PSEUDOMONAS PSEUDOMALLEI: 1. INFECTION IN THAILAND

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INTRODUCTION

Melioidosis is an infectious disease caused by the gram negative bacillus, *Pseudomonas pseudomallei*. Whitmore and Krishnaswami (1912) recorded postmortem observations in a subject in Rangoon, the first reported case of melioidosis, and their report was published along with a description of the etiologic agent and the proposed name of *Bacillus pseudomallei*. The organisms have been isolated from soil, stagnant water and rice paddies which are widely found throughout Vietnam, Malaysia, other parts of Southeast Asia and other tropical areas (Chambon, 1955; Ellison *et al.*, 1969; Strauss *et al.*, 1969). The disease is known to occur in a rather limited area in Southeast Asia including Burma, Ceylon, Indochina, Malaysia, Singapore, Saigon, Thailand and Guam (Merick *et al.*, 1946; Robin *et al.*, 1963). The first case of melioidosis in Thai people was reported by Chittvej *et al.*, in 1955. Recently two cases were reported from the Children Hospital, Bangkok (Lampe *et al.*, 1974).

The purpose of this paper is to report 4 more cases and to bring to attention the significant aspects of this disease which is suspected to occur quite commonly in Thailand.

CASE HISTORIES

During the period of March through November 1973, four cases of melioidosis, proven by cultures of *Pseudomonas pseudomallei*, were diagnosed at Ramathibodi Hospital, Bangkok.

Case I was a 57-year-old Thai army soldier, a known diabetic patient, who suffered from 2nd degree burns of the arm and a compound fracture of the left humerus after a helicopter crash. He developed septicaemia 5 days after the accident. *Pseudomonas pseudomallei* was isolated from his blood continously for two weeks. The patient had a stormy course of septicaemia with septic shock but recovered after vigorous treatment with massive doses of chloramphenicol, tetracycline, kanamycin and gentamicin. The melioidosis agglutinating antibody was 1:8 and the fluorescent antibody was 1:320.

Case II was a 56-year old Chinese woman, a known case of diabetes mellitus, who was admitted with a history of high fever for 2 weeks and pain in the left hip for one week. She had osteomyelitis of the left shoulder which was apparently cured with methicillin about one year before the present illness. Following admission she was diagnosed as having septicaemia, pneumonitis of left upper lobe and possible disseminated infection of the left hip, brain and liver. There was also a residual sign of bony destruction of the proximal left humerus. She was treated initially with kanamycin without any improvement. The blood culture subsequently became positive for *Pseudomonas pseudomallei* from three consecutive samples. The treatment was switched to tetracycline and chloramphenicol. She made a rapid response only to die later with *Klebsiella* and *Pseudomonas aeruginosa* septicaemia. The antibody titer was not performed.

