Brucella melitensis prosthetic joint infection in a traveller returning to the UK from Thailand: Case report and review of the literature

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Summary  Background: Brucella spp. prosthetic joint infections are infrequently reported in the literature, particularly in returning travellers, and optimal treatment is unknown.
Method: We describe a prosthetic joint infection (PJI) caused by Brucella melitensis in a traveller returning to the UK from Thailand, which we believe to be the first detailed report of brucellosis in a traveller returning from this area. The 23 patients with Brucella-related PJI reported in the literature are summarised, together with our case.
Results: The diagnosis of Brucella-related PJI is difficult to make; only 30% of blood cultures and 75% of joint aspiration cultures were positive in the reported cases. Culture of intraoperative samples provides the best diagnostic yield. In the absence of radiological evidence of joint loosening, combination antimicrobial therapy alone may be appropriate treatment in the first instance; this was successful in 6/7 [86%] of patients, though small numbers of patients and the likelihood of reporting bias warrant caution in drawing any firm conclusions about optimal treatment. Aerosolisation of synovial fluid during joint aspiration procedures and nosocomial infection has been described.

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1. Introduction

Brucellosis is a zoonotic infection transmitted to humans from fluids of infected animals or through consumption of unpasteurised dairy products [1]. It is caused by Brucella spp., intracellular Gram-negative coccobacilli. Four species cause most cases of human disease, each with a different animal host reservoir: Brucella melitensis (goats, camels) is most common, followed by Brucella abortus (cattle), Brucella suis (pigs) and Brucella canis (dogs). Infections with new species such as Brucella pinnipedialis and Brucella ceti (marine animals) are occasionally recognized [2]. It can cause an acute febrile illness after a usual incubation period of 1–4 weeks, ranging up to 6 months, or chronic infection, which can be without focus or can affect any organ system. Osteoarticular involvement is the most common focal presentation. Diagnosis is usually based on serology, augmented when possible by culture of Brucella organisms from blood, synovial fluid, or bone. Promising molecular methods are in development. Treatment is usually with combination therapy of doxycycline, rifampicin ± an aminoglycoside for 6–12 weeks [1]. Prosthetic joint infections (PJI) caused by Brucella spp. are uncommonly reported in the literature. We describe a PJI caused by B. melitensis in a traveller returning to the UK from Thailand, the first detailed report of brucellosis in a travellr returning from this area; we also present a review of the 24 reported cases of Brucella-related PJI in the literature.

2. Materials and methods

2.1. Case report

A 51-year old UK resident attended our clinic on 5 May 2015 with a 21-day history of daily rigors, profuse sweating attacks and high fever. He had returned from Thailand three months earlier. He also had pain and swelling in his left knee, in which he had an uncomplicated total knee replacement 5 years previously for early onset osteoarthritis following trauma. The only abnormalities on examination were fever of 38.3°C and a small effusion in the symptomatic knee. Blood cultures yielded Gram-negative coccobacilli after 3 days (BioMerieux Bact/ALERT blood culture system), identified as B. melitensis by matrix-assisted laser desorption/ionization/time-of-flight (MALDI-TOF) mass spectrometry (Bruker microflex LT), but not before two laboratory scientists had been exposed to open bacterial culture plates. The organism was confirmed as B. melitensis biotype 3 in the Veterinary Investigation Centre in Weybridge. Standard agglutination tests for brucellosis were suggestive of chronic infection, with IgG titres of >1:2560 and IgM 1:80.

Aspiration of the knee was carried out by the orthopaedic team, equipped with personal protective equipment (PPE) consisting of gown, gloves, apron, visor and filtering face piece-3 (FFP3) respirator. Cloudy fluid was aspirated; this contained over 6000 lymphocytes/mm³ and cultured B. melitensis after 7 days. The patient commenced doxycycline and rifampicin 600 mg daily for 6 months, together with parenteral gentamicin 5 mg/kg/day for the first 14 days, with resolution of his symptoms and preservation of his implant without revision surgery. Twelve months later he has fully recovered with no signs of loosening of the joint prosthesis on plain x-rays. The exposed laboratory personnel were given doxycycline 100 mg twice daily for 21 days as postexposure prophylaxis according to UK guidelines [3].

