รายงานผู้ป่วย

Melioidosis with erythroderma and meningitis A case report.

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A case of a 52-year-old Thai male patient from Amnat Charoen Province with fever, erythroderma and meningitis which subsequently progressed to septicemia and septic shock is reported. Disseminated septicemic melioidosis was later diagnosed. Despite intensive antimicrobial therapy and critical care management his condition deteriorated and he died 13 days after admission.

Key words: *Melioidosis, Erythroderma, Meningitis.*

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นรินทร์ หิรัญสุทธิกุล, ธีระพงษ์ ตัณฑวิเชียร. เมลิออยโดสิสร่วมกับภาวะผิวหนังแดงและเยื่อหุ้มสมองอักเสบ. จุฬาลงกรณ์เวชสาร 2539 ต.ค.;40(10): 837-43

ได้รายงานผู้ป่วยชายไทย อายุ 52 ปี จากจังหวัดอำนาจเจริญ มาโรงพยาบาลด้วยเรื่องไข้, ผิวหนังแดงและเยื่อหุ้มสมองอักเสบ ต่อมาลุกลามจนเกิดภาวะติดเชื้อในเลือดและภาวะช็อคจากการติดเชื้อ การวินิจฉัยในเวลาต่อมาพบว่าเป็นเมลิออยโดสิสที่มีภาวะติดเชื้อในเลือดชนิดแพร่กระจาย แม้จะได้รับการรักษาด้วยยาปฏิชีวนะและการบริบาลในภาวะวิกฤติอย่างเต็มที่ ผู้ป่วยมีอาการเลวลงและเสียชีวิตหลังเข้าพักรักษาตัวในโรงพยาบาล 13 วัน

Melioidosis is a tropical infectious disease caused by Burkholderia pseudomallei (B. pseudomallei), previously known as Pseudomonas pseudomallei, which is a small, obligatory aerobic, motile, non-spore forming and poorly stained gram-negative bacilli. In humans, melioidosis is transmitted mainly by direct contact with contaminated soil or water through a skin abrasion or wound, or by inhalation of infectious dust particles. In Thailand, B. pseudomallei has been isolated from samples of surface soil and deep fresh water mainly in the northeast and south.[1,2] We report here a case from northeastern Thailand who had a history of a traumatic wound and who later developed disseminated septicemic melioidosis with erythroderma and meningitis.

Case report

A 52 year-old Thai male farmer living in Amnat Charoen Province was admitted to Chulalongkorn Hospital with fever, chills, jaundice and erythrematous rash which he had suffered for one day. One week prior to admission he had experienced a thorn-puncture wound on his left sole. Three days prior to admission his left foot began progressive swelling and there was a purulent discharge from the puncture wound. After incision and drainage of the wound and application of oral doxycycline treatment at a local private clinic, but without clinical improvement, he was transferred to Chulalongkorn Hospital. He had experienced right cervical tuberculous lymphadenitis one year ago and had been treated with isoniazid, rifampicin, ethambuthol and pyrazinamide. After two weeks of this therapy the isoniazid was stopped due to hepatitis but rifampicin and ethambuthol were continued without adverse reactions until his admission.

Physical examination revealed a thin drowsy, febrile middle-aged man with generalized erythroderma. The vital signs included body temperature of 38.7°C, pulse rate of 100 per minute, blood pressure of 130/70 mmHg and respiratory rate of 28 per minute. There was a mild pallor and mildly icteric sclera. A non-tender, firm, left cervical lymph node enlargement of approximately 1.5 cm. diameter was found. Hepatomegaly, 2 cm. below the right costal margin, was also detected. The spleen was not palpable. At the left sole there was a dry, recently incisioned wound without signs of inflammation. A neurological examination revealed that the neck was stiff in all directions. Other physical examinations were unremarkable.

The hematological studies upon admission showed hemoglobin of 11 gm/dl, hematocrit of 33.1%, WBC of 17,000/cu.mm. with 80% neutrophil, 11% lymphocyte, 4% monocyte, 3% eosinophil and 2% basophil. The platelet count was 57,900/cu.mm. The prothrombin time was 27.3 sec. (control 11.8 sec) and the partial thromboplastin time was 47.8 sec. (control 30.8 sec). The blood chemical studies revealed total bilirubin of 3.9 mg/dl, direct bilirubin 2.7 mg/dl, aspartate aminotransferase 116 u/l, alanine amino transferase 87 u/l, alkaline phosphatase 402 u/l, albumin 2.1 gm/dl, globulin 3.4 gm/dl, sodium 127 mEq/l, potassium 4 mEq/l, chloride 99

mEq/l and carbon dioxide 16 mEq/l. A chest X-ray showed unremarkable findings.

