An imported case of melioidosis presenting as pyelonephritis/urosepsis

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Introduction: Melioidosis is a tropical disease that is commonly encountered especially in south-east Asia and Northern Australia. It is caused by Burkholderia pseudomallei. Although the disease is not endemic in western European countries, imported cases have been reported with very different presentations and outcome (Cuadros et al., 2011; Dance et al., 1999; Frangoulidis et al., 2008; Gétaz et al., 2011). Infection is usually acquired by exposure to contaminated water, soil or dust particles, by inhalation of aerosols caused for example by helicopters (Howe et al., 1971) or by ingestion such as in near-drowning accidents (White, 2003). Laboratory infections, transmission at childbirth and sexual transmission have also been reported (Abbink et al., 2001; Green & Tuffnell, 1968; Lumbiganon et al., 1988; McCormick et al., 1975). Clinical presentations of melioidosis are variable, ranging from wound infections,
parotitis and urogenital infections to pneumonia and septicemia.

**Case report**

The patient was a 63-year-old male who was admitted with fever (38.5 °C), renal tenderness and vomiting. His level of C-reactive protein (CRP) at admission was 175 mg l⁻¹, rising to 217 mg l⁻¹ 3 h later. His leukocyte count was 9.1 × 10⁹ l⁻¹. A chest X-ray was normal, but ultrasound showed bilateral enlargement of the kidneys. His past medical history included increased blood pressure, an asymptomatic choledolithiasis and an unexplained CRP increase in the year before. One month prior to admission, he presented to a county hospital with a urinary tract infection. *Proteus penneri* was diagnosed and treated with cefotaxime. His previous travel history included a journey to Vietnam 2 months prior, to Thailand 1 year prior and to Sri Lanka and the Maldives 2 years prior to admission.

**Investigations**

Blood cultures and urine samples were repeatedly taken and yielded bacterial growth. Gram stains of colony material and of positive blood cultures yielded short Gram-negative rods with bipolar staining. Colonies from urine samples and subcultures from positive blood culture bottles on Columbia blood agar were white with a wrinkled surface. After prolonged incubation (approx. 72 h), the colonies were pale cream coloured and showed a ‘wheel-shaped’ pattern of radial and concentric wrinkles (Fig. 1), diffuse haemolysis and a brownish discoloration of the agar around the colonies. A very strong sweetish–putrid odour was noted resembling a neglected, uncleaned aquarium.

On bile-chrysoidin-glycerol broth (Ziesché et al., 1985), the colonies were small and dark bluish green as commonly observed for various non-fermenters.

An API 20NE assay (bioMérieux) was used to identify the species.

**Diagnosis**

The biochemical profile was consistent with *B. pseudomallei*. For further confirmation, hybridization of labelled DNA from culture preparations against a set of previously described probes for identification of 12 *Burkholderia* spp. (Schmoock et al., 2009) was performed. This confirmed *B. pseudomallei* and ruled out *Burkholderia mallei* as well as other species.

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**Fig. 1.** Morphology of colonies on Columbia blood agar after 24 h (left) and approximately 72 h (right) of incubation at 37 °C. Note the wrinkled surface of the colonies. The colony size ranges from 4 to 10 mm.

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Antibiotic susceptibility testing revealed resistance to ampicillin, tobramycin, gentamicin and amikacin, as well as susceptibility to piperacillin, piperacillin-tazobactam, piperacillin-sulbactam, cefazidime, cefepim, imipenem, meropenem, ciprofloxacin, levofloxacin, moxifloxacin and co-trimoxazole.

**Treatment**

Antibiotic therapy was started upon admission with cefotaxime. Later, when the susceptibility test results became available, it was changed to levofloxacin.

**Outcome and follow-up**

Urine cultures taken 2 days after initiation of therapy remained sterile, and body temperature and CRP returned to normal within a few days. The therapy was continued for 2 weeks, and afterwards the patient received co-trimoxazole for 6 months.

