

Case Reports

Disseminated Melioidosis

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Melioidosis is endemic to several Southeast Asian countries(1) but it has only rarely been reported from India(2-4). We report the clinical, microbiological and histopathological features of a child with disseminated melioidosis, reported earlier as a preliminary communication(5).

Case Report

A 9-year-old boy from Thrissur in Kerala state presented with a febrile illness of 3 months duration. He was diagnosed to have insulin dependent diabetes mellitus (IDDM) in April 1994. Four months later he developed fever and a right anterior cervical lymph node swelling. An excision biopsy of the lymph node showed granulomatous lesions suggestive of tuberculosis. Hence, anti-tuberculosis treatment was started though the fever had subsided spontaneously following the biopsy. However, when the fever recurred a month later, abdominal ultrasonography revealed

multiple hypoechoic lesions in the spleen and the bone marrow biopsy was reported non-diagnostic. Three weeks after the recurrence of fever, the child was referred to this hospital.

On examination, he was febrile, looked ill and was pale. He had no cutaneous lesions, significant lymphadenopathy or any other abnormality. Laboratory investigations revealed hemoglobin concentration of 8 g/dl, white blood cell count of 9000/cu mm with band forms 2%, neutrophils 56% and lymphocytes 42%, platelet count of 410,000/cu mm and ESR of 100 mm/hr. His diabetic control was poor with blood sugar values fluctuating greatly; most readings were between 250 to 400 mg/dl. The Mantoux test was negative and the chest roentgenogram was normal. An abdominal ultrasound examination showed hepato-splenomegaly with multiple hypoechoic areas in the spleen (*Fig. 1*). Of the three blood cultures performed, two were sterile while contaminating bacteria (coagulase negative staphylococcus and a non-fermenting, non-motile, gram negative bacterium) were isolated from the third. Urine and bone marrow were sterile on culture. Echocardiogram did not show vegetations on any of the heart valves.

The lymph node biopsy and bone marrow slides prepared at the referring hospital were reviewed. They showed epithelioid granulomas suggestive of mycobacterial infection. The patient was restarted on treatment with isoniazid, rifampicin, pyrazinamide and streptomycin. However, he remained febrile and an abdominal ultrasound examination repeated 10 days later revealed new hypoechoic areas in the liver. Ultrasound guided aspiration of one of the

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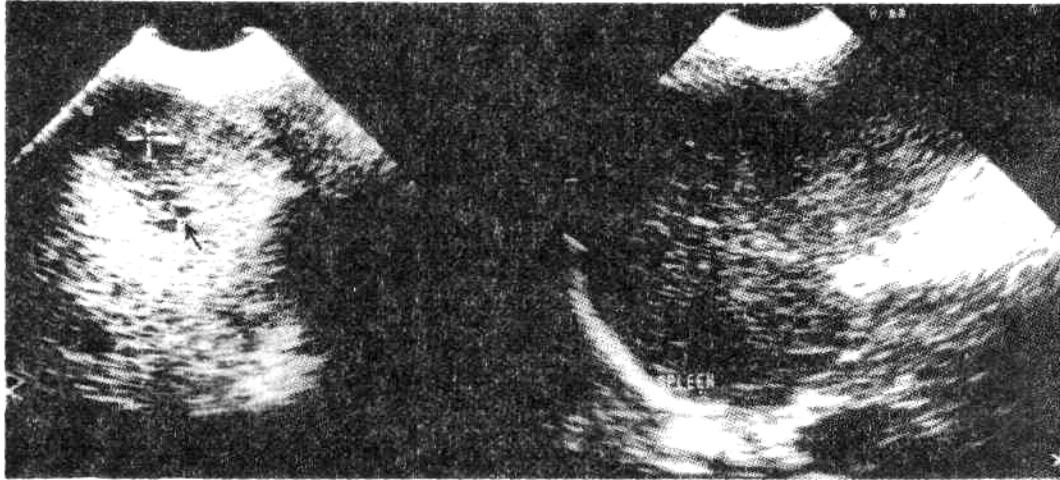