Community-acquired septicemia with toxic shock syndrome was suspected. A lumbar puncture was performed and the CSF finding revealed an opened pressure of 16 cm. H_2O, closed pressure of 10 cm. H_2O, protein 149 mg/dl, sugar 20 mg/dl, white blood cells 265 per mm^3 with mononuclear cells 94% and neutrophils 6%. Gram's stain, AFB stain and Indian ink stain did not find any organisms. Tuberculous meningitis was the second provisional diagnosis. After blood cultures were performed he was empirically treated with 1 gram cefotaxime intravenously every 4 hours and anti-tuberculous drugs, including rifampicin (450 mg/day), ethambutol (800 mg/day), pyrazinamide (1000 mg/day) orally and streptomycin (750 mg/day) intramuscularly.

On the third day of hospitalization his condition deteriorated with high fever, drowsiness and respiratory failure. Follow-up chest x-rays showed diffuse patchy infiltration invoving both lungs. Staphy-lococcus aureus septicemia and disseminated septicemic meliodosis were included in the differential diagnosis. Accordingly, the antibiotics were switched to 2 grams cloxacillin intravenously every 6 hours and 2 grams ceftazidime intravenously every 8 hours. Mechanical ventilation was also given.

On the fifth day of hospitaliation several pustules on the left thigh were detected and a gram stain of the pus revealed small gram-negative rods. On the same day, it was reported that blood culture and spinal fluid culture grew B. pseudomallei. Disseminated septicemic melioidosis with meningitis was thus microbiologically documented. Cotrimoxazole 160 mg (of trimethoprim) intravenously every 8 hours was added. However, he deteriorated with refractory septic shock, multiple organ failure and expired on the thirteenth day of admission.

Discussion

The clinical presentations of disseminated septicemic melioidosis in this patient were fever and generalized erythroderma mimicking toxic shock syndrome caused by Staphylococcus aureus or group A Streptococci. Generalized erythroderma is an unusual manifestation of melioidosis. Bonnma P. reported two cases of melioidosis with clinical manifestations of fever, diarrhea, erythroderma and shock which were initially considered and treated as toxic shock syndrome due to Staphylococcus aureus. But blood cultures later revealed to be B. pseudomallei.[3,4] The pathogenesis of erythroderma in meliodosis is still not understood, although in mice it has been demonstrated that B. pseudomallei can produce two exotoxins; lethal toxin and dermonecrotic toxin.[5,6] Whether these exotoxins can cause erythroderma or other clinical findings in humans needs to be confirmed by further studies.

In our case, meningitis caused by B. pseudomallei was also detected. Interestingly, the cerebrospinal fluid (CSF) analysis revealed mononuclear pleocytosis with hypoglycorrhachia which is similar to findings in tuberculous meningitis.

CNS involvement in melioidosis is infrequent. Reports in Thailand reveal CNS involvement to be 1-6% of all manifestations,[7-9] and most of the cases described have been associated with brain abscess, focal cerebritis and meningitis. Clinical settings are not specific and cannot be distinguished from other pyogenic bacterial or tuberculous infections of the CNS.[9-13]

Sukpranee M. and colleagues reported 141 cases of melioidosis and they found five cases of meningitis (3.5%).[8] CSF analysis showed mononuclear pleocytosis in all cases but there were neither reports of CSF culture nor any explanation of this finding.

Marion L. and colleagues found seven cases of neurological melioidosis in the northern territory of Australia.[14] They found meningitis in all cases, however, CSF culture grew B. pseudomalei in only one case with a purulent profile. Three cases showed mononuclear pleocytosis with normoglycorrhachia, two cases showed polymorphonuclear pleocytosis (purulent profile) and one case was initially polmorphonuclear pleocytosis followed by mononuclear pleocytosis with normoglycorrhachia. CSF analysis was not done in one case. CT or MRI was done in 5 of 7 cases but revealed no focus of infection in the CNS. One case had encephalitis consistent with a toxin-induced etiology and was virtually identical to that described in diphtheric infections.[15] Therefore, they postulated that neurologic melioidosis, apart from direct bacterial infection of the CNS, could be exotoxin-induced with profound neurological disease occurring in the absence of apparent direct infection of the CNS. In our cases, despite the isolation of B. pseudomallei from CSF, the CSF findings were not typical of purulent meningitis. We can only speculate that it might possibly be affected by doxycycline treatment prior to hospitalization.

