Imported melioidosis with an isolated cutaneous presentation in a 90-year-old traveller from Bangladesh.

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Introduction

Melioidosis, the infection with *Burkholderia pseudomallei*, is recognized as an important cause of sepsis in some tropical areas (23). It mostly infects adults with an underlying predisposing condition (4, 15, 19). With the increase of international travel, melioidosis has been identified among patients returning from endemic areas (5, 8, 13, 15, 20).

We report the case of a 90-year-old Belgian woman with diabetes mellitus who spent three weeks in Bangladesh during the rainy season in September 2003, and was diagnosed 5 weeks after her return to Belgium with melioidosis without any systemic involvement at a very first stage of cutaneous inoculation. Early diagnosis and specific suppressive treatment led to a favourable outcome, without relapse at long term follow-up.

Case report

A 90-year-old Belgian woman consulted our outpatient clinic with a single, non healing erythematous and ulcerated cutaneous lesion involving the external side of the left elbow. The lesion had appeared spontaneously as a papule which gradually increased in size up to 3 cm of diameter. The patient had diabetes mellitus for the past 20 years which was initially treated with orally administered hypoglycaemic agent and recently became insulin-dependent. She had anginal pectoris managed by the administration of nitous derivates.

She had been immunized against hepatitis A, hepatitis B and typhoid fever. The patient had been considered in vigorous health eight weeks earlier, when she began a three-week trip in Bangladesh. This trip was the third one throughout this area, as she previously travelled there two and four years before to visit her son who was involved in a local humanitarian assistance project. She stayed in a village of the northwest area located in the Rangpur district during the flooding
Imported melioidosis in a 90-year-old traveller from Bangladesh.

Melioidosis was first described in 1911 by Frank Whitmore, who isolated the causative bacillus, *Bacillus pseudomallei*, from a patient who died of a pneumonia-like illness in Rangoon, Burma. Since then, melioidosis has been recognized as a serious disease in the tropics, with symptoms ranging from mild respiratory illness to invasive infection. The disease is caused by *B. pseudomallei*, a Gram-negative bacillus that is commonly found in soil, water, and vegetation in regions with high humidity and heavy rainy season. Because of local environmental conditions, she had to use well water for bathing and other domestic use. She acknowledged having received multiple insect and mosquito bites which developed into intense pruritic papules. This had led her to uncontrollable scratching and repeated washing of bite lesions with untreated well water. During her stay, she did not take prophylaxis medication against malaria. Two weeks after her return, she presented with an irregularly shaped, tender, non-healing cutaneous papule on the external side of the left elbow, which grew steadily in size despite application of topical ointment with fusidic acid. Three weeks later, after consulting different physicians, she was admitted to our institution and investigated. She reported no fever, rigors, sweating, malaise, weight loss, nor respiratory symptoms. Skin examination revealed an irregular, erythematous, fluctuant, tender and painful 3.2 cm x 4.0 cm ulcerated plaque on the external side of the left elbow (photo 1). There were no palpable regional lymph nodes. The physical examination was otherwise normal. Laboratory investigations revealed a haemoglobin (Hb) at 12.0 g%, total leucocyte count at 5.97 G/l (n, 3.6-10), a normal differential leucocyte count, erythrocyte sedimentation rate (ESR) of 16 mm in the first hour and a C-reactive protein level at 0.6 mg/100 ml (n < 1). Fasting blood sugar was 151 mg/100 ml (n, 60-110). Creatininemia was 82 µmol/l (n, 70-120). Electrolytes and liver functions tests were normal. Serum venereal disease research laboratory (VDRL) test was non-reactive. Serology for human immunodeficiency virus (HIV) was negative. Blood cultures were repeated five times but failed to isolate any micro-organism. Skin biopsy from the plaque revealed an inflammatory granulomatous reaction. Gram stain of biopsy imprints showed scanty lymphocytes, no polymorphonuclear leukocytes and no micro-organisms. Biopsy specimens were grinded with a tissue blender and inoculated onto Columbia agar with 5% horse blood and Schaedler enrichment broth incubated aerobically for 3 days as well as Schaedler agar with 5% horse blood incubated for 10 days anaerobically. After 72 hours, the Schaedler broth grew few colonies of an aerobic Gram negative bacillus which was identified as *B. pseudomallei* based on typical biochemical characteristics. The strain was mobile at 37°C, able to grow at 42°C, able to oxidize but not to ferment glucose, produced cytochrome oxidase, arginine dihydrolase and gelatinase and was resistant to polymyxin B 300 U.I. (DiaTabs, Rosco, Taastrop, Denmark). The isolate had a negative reaction for arabinose. Antibiotic susceptibility testing was performed on Mueller-Hinton II medium using the disk diffusion technique (Neo-Sensitabs, Rosco) and E-test method (AB Biodisk, Solna, Sweden) for minimal inhibitory concentration (MIC) determination. The strain was susceptible to temocillin, amoxicillin-clavulanic acid (MIC, 2 mg/l), piperacillin-tazobactam, ceftazidime, cefepime, meropenem (MIC, 0.75 mg/l), doxycycline, cotrimoxazole; it was resistant to cefazolin, cefoxitin, ampicillin, gentamicin, ciprofloxacin and amikacin. Chest X-ray, abdominal echography, transoesophagial cardiac echography as well as computed thoraco-abdominal tomographic scan were normal. Sputum and urine cultures were negative. For personal reasons, the patient was not willing to stay in hospital to receive a parenteral intravenous therapeutic regimen. Therefore, and against our firm recommendations, she was discharged with a combination of oral doxycycline 100 mg twice a day and amoxicillin/clavulanic acid 875 mg twice a day up to 32 weeks. At follow-up visits, the cutaneous lesion had dramatically improved 8 weeks after the onset of treatment (photo 2) and had completely disappeared 20 weeks later (photo3). Fifteen months after the diagnosis, the patient presented for evaluation. The skin lesion was replaced by a flexible, pale and painless scar. She reported no episode of fever or any systemic symptoms. The patient agreed for using her history and photographs for this report and an agreement form was completed.