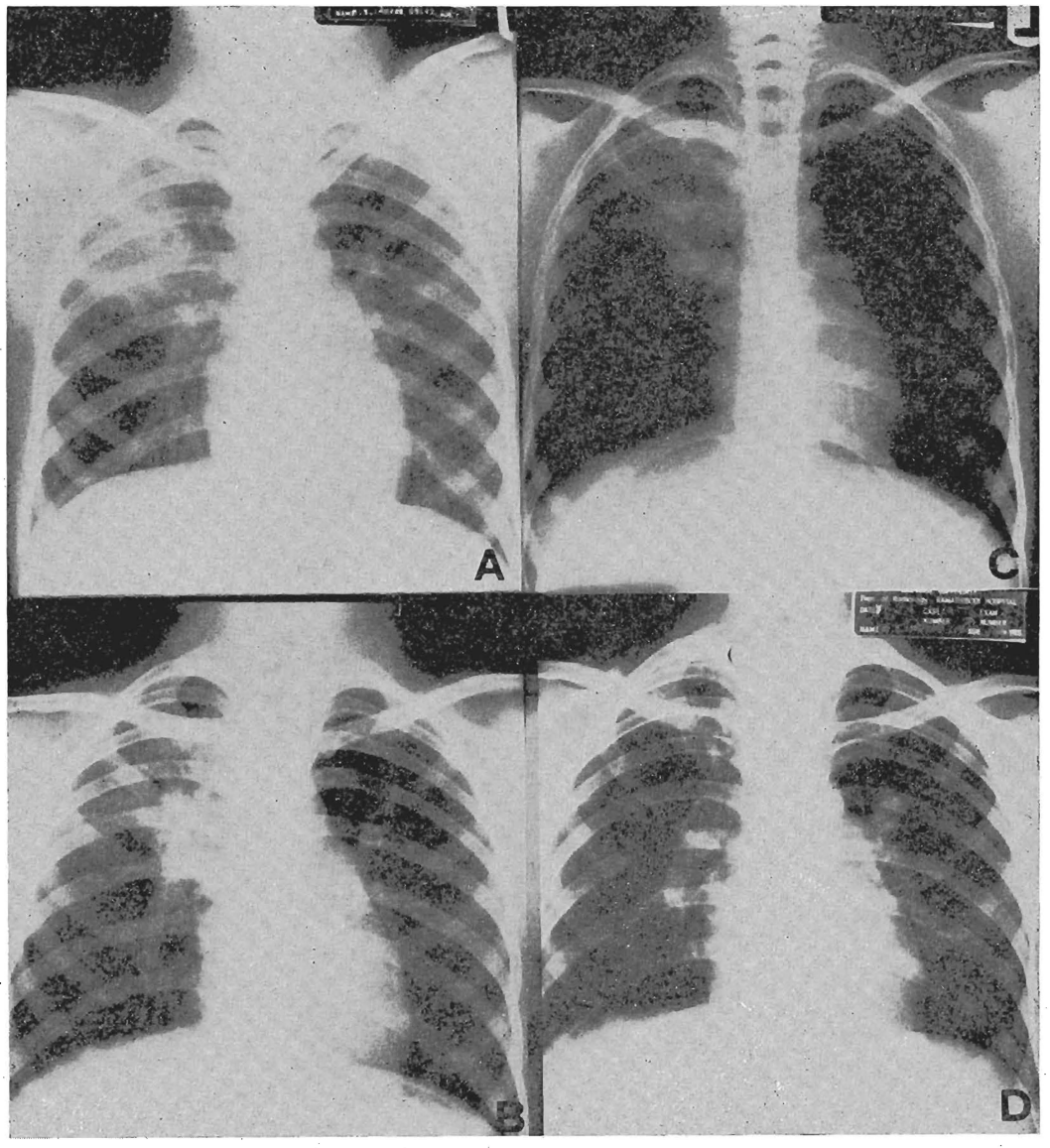

Fig. 1 — Chest PA: A) Right upper lobe infiltration. B) Improvement of right upper lobe infiltration. C) Further resolution of right upper lobe pneumonia. D) Clearing of right upper lobe pneumonia.

Case III was a 14-year-old Thai boy who was admitted for right upper lobe pneumonia (Fig. 1A). He had chest pain at the right costal margin 7 months prior to the illness. He was treated with penicillin for possible bacterial pneumonia. He made an initial improvement both clinically and radiologically (Fig. 1B). However, radiological findings 6 weeks later showed persistent "right upper lobe infiltration". In addition,

the tuberculin test became positive which led to the diagnosis of pulmonary tuberculosis and treatment with INH, PAS and streptomycin. He responded well during the first month (Fig. 1C). Unfortunately he did not return to the clinic for follow-up until 6 months later when he was readmitted in a moribund state with marked abdominal distension and severe dehydration. The positive laboratory findings included WBC 15,200 c.mm, polymorphonuclear 96%. He had proteinuria of 2 + and WBC 1-2 cells/hpf. Blood cultures were negative.

His chest X-ray showed clearing of the lesions of the right upper lobe (Fig. 1D). The initial diagnosis was peritonitis, most likely of tuberculous origin, and the antituberculous drug was restarted. His abdominal distension increased, and an abdominal tap on the following day yielded cloudy, straw-coloured fluid with numerous polymorphonuclear cells. On the third day, the abdominal distension still increased, and the possibility of secondary peritonitis led to the decision to perform exploratory laporatomy.

At surgery, generalized depositions of small whitish nodules were found on both parietal and visceral peritoneal surfaces, on the liver, and on the small and large intestine, and 700 ml. of ascitic fluid were aspirated. The patient died the day following surgery. Autopsy consent was denied. *Pseudomonas pseudomallei* was isolated in pure culture from ascitic fluid and omentum. The melioidosis fluorescent antibody titer was 1 : 320 and the agglutinating antibody was 1 : 160.