In our patient, the diagnosis of disseminated septicemic melioidosis was based on a rapidly progressing course of septicemia and community-acquired pneumonia plus epidemiologic clues. However the initial diagnosis was misleading due to clinical findings of erythroderma and meningitis. In spite of effective antimicrobial therapy and aggressive respiratory and hemodynamic supports, the patient still deteriorated.

Disseminated septicemic melioidosis and meningitis have very high morbidity and mortality rates. The mortality rate of disseminated septicemic melioidosis is over 80%, and most of the cases develop rapidly progressing septic shock. With the introduction of ceftazidime, the mortality rate has declined to about 40%.[16,17] Therefore, this group of patient needs a very urgent effective antimicrobial therapy (such as high dosages of ceftazidime) as well as aggressive critical care in order to reduce the morbidity and mortality.

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References

1. Patamasucon P. National workshop on Melioidosis organized by the Infectious Disease Association of Thailand at Ambassador Hotel, Bangkok, Thailand, 23-24 November, 1985. Bangkok: Infectious Disease Association of Thailand, 1985.
2. Leelarasamee A, Punyakuypta S. Melioidosis : Epidemiology with Thai Experience. In: Punyagupta S, Sirisanthana T, Satapatayavong B,eds. National Workshop on Melioidosis. Bangkok : Bangkok Medical Publisher, 1989:238-52
3. Boonma P, Srisukh V. Myocarditis and myositis in melioidosis. J Infect Dis Antimicrob Agents 1993 Sep-Dec;10(3):149-53
4. Boonma P, Chetchotisakd P. Interesting infectious disease cases presentation: (No:22); fever, diarrhoea, erythroderma and shock. J Infect Dis Antimicrob Agents 1989 Apr-Jun;6(2):89-92
5. Heckly RJ. Differentiation of exotoxin and other biologically active substance in Pseudomonas pseudomallei filtrates. J Bacteriol 1964 Dec;88(6):1730-6
6. Heckly RJ. Toxins of Pseudomonas. In: Jeliaszewicz J, Wadstrom T, eds. Bacterial Toxin and Cell Membrane.London : Academic Press, 1978:473-91
7. Chaowagul V, Saipan P, Naiyakowit P, Thirawattanasuk N. Melioidosis: a 3-year retrospective study of 169 patients at Ubon Hospital. In: Punyagupta S, Sirisanthana T, Stapatayavong B, eds. Melioidosis. Bangkok: Bangkok Medical Publisher, 1989:22-33
8. Sookpranee M, Boonma P, Bhuripanyo K, Nuntirooj K, eds. Melioidosis at Srinagarind Hospital. In: Punyagupta S, Sirisanthana T, Stapatayavong B, eds. Melioidosis. Bangkok : Bangkok Medical Publisher, 1989:34-47
9. Punyagupta S. Melioidosis: Review of 686 cases and presentation of a new clinical classification. In: Punagupta S, Sirisanthana T, Stapatayavong B,eds. Melioidosis, Bangkok: Bangkok Medical Publisher, 1989:217-29
10. Brundage WG,Thuss GJ Jr, Walden DC. Four fatal cases of melioidosis in U.S. soldiers in Vietuam. Bacteriologicand pathologic characteristics. Am J Trop Med Hyg 1968 Mar;17(2):183-91
11. Pit S, Chea FKC, Jamal F. Melioidosis with brain abscess. Postgrad Med J 1988 Feb;64(748):140-2
12. Tremonti LP, Dart LH. Focal encephalitis due to Pseudomonas pseudomallei. JAMA 1971 Jan 4;215(1):112-3
13. Visudhiphan P, Chiemchanya S, Dheandhanoo D. Central nervous systemmelioidosis in children. Pediatr Infect Dis J 1990 Sep; 9(9):658-61
14. Marion ML 2d, Currie BJ, Howard DM, Tierney A, Watson A, Anstey NM,

Philpott J, Asche V, Withnall K. Neurological Melioidosis : seven cases from the Northern Territory of Australia. Clin Infect Dis 1992 Jul;15(1):163-9

15. Weil A. Textbook of neuropathology. 2 nd ed. New York: Grune & Strattion, 1945:187-209

16. White NJ, Dance DAB, Chaowagul W, Wattanagoon Y, Wuthiekanum V, Pitakwatchara N. Halvingof mortality of severe melioidosis by ceftazidime. Lancet 1989 Sep 23;2(8665):697-701

17. Sookpranee M, Boonma P, Susaengrat W, Bhuripanyo K, Punyagupta S. Multicenter prospective randomized trial comparing ceftazidime plus co-trimoxazole with chloramphenicol plus doxycycline and co-trimoxazole for treatment of severe melioidosis. Antimicrob Agents Chemother 1992 Jan;36(1):158-62