Fig. 1. Ultrasound picture showing multiple hypoechoic lesions in the spleen (left, marked with arrow) and the follow up ultrasound done after 3 months of treatment showing absence of the lesions (right).

abscesses in the liver, yielded thick, white, cheesy pus, smears from which showed polymorphs but no bacteria, fungi or acid fast bacilli. A non-fermenting Gram negative (NFGN) bacillus, presumed to be a contaminant, was isolated by culturing this fluid. An open liver biopsy was performed, which showed areas of stellate necrosis containing many neutrophils and bounded by lymphocytes, histiocytes and epithelioid cells. Occasional plasma cells and a few ill-formed giant cells were also seen. Fibro-blastic proliferation was present at the periphery. Since the histology was not typical of tuberculosis, the possibility of melioidosis was suggested.

Motile NFGN bacilli were again isolated on culture from the liver tissue as well as from the pus aspirated at surgery from one liver abscess. On further speciation all the 3 isolates were identified as *Burkholderia pseudomallei* (*Pseudomonas pseudomallei*) based on motility, positive tests for oxidase, gelatinase and arginine dihydrolase; oxidative utilization of glucose and lactose; ability to grow at 42°C; and resistance to gentamicin and

polymyxin B (300 units)(6). The organism was sensitive to ceftazidime, cotrimoxazole and tetracycline and resistant to penicillin, chloramphenicol, cefotaxime, gentamicin, amikacin and ciprofloxacin. The stained smears showed bipolar staining of the bacilli, usually described as "safety-pin" appearance.

The patient was treated with intravenous ceftazidime and oral cotrimoxazole. The fever defervesced gradually and he became afebrile three weeks later. The diabetes was brought under control after antibiotic therapy was commenced. Parenteral ceftazidime was stopped after four weeks and oral cotrimoxazole was recommended for 5 more months. On review three months later he had no fever and had gained weight. A repeat ultrasound examination of the abdomen showed no abscesses in the liver, spleen or kidney (Fig. 1). He was continuing to do well six months after discharge.

Discussion

This patient presented with many of the classical features described with chronic disseminated melioidosis including IDDM which is a well recognized predisposing factor, persistent fever and multiple

abscesses in the liver and spleen(1). Yet, in this child melioidosis was not suspected, because of our unfamiliarity with this condition and the belief that melioidosis was not prevalent in southern India. Again, in the microbiology laboratory, the diagnosis was missed initially because NFGN bacilli are not often speciated since many of them turn out to be contaminants.

B. pseudomallei is a saprophyte soil organism, found in many regions of South-East Asia(1). In Thailand it is a major cause of community acquired septicemia and pyogenic liver abscesses(7,8). There have been a few case reports from our country, mainly from central India (2,4). Infection with this organism may be subclinical, focal or disseminated and the course self-limiting, acute fulminant or chronic(1). It is not uncommon for the disease to manifest itself after years of latency(1).

Chronic infection with *B. pseudomallei* produces granulomatous inflammation with epithelioid cells, Langhans giant cells and a central area of necrosis which resembles caseation(9). This makes histopathological differentiation from tuberculosis very difficult as in this patient. However, in an unusual clinical setting, the presence of coexistent acute inflammation and a granulomatous reaction with necrosis should raise the possibility of this condition.

This report emphasizes that NFGN bacilli are not always contaminants, specially so when isolated from a normally sterile site or when isolated persistently from one or more sites. In such cases, consultation with the microbiologist and further speciation of the organism is required. Experience from this case contributed to correct diagnosis being made promptly in two subsequent

cases in our hospital. Both were adults and had diabetes mellitus; one of them also had chronic renal failure (unpublished).

The treatment of choice in patients with disseminated melioidosis is parenteral ceftazidime(10). Since relapse with melioidosis is common, treatment with an oral antibiotic such as doxycycline or cotrimoxazole should be continued for at least 2 months and the patient followed up to ensure that remission is maintained. We suspect that the prevalence of melioidosis in India may be higher and more widespread than previously recognized. Increased alertness of physicians to the possibility of this infection is therefore recommended.

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