Case IV was a 41-year-old Thai male with a previous history of HbE disease following splenectomy. He developed epididymo-orchitis during an acute episode of haemolysis and congestive heart failure one year after splenectomy. He did not respond to Ampicillin and the infection progressed to an abscess localized in the left testis. The abscess was drained and the pus yielded a pure culture of *Pseudomonas pseudomallei.* There was no rise in agglutinating or fluorescent antibodies to *Pseudomonas pseudomallei.* The patient made a rapid recovery after treatment with tetracycline.

DISCUSSION

The clinical pictures of four patients described here are good examples of the wide spectrum of the disease. The first case presented a picture of acute septicaemia with septic shock. The source of infection was most likely from soil stirred up during the explosion of the helicopter and entering through skin abrasions, one of the common, sites of entrance of this organism (Thin *et al.*, 1970). *Pseudomonas pseudomallei* is known to contain both heat labile and heat stable toxin. The heat labile component is necrotoxic and the heat stable component possesses classical endotoxic activity (Nigg *et al.*, 1955; Colling *et al.*, 1958; Heckly and Nigg, 1958; Rapaport *et al.*, 1961). Furthermore, experimental studies in mice showed evidence of intraglomerular deposition of fibrinoid material resembling those of a generalized Schwartzman reaction. The rapid death of the animal without adequate pathology suggested the cause of death to be due to toxaemia (Dannenberg and Scott, 1958). The clinical shock in this case was most likely endotoxic in origin.

The second case had subacute form of the disease with acute flare-up and a fatal outcome. The patient had osteomyelitis of the shoulder which remained in a quiet stage for about one year before the disease flare-up. A case of chronic melioidosis of the lung and kidney for 19 years has been reported from Sydney (Newland, 1969). Both case I and case II had diabetes mellitus which is

an underlying disease known to be a predisposing factor in melioidosis (Remington, 1962).

The third case presented a picture of pneumonitis mimicking pulmonary tuberculosis which spread to systemic infection. This form of melioidosis is common, (Murray *et al.*, 1967) and it is quite a problem in management particularly in the areas where tuberculosis is very common. One of the most perplexing problems about melioidosis is its ability to exist in an inactive state and flare up at a later time, expecially after stress or trauma. The fourth case represented a localized form of melioidosis which was benign, and the course of the disease was short since the patient received proper treatment.

The clinical picture in melioidosis is not diagnostic nor are the radiographic appearances specific. Furthermore in an endemic area of the disease such as Thailand there is high percentage of healthy people with antibody to the organisms (Nigg, 1963). Therefore, serology is of little value in diagnosing the disease. Isolation of the organisms is an important clue for the diagnosis. This is usually easy in the acute form and the organism is readily isolated from the blood, exudates and tissues of various infected organs.

Most strains of *Pseudomonas pseudomallei* are sensitive to chloramphenicol and tetracycline and resistant to colymycin (Eickhoff *et al.*, 1970). Clinically, the majority of cases likewise respond to chloramphenicol and tetracycline and both antibiotics are recommended particularly in severe cases. In septicaemic and pulmonary forms with cavities, vigorous treatment is necessary and large doses of chloramphenicol and tetracycline are recommended. The duration of treatment should be prolonged at least 30 days. Short courses of antibiotics are dangerous because relapse with production of resistant organisms may occur (McDowell and Varney, 1947). In chronic cases which resist medical treatment, particularly in cases with persistent high antibody titer, surgical removal of the infected organ is recommended (Zajtchuk *et al.*, 1973).

SUMMARY

Four cases of melioidosis admitted to Ramathibodi Hospital, Bangkok, during March through November, 1973, were reported. One case died of acute septicaemia, one died of peritonitis following subacute pulmonary infection, one case recovered from persistent septicaemia and one recovered from acute testicular abscess. *Pseudomonas pseudomallei* was isolated in pure culture from blood, peritoneal fluid, omentum and pus aspirated from testes. The organisms were sensitive to chloramphenicol and tetracycline but resistant to colimycin. Only three patients were treated with tetracycline and chloramphenicol with good results.

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