Cautionary Tale

Reactivation of latent melioidosis

A.B. Johnson and N. Ali

Norfolk and Norwich Hospital, Norwich, UK.

Summary: Reports of melioidosis in residents of European countries are rare. We describe a case of reactivation of latent melioidosis in a United Kingdom resident. The case demonstrates the lack of clinical response to chemotherapy despite proven *in vitro* sensitivity of the organism to the drugs used. It is important to consider melioidosis as a cause of septicæmic illness in patients who have travelled to, or been resident in South-East Asia.

Introduction

Melioidosis is an uncommon infectious disease, caused by the Gram-negative organism *Pseudomonas pseudomallei*. The main endemic areas are South-East Asia and northern Australia, although sporadic cases have been reported from countries located between latitudes 20° north and 20° south. The organism is found in soil and surface water, and is presumed to enter the body by inhalation or in association with trauma.¹ Many cases have been reported in servicemen on duty in South-East Asia, but reactivation of latent disease can also occur many years after leaving the endemic area.^{2,3} We report such a case in a United Kingdom resident.

Case report

Over a period of a month a 48 year old man became progressively unwell with fever, malaise and weight loss. Two days before admission he developed a painful swollen right elbow. Apart from longstanding hypertension treated with methyldopa and diuretics, he had been fit and well prior to admission. He was an ex-American marine and had served in South-East Asia 12 years previously during the Vietnam war without being wounded.

On examination he was febrile, 38.4°C, and unwell. He was overweight and had a subcutaneous abscess over his left deltoid muscle and a painful inflamed right elbow. He had a regular tachycardia and was normotensive. The liver and spleen were enlarged 3 cm below the costal margin and were non-tender.

Admission investigations revealed a white cell count of $10.2 \times 10^9/l$, with a normal differential,

and an ESR of 82 mm/h. Serum glucose was 14.2 mmol/l, aspartate transaminase 47 IU/l, and alanine transaminase 52 IU/l. A chest X-ray was normal. Ultrasound examination of the abdomen confirmed an enlarged liver and spleen but no other abnormalities were demonstrated.

Intravenous benzylpenicillin and flucloxacillin were commenced after aspiration of the right elbow and the subcutaneous abscess. Blood glucose was controlled with soluble insulin. The antibiotics were changed to amoxycillin-clavulanic acid (Augmentin), gentamicin and metronidazole when Gram-negative rods were isolated and sensitivities were available. However, on the sixth day of admission, a septic arthritis of the right knee and more subcutaneous abscesses developed. On the eighth day the organism was identified as *Pseudomonas pseudomallei* and therapy was further changed to chloramphenicol 12 grams, tetracycline 4 grams, and cotrimoxazole 1.92 grams daily. He became afebrile within 48 hours.

On the fourteenth day he had a large haematemesis and required transfusion. Gastroscopy demonstrated a bleeding point high on the junction of the greater and lesser curves of the stomach. Due to persistent bleeding he required surgery. At laparotomy a large abscess was found in the pedicle of the spleen adjacent to the bleeding point, and splenectomy and partial gastrectomy were performed. He died 24 hours post-operatively following a cardiac arrest.

Discussion

P. pseudomallei appears to have the ability to remain quiescent in infected individuals. As a consequence such people remain at risk of recrudescence of disease many years after leaving an endemic area. This report illustrates such a case in a

Correspondence: A.B. Johnson, M.R.C.P., Ward 12 Office, Royal Victoria Infirmary, Queen Victoria Road, Newcastle upon Tyne NE1 4LP, UK.

Accepted: 20 April 1990

United Kingdom resident. The incidence and exact cause of reactivation is unknown, but cases have been reported in association with diabetes,^{4,5} influenza A,⁶ trauma and other illnesses compromising the immune system of the host. Prior to admission this patient was not known to have diabetes mellitus. Its development, therefore, could have contributed to the recrudescence of *P. pseudomallei* acquired in Vietnam.

The clinical manifestation of melioidosis varies from subclinical disease to an overwhelming septicæmia.¹ Septicæmic melioidosis may follow overwhelming initial exposure or, as reported here, reactivation of latent disease. The septicæmia is typically of abrupt onset, with widespread dissemination of the infection as evidenced by the development of subcutaneous, joint, chest and visceral abscesses.⁵ In this patient repeat chest X-rays remained free of visible lesions despite the widespread dissemination of infection. The overall mortality rate for overwhelming septicæmic melioidosis remains high and exceeds 65% even with prompt, intensive antibiotic therapy.⁵

Satisfactory treatment regimens for septicæmic melioidosis are not well established as *P. pseudomallei* is resistant to many antimicrobials. A combination of tetracycline, chloramphenicol and a third agent, usually trimethoprim-sulphamethoxazole, is recommended, but unfortunately disparate results commonly occur between *in vitro* susceptibility and clinical response² particularly in the disseminated septicæmic form of melioidosis. In this patient the cultures taken from the abscess and intravenous catheter tips prior to death were still positive for the organism, despite proven inhibition by the patient's blood at a dilution of 1:8. Currently the third-generation cephalosporin ceftazidime is being evaluated as it is highly active *in vitro*,⁷ but to date clinical experience is limited.