The patient made frequent visits to Thailand where he had most recently stayed with a friend on his farm in Nakom Pathom province from 11 December 2014 to 8 January 2015. During that time, he helped deliver several parturient goats and handled newly born kids and other products of conception with his bare hands. He had not consumed unpasteurised dairy products and had no contact with cattle or buffaloes. Two farm workers had contemporaneous fevers, only recognised to be due to brucellosis and treated appropriately after our patient was diagnosed.

2.2. Literature review

PubMed and Scopus databases were searched using the search string ((((((prosth*) OR replacement)) OR arthroplasty)) AND (((knee) OR hip) OR joint)) AND brucell*. Studies were reviewed and data extracted by one author (JL), with no restriction on date or language. Prosthetic joint brucellosis was defined as either a) Brucella spp. recovered from prosthetic joint synovial fluid culture OR b) signs and symptoms consistent with PJI AND Brucella spp. recovered from blood OR positive serology (standard agglutination test [SAT] titre > 1:160 OR fourfold rise in titre between acute and convalescent samples).

3. Results and discussion

The search returned 48 results in Scopus and 26 in PubMed. After removal of duplicates, 47 remained. 18

Conclusions: Brucella-related PJI should be considered in the differential of travellers returning from endemic areas with PJI, including Thailand. Personal protective equipment including fit tested filtering face piece-3 (FFP3) mask or equivalent is recommended for personnel carrying out joint aspiration when brucellosis is suspected. Travellers can reduce the risk of brucellosis by avoiding unpasteurised dairy products and animal contact (particularly on farms and abattoirs) in endemic areas and should be counselled regarding these risks as part of their pre-travel assessment.