Multilocus sequence typing of the causative agent yielded sequence type (ST) 99 (ace-1, gltB-1, gmhD-4, lepA-1, lipA-1, narK-4 and ndh-1). This type has been found previously in Thailand, Malaysia and the Philippines (http://bpsseudomallei.mlst.net/). BURST analysis (an algorithm for comparing sequence types and inferring their phylogenetic relationship; http://eburst.mlst.net/) showed that it belonged to a cluster of STs with the founder ST48 from Thailand. Related STs have been found in Vietnam. From Sri Lanka, other STs from the same phylogenetic group as well as an entirely unrelated ST (ST421) have been multilocus sequence typed. From the Maldives, no sequence data are available. Therefore, it cannot be determined conclusively on which journey the patient contracted the infection.

Sera taken during the acute phase of the infection reacted positively in an indirect haemagglutination assay. Earlier serum samples were not available. Sera taken from three other fellow travellers to Vietnam were negative by indirect haemagglutination assay.

**Discussion**

Definitive diagnosis of melioidosis depends on the isolation and identification of *B. pseudomallei* from clinical specimens, as the clinical features of melioidosis can widely vary. *B. pseudomallei* is classified as a Biosafety Level 3 agent, so it is compulsory for the analysing laboratory to be appropriately equipped. Due to the low clinical experience with melioidosis in western European countries and the lack of pathognomonic symptoms, identification is challenging for laboratories when unexpectedly confronted with an imported case. The described case highlights that this diagnosis might be rather surprising to a routine diagnostic laboratory. Accidental and unwitting exposure of laboratory staff may occur, as the time span between initial cultivation of a patient specimen and a definite identification can realistically be 48 h or longer. However, only a few laboratory-acquired cases have been described (Green & Tuffnell, 1968; Schlech et al., 1981), so the actual risk may be assumed to be low if safe work practices are provided. Good communication between the clinician and laboratory staff is crucial, especially with respect to information on the travel history of the patient.

*B. pseudomallei* is rarely encountered in Western Europe, but is common in Thailand, Vietnam and Northern Australia, especially during the rainy seasons. In our case, a recent travel history to Vietnam was noted. Due to previous journeys to other endemic areas and due to the long and variable incubation time (Howe et al., 1971), it was not possible to safely assume when and where the patient contracted melioidosis. Multilocus sequence typing could theoretically help to localize the region where travellers acquired an infection, but in our case this analysis remained inconclusive.

It can be assumed that tourists travelling in a group might all be exposed to contaminated aerosols, mud, water, etc. As tourist groups separate after returning home, and because melioidosis can have a very long incubation time, it is nearly impossible to draw connections between apparently isolated cases. Unfortunately, melioidosis is not a notifiable disease in Germany, although a notification to public health authorities would facilitate serological screening as well as pre-emptive therapy of fellow travellers. We were able to test the sera of three fellow travellers (all of which were negative), but we were not able to contact any other members of the tourist groups.

Various risk factors for developing melioidosis have been defined previously including diabetes mellitus, renal disease, thalassaemia, ethanol abuse, chronic lung disease, male gender, age ≥ 45 years and immunosuppression (Currie et al., 2000, 2004; Suputtamongkol et al., 1994, 1999). Except for age and gender, our patient did not present any of these risk factors.

The gold standard in diagnosis remains the isolation of *B. pseudomallei* from patient samples. *B. pseudomallei* grows readily on most routine culture media including blood culture bottles. Colony morphology on blood agar (see above) and on selective media (such as Ashdown’s medium) should raise suspicion. Species identification is commonly achieved by commercial kits such as API 20NE (Dance et al., 1989), although some strains might yield indeterminate results or misidentifications, mostly as *Chromobacterium violaceum* (Inglis et al., 1998). Automated systems like the Vitek 1 system, but not the Vitek 2 system, seem to identify *B. pseudomallei* reliably (Lowe et al., 2002). 16S rRNA gene sequencing for the identification of culture material does not reliably differentiate *B. pseudomallei* from *B. mallei*. Hybridization against specific probes using diagnostic microarray technology might be helpful to facilitate rapid genotypic identification.
B. pseudomallei is resistant to penicillins, first-/second-generation cephalosporins, colistin and aminoglycosides (Cheng & Currie, 2005; Schweizer, 2012). Additionally, it exhibits relative resistance to quinolones. Ceftazidime, (Cheng & Currie, 2005; Schweizer, 2012). Additionally, it generation cephalosporins, colistin and aminoglycosides is resistant to penicillins, first-/second-

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References


