series on CNS meliodiosis where they mentioned that CNS melioidosis can present as encephalomyelitis, brain abscess, isolated meningitis or isolated extra-axial collection. According to them, unlike brain abscess from other causes, presentation with fever is more prevalent in melioidosis brain abscess (74%) [10]. Our case also presented to us only fever and headache without any localisisng symptoms.

Culture remains the gold standard method for the diagnosis of melioidosis .As per CDC guideline, blood, throat, and urine cultures is performed on all patients with suspected melioidosis, regardless of their symptoms. Specimens from localized disease, such as aspirates from abscesses, should also be collected [11].Our first case at initial presentation was abdominal pain and fever, but blood culture was positive for burkholderia pseudomallei , while the second case was confirmed on the basis of positive pus culture.

The risk factors for melioidosis include diabetes mellitus, alcoholism, renal disease and immunosuppression. In all these cases, the poor cell-mediated immune response can cause poor neutrophil function. Suputtamongkol et al.reported in their study that diabetes mellitus was the only factor significantly associated with bacteremic melioidosis and confirms that impairment of host immunity plays a major role in the pathogenesis of melioidosis [12]. In our both cases, patients were diabetic which is a major risk factor for meliodiosis.

As the course of the disease in Melioidosis is prolonged, it usually requires a lengthy course of antimicrobial treatment [13]. Burkholderia pseudomallei are usually resistant to penicillin, ampicillin, aminoglycoside and first & second generation cephalosporin [14]. The main therapeutic options for melioidosis include broad spectrum cephalosporin (ceftazidime), carbapenems, Trimethoprim- sulphamethoxazole and Doxycycline. The treatment in non-neurologic meliodiosis typically consisting of 10 to 14 days of ceftazidime, meropenem, or imipenem intravenously in the intensive phase followed with oral trimethoprim-sulfamethoxazole for 3 to 6 months in the maintenance phase [13]. In our two cases; we have started meropenem as the initial treatment after reaching the diagnosis of meliodiosis. In our first case, after 12 days of treatment, patient succumbed while in second case we continued meropenem for 14 days. Purabi et al reported a case of meliodiosis having pneumonia, leg ulcer and bacteremia where they have found the organism was resistant to ceftazidime and sensitive to carbapenem and doxycline [15]. Also carbapenem having the lowest MICs (Minimum inhibitory concentration) against Burkholderia pseudomallei [16]. Furthermore in a retrospective study done in australia between 1989 to 2013 in ICU patients having severe meliodiosis, mortality decreased from 92 percent in first eight years to 26 percent in last eight years when patients treated with meropenem [17].

In neurologic meliodiosis,ceftazidime and meropenem are the drugs of choice for intensive-phase therapy, while trimethoprim/ sulfamethoxazole is the first-line drug for eradication-phase therapy [18]. Some medications including chloramphenicol and doxycycline were used in intensive-phase therapy in some CNS melioidosis cases; however, they are not effective thus should be avoided. The treatment duration is also a key to success that eight weeks and six months are the minimal duration for intensive- and eradication-phase therapy, respectively [19]. In our case meropenem was given for 6 weeks followed by oral trimethoprim- sulfamethoxazole.

Monitoring of treatment compliance is very important as adherence may be the most important factor in determining recurrence, which is the most serious complication of melioidosis. True recurrences are due to failed eradication rather than new infection. Recurrent melioidosis occurs in 5% to 25% of cases and has a high mortality rate of 25% [20].

Mortality in cases of meliodiosis is usually less if early diagnosis and institution of treatment in suspected cases. In a randomized control trial done by chierakul etal in thialand, there are some independent risk factors for mortality like bacteremia, respiratory failure and renal failure in meliodidosis [21]. In one of our cases, patient had all three factors leading to mortality.

Conclusion

Timely diagnosis of the disease and prompt initiation of treatment play important roles in determining the treatment outcome. Neurologic disease is an uncommon manifestation of melioidosis,a high clinical index of suspicion is therefore essential in early assessment and management of this disease. Outcome in severe melioidosis is good in healthy person, when infection is diagnosed early, early appropriate antibiotics, critical care support whenever required and compliance to treatment.

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