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| Reference                      | Age | Sex | Country of exposure | Traveller Occupation | Prosthetic implant | Time since implantation (months) | Brucella SAT titre | Radiographic changes | Blood cultures positive | Joint aspirate culture positive | Species | Antibiotics used | Antibiotic course length (weeks) | Surgical management | Follow up (months) | Outcome       |
|-------------------------------|-----|-----|---------------------|----------------------|--------------------|-------------------------------|------------------|---------------------|-----------------------|-------------------------|----------|-----------------|------------------------------|----------------------|------------------|---------------|
| Jones et al., 1983 [4]        | 54  | M   | USA                 | Dairy farmer         | R THR              | 6                             | 640              | No                  | No                    | No                      | B. abortus | Tetracycline 500 mg QID, Streptomycin 500 mg QID | 6 – failed therapy; followed by 52 weeks; Streptomycin first 6 only 76 | One-stage revision once medical treatment failed | None          | 24            | Asymptomatic |
| Agarwal et al., 1991 [5]      | 24  | F   | Saudi Arabia        | No NR                | Bilateral TKR      | 2                             | 2560             | No                  | No                    | Yes                     | B. melitensis | Rifampicin 100 mg BID, Doxycycline 100 mg BID, Streptomycin 1 g QD | 6 | Streptomycin first 3 only | None | 19 | Pain free, flexion 0–90 |
| Ortí et al., 1997 [6]         | 60  | M   | Spain               | "Works with goats"  | R TKR              | 14                            | 160              | No                  | No                    | Yes                     | B. melitensis | Doxycycline 100 mg BID, Streptomycin 900 mg QD | 34 | Gentamicin first 1 only | None | 8 | Symptom free |
| Navarro et al., 1997 [7]      | 54  | M   | Spain               | Shepherd             | L. internal fixation of femur | 324                         | 160              | Loosening           | No                    | NR                      | B. melitensis | Doxycycline 100 mg BID, Gentamicin 240 mg QD, Streptomycin 1 g QD | 20 | Streptomycin first 3 only | None | 18 | Asymptomatic |
| Malizos et al., 1997 [8]      | 74  | M   | Greece              | Shepherd             | Bilateral TKR      | 5                             | 160              | No                  | Yes                   | Yes                     | B. melitensis | Doxycycline 100 mg BID, Streptomycin 900 mg QD | 12 | Streptomycin first 3 only | Two-stage revision | 6 | “Satisfactory” |
| Ortega et al., 2002 [9]       | 63  | M   | Spain               | Cattle owner         | R THR              | 60                            | NR               | No                  | NR                    | No                      | B. melitensis | Doxycycline 200 mg QD, Rifampicin 600 mg QD, Streptomycin 1 g QD | 12 | 6 prior to surgery, 6 after | Two-stage revision | 12 | Asymptomatic |
| Weil et al., 2003 [10]        | 38  | M   | Israel              | Artist               | L THR              | 48                            | 1600             | Loosening           | NR                    | No                      | B. melitensis | Doxycycline 200 mg QD, Rifampicin 600 mg QD, Streptomycin 1 g QD | 12 | 6 prior to surgery, 6 after | Two-stage revision | 12 | Asymptomatic |
| Weil et al., 2003 [10]        | 61  | M   | Israel              | Retired              | R TKR              | 60                            | 1600             | Loosening           | NR                    | No                      | B. melitensis | Doxycycline 200 mg QD, Rifampicin 600 mg QD, Streptomycin 1 g QD | 12 | 6 prior to surgery, 6 after | Two-stage revision | 12 | Free of joint pain |
| Weil et al., 2003 [10]        | 67  | M   | Israel              | Retired              | L TKR              | 168                           | 1600             | Loosening           | NR                    | Yes                     | B. melitensis | Doxycycline 200 mg QD, Rifampicin 600 mg QD, Streptomycin 1 g QD | 12 | 6 prior to surgery, 6 after | Two-stage revision | 12 | Free of joint pain |
| Kasim et al., 2004 [11]       | 47  | F   | Lebanon             | No NR                | L THR              | 168                           | 640              | Loosening           | NR                    | NR                      | Brucella spp. | Doxycycline 100 mg BID, Rifampicin 600 mg QD, Streptomycin 1 g QD | 20 | One-stage revision | 48 | Symptom free, negative Brucella titres |
| Cairo et al., 2006 [12]       | 50  | M   | Spain               | No NR                | L THR              | 0                             | 320              | No                  | Yes                   | NR                      | B. melitensis | Doxycycline 100 mg BID, Streptomycin 1 g QD | 104 Streptomycin first 2 only | None | 60 | Well, negative Brucella titres |
| Authors          | Gender | Age  | Occupation | Site | Stage | Duration (months) | Causes       | Treatment                    | Revision Details                                                                                   | Outcome                                                                                     | Notes                                                                                          |
|------------------|--------|------|------------|------|-------|-------------------|--------------|-------------------------------|-------------------------------------------------------------------|-----------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------------|
| Cairo et al.,    | M      | 71   | Farmer     | R    | THR   | 36                | *B. melitensis* | Doxycycline 100 mg BID, Rifampicin 600 mg QD, Streptomycin 750 mg QD | 24 Streptomycin first week only, initially one stage revision (infection not suspected) | Initially bone graft and medical therapy—failed—then two-stage revision | Debridement, 60 Asymptomatic                                                             |
| 2006 [12]        |        |      |            |      |       |                   |              |                               |                                                                    |                                                                                               |