Discussion

In 1911, Whitmore first isolated from a patient dying from pneumonia in Rangoon, Burma, a newly discovered bacterium he called *Bacillus pseudomallei* (24). By 1917, over 100 cases of “Whitmore’s disease” were reported in Rangoon, mainly among neglected or emaciated morphine addicts who languished on the streets of the city. The term “melioidosis” was chosen in 1921. It is derived from the Greek word “melis” meaning “a distemper of asses” because it shows similar pathological features to glanders, a disease of asses caused by infection with the related bacterium *B. mallei* (16). Sporadic cases were reported in French soldiers fighting in Vietnam during the war of independence and among US soldiers during the later conflict there with the USA, skewing their focus elsewhere.
clinical descriptions towards more chronic forms of reactivation long after exposure (11). In the past two decades melioidosis has been recognized as an public health problem in parts of Southeast Asia such as Malaysia, Singapore, Thailand, Southern China, Taiwan, South India, Bangladesh and across the northern part of Australia (3, 4, 9, 18, 23). The organism has also re-emerged as a veterinary pathogen, since the event of the “Jardin des Plantes”. A panda imported from China was thought to be the index case in an epidemic which decimated the mammals of the Paris zoological garden and affected horses of the neighbouring stud farms over a decade.

The bacterium is now incorporated into the genus *Burkholderia* as *B. pseudomallei*. It is a mobile, aerobic, non-spore forming, gram-negative, oxidase-positive bacillus causing a characteristic sweet smell of putrefaction in fresh culture. It typically shows resistance to aminoglycosides, penicillins and cephalosporins of first and second generation. *B. pseudomallei* is a soil and water saprophyte of the tropics which can be recovered readily from water and mud in rice paddy fields in endemic areas (26). Like many soil bacteria, it is difficult to destroy, and is particularly abundant during high levels of rainfall in the wet season. Infection usually occurs by direct contact and inoculation of minor cutaneous trauma with contaminated water or soil, and less frequently by inhalation or ingestion of contaminated materials. The risk of disease seems roughly proportional to concentration of the micro-organism in soil.