The frequency of asymptomatic infection is not accurately known, but haemagglutination titres greater than 1:40, suggestive of a recent or past infection have been found in 3 to 9% of Vietnam veterans⁸ and 2% of Commonwealth soldiers serving in peninsular Malaysia.⁹ As 2.5 million people served in Vietnam, it has been calculated that up to 225,000 ex-servicemen remain at risk. More recently the prevalence of melioidosis has been estimated in various populations in northern Queensland.¹⁰ There, 5.7% of the total population tested was found to have titres greater than 1:40. The prevalence in the population of Vietnamese refugees in this area was 29%. In Hong Kong 36% of a randomly selected group of elderly patients were found to be seropositive. Thus these data strongly suggest that there is a large group of asymptomatic people at risk.

Despite sporadic case reports in military personnel who have resided in endemic areas^{2,3} and more recently in travellers to these areas,^{11,12} melioidosis has still not attracted much attention in Europe. However, with the resettlement of South-East Asian refugees and the increasing importance of South-East Asia as a tourist and trading area, there is now a relatively large number of asymptomatic people potentially at risk in Europe. Activation of latent *P. pseudomallei* must therefore be considered in the differential diagnosis of a febrile illness in any patient who has lived in or travelled to an endemic area, particularly South-East Asia. This is especially true of febrile illness that follows trauma, illness or treatment which compromises the host-defence system.

Acknowledgement

We would like to thank Dr A. Page for allowing us to present this patient.

References

1. Leelarasamee, A. & Bovornkitti, S. Melioidosis: review and update. *Rev Infect Dis* 1989, **11**: 413–425.
2. Shaefer, C.F., Trinchler, R.C. & Rissing, J.P. Melioidosis: recrudescence with a strain resistant to antimicrobials. *Am Rev Respir Dis* 1983, **128**: 173–175.
3. Morrison, R.E., Lamb, A.S., Craig, D.B. & Johnson, W.M. Melioidosis: a reminder. *Am J Med* 1988, **84**: 965–967.
4. So, S.Y., Chau, P.Y., Leung, Y.K. & Lam, W.K. First report of septicæmic melioidosis in Hong Kong. *Trans R Soc Trop Med Hygiene* 1984, **78**: 456–459.
5. Chaowagul, W., White, N.J., Dance, D.A. *et al.* Melioidosis: a major cause of community-acquired septicæmia in north-eastern Thailand. *J Infect Dis* 1989, **159**: 980–999.
6. Mackowiak, P.A. & Smith, J.W. Septicæmic melioidosis. Occurrence following acute influenza A, six years after exposure in Vietnam. *JAMA* 1978, **240**: 764–766.
7. Chou, P.Y., Ng, W.S., Leung, Y.K. & Lolekha, S. *In vitro* susceptibility of strains of *Pseudomonas pseudomallei* isolated in Thailand and Hong Kong to some newer β -lactam and quinolone derivatives. *J Infect Dis* 1986, **253**: 167–170.
8. Kishimoto, R.A., Brown, G.L., Blair, E.B. & Wenkheimer, D. Melioidosis: serologic studies on US Army personnel returning from Southeast Asia. *Milit Med* 1971, **21**: 694–698.
9. Thin, R.N.T. Melioidosis antibodies in Commonwealth soldiers. *Lancet* 1976, **i**: 31–33.
10. Ashdown, L.R. & Guard, L.W. The prevalence of human melioidosis in northern Queensland. *Am J Trop Med Hyg* 1984, **33**: 474–478.
11. Bremmelgaard, A., Bygbjerg, I.B. & Hoiby, N. Microbiological and immunological studies in a case of human melioidosis diagnosed in Denmark. *Scand J Infect Dis* 1982, **14**: 271–275.
12. Bouvy, J.J., Degener, J.E., Stijnen, C., Gallee, M.P. & van der Berg, B. Septic melioidosis after a visit to Southeast Asia. *Eur J Clin Microbiol* 1986, **5**: 655–666.