Three forms of melioidosis are recognized, acute, sub-acute and chronic. After an incubation period of 1 to 21 days, the disease typically presents as a febrile illness, ranging in severity from an acute fulminating septicemia to a chronic debilitating localized or disseminated disease with multi-organ involvement. Any organ may be affected especially the lung (causing acute fulminating pneumonia or indolent cavitary disease) (6), subcutaneous tissues, bones and joints, liver, spleen, kidneys and brain (25). Severe melioidosis is frequently seen, especially in immuno-compromised patients such as those with diabetes mellitus, renal disease, cystic fibrosis or those who are immunosuppressed because of a disease or drug treatment (4, 15, 19, 22). Up to 50% of patients with melioidosis have diabetes mellitus, usually maturity onset diabetics, often with evidence of poor control of blood glucose before disease onset (4, 15, 19).

With the increase of international travel and adventure tourism in endemic regions, melioidosis has become more likely to develop among travellers, even among those experiencing short-term exposure. The recent tsunami disaster has caused an increase of cases among surviving victims of trauma in coastal areas of Southeast Asia (12). The vast majority of cases diagnosed in temperate countries were imported from Southeast Asia and tropical Australia. Recent reports suggest that melioidosis is probably widespread but poorly recognized throughout Bangladesh (5). The occurrence of cases in India and Pakistan adds further weight to the mounting evidence that the disease is more prevalent in the Indian sub-continent than it was previously considered (9, 26).

The case of imported melioidosis reported here had a quite unusual clinical course. She had never been febrile and presented an uncomplicated infection of the skin localized to an inoculation lesion, without any sign or symptom of systemic involvement despite her predisposing diabetic condition (15, 19). To our knowledge, this exclusively cutaneous localization has been rarely described among travel-associated cases of melioidosis. Indeed, similar feature has been recently reported among two Finnish tourists after the December 2004 tsunami in Thailand (12). Most imported cases present with pulmonary involvement (5, 13, 14) or multi-organ abscesses or mycotic aneurysms (17, 20) associated with very severe prognosis. Cutaneous symptoms may accompany these outcomes, mainly represented by recurrent scattered pustular skin lesions (11, 13, 20). In endemic cases, melioidosis can present with cutaneous infection without severe complications in about 10 percent of cases (4, 21). In such situations, manifestations can also involve abscess formation in subcutaneous tissues or the eye (21).

The mode of acquisition in the patient described here was probably inoculation of insect bites by contaminated water or direct contact with wet soil during the rainy season. Regardless of the advanced age of our patient and considering her diabetes condition, an oral treatment with a two-drug combination was given for 32 weeks. Despite healing of the lesion in 20 weeks, the patient was maintained on a longer term suppressive regimen to prevent relapse. She was advised to require lifelong follow-up as relapse have been rarely observed several years after infection. Combination therapy has been reported to reduce the risk of relapse (2).

Imported melioidosis is no longer the rarity it once was. Clinicians managing patients returning from endemic tropical areas, including the Indian sub-continent, should consider melioidosis in the differential diagnosis of febrile illnesses but also of isolated skin ulcers, particularly in patients with underlying diseases. Concurrently, clinicians and laboratory staff working throughout tropical areas where the disease has not ever been recognized, should be aware of the condition. Indeed first cases of human melioidosis have been recently described in the islands of the southwest Indian Ocean (7, 10). A first case of autochthonous human melioidosis has been reported in Mauritius, where *B. pseudomallei* has never been isolated (7). Moreover, a first human case of the disease has been diagnosed in La Reunion among a sixty-year old French man living in Madagascar (10).

Conclusion

Diagnosis is based on isolation of *B. pseudomallei* from blood, sputum or biopsy specimens from lesions. Microbiologists should also be aware of the characteristics of the agent and informed when such infection is suspected as cultures should be handled under laboratory biosafety level 3 containment. *B. pseudomallei* is considered a potential bio-weapon agent (1). Assessment of geographic and seasonal exposure remains an important criterion for suspecting this polymorphic “exotic” disease which is likely to expand with the growth of international travel and adventure tourism in endemic areas.

Références bibliographiques


4. CURRIE BJ, FISHER DA, HOWARD DM, BURROW JN, LO D et
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7. ISSACK MI, BUNDHUN CD, GOKHOOL A – Melioidosis in Mauritius. Emerg Infect Dis, 2000, 11, 139-140
16. STANTON AT & FLETCHER W – Melioidosis: studies from the Institute of Medical Research, Federated Malay states; 21 London: John Bale and Sons and Danielson Ltd, 1932.