| Cairo et al.,    | F      | 74   | No NR L    | L    | THR   | 180               | *B. melitensis* | Doxycycline 100 mg BID, Rifampicin 300 mg TID, Streptomycin 1 g QD | 32 Doxycycline/streptomycin first week, Doxycycline/rifampicin for remainder | Two-stage revision | Satisfactory range of movement 0 -100° knee                                               |
| 2006 [12]        |        |      |             |      |       |                   |              |                               |                                                                    |                                                                                               |
| Ruiz-Iban et al.,| F      | 66   | Housewife  | THR  | 36    | No NR            | *B. abortus*  | Doxycycline 200 mg QD, Rifampicin 900 mg QD, Streptomycin 200 mg QD | 24 Streptomycin first 6 only, Doxycycline/streptomycin first week | Initially two-stage revision | Asymptomatic                                                                      |
| 2006 [13]        |        |      |            |      |       |                   |              |                               |                                                                    |                                                                                               |
| Ruiz-Iban et al.,| M      | 71   | Agricultural worker | THR | 28    | 640               | *B. melitensis* | Doxycycline 200 mg QD, Rifampicin 900 mg QD, Streptomycin 200 mg QD | 12 Two-stage revision | None | 12 Pain free, walking distance > 1 km    |
| 2006 [13]        |        |      |            |      |       |                   |              |                               |                                                                    |                                                                                               |
| Marbach et al.,  | M      | 67   | Sicily Yes | Bilateral TKR | 48 | NR  | Loosening NR NR | Brucella spp.        | Doxycycline 100 mg BID, Rifampicin 450 mg BID, Streptomycin 1 g QD | 15 Two-stage revision | Good range of movement                                                                 |
| 2007 [14]        |        |      |            |      |       |                   |              |                               |                                                                    |                                                                                               |
| Tena et al.,     | M      | 56   | Farmer     | L    | THR   | 60                | *B. melitensis* | Doxycycline 100 mg BID, Rifampicin 900 mg QD, Streptomycin 1 g QD | 8 Doxycycline/streptomycin first 2 weeks, Doxycycline/rifampicin for remainder | Two-stage revision | Asymptomatic, good joint function                                                               |
| 2007 [15]        |        |      |            |      |       |                   |              |                               |                                                                    |                                                                                               |
| Tassinari et al.,| M      | 68   | Italy No NR | R TKR | 24 | 800  | No loosening NR NR | *B. melitensis* | Doxycycline 100 mg BID, Rifampicin 250 mg QD, Streptomycin 1 g QD | 8 None | 12 Pain disappeared, no radiographic changes (continued on next page) |
| 2008 [16]        |        |      |            |      |       |                   |              |                               |                                                                    |                                                                                               |
| Dauty et al.,    | F      | 65   | Portugal Yes | Bilateral TKR | NR | NR | Loosening NR NR | *B. melitensis* | Doxycycline 200 mg QD, Rifampicin 250 mg QD, Streptomycin 1 g QD | 12 Two-stage revision | 120 Pain free, walking distance > 1 km Free of joint pain, negative serology                |
| 2009 [17]        |        |      |            |      |       |                   |              |                               |                                                                    |                                                                                               |
| Erdogan et al.,  | F      | 63   | Turkey No NR | R TKR | 24 | 160  | NR NR NR NR | *B. melitensis* | Doxycycline 200 mg QD, Rifampicin 250 mg QD, Streptomycin 1 g QD | 36 One-stage revision | Free of joint pain, negative serology                                                      |
| 2010 [16]        |        |      |            |      |       |                   |              |                               |                                                                    |                                                                                               |
| Nichols et al.,  | F      | 67   | Mexico No NR | THR  | 24 | NR  | Loosening NR NR | B. abortus | Doxycycline Rifampicin | 12 Two-stage revision | No evidence of infection recurrence                                                      |
| 2014 [19]        |        |      |            |      |       |                   |              |                               |                                                                    |                                                                                               |
| Lowe et al.,     | NR     | 68   | India Yes NR | THR  | NR | NR  | NR NR NR | B. melitensis | None — lost to follow up | None | 0 Unknown                                  |
| 2015 [20]        |        |      |            |      |       |                   |              |                               |                                                                    |                                                                                               |
| Reference | Age | Sex | Country of exposure | Traveller | Occupation | Prosthetic implant | Time since implantation (months) | Brucella SAT titre | Radiographic changes | Blood cultures positive | Joint aspirate culture positive | Species | Antibiotics used | Antibiotic course length (weeks) | Surgical management | Follow up (months) | Outcome |
|-----------|-----|-----|---------------------|-----------|------------|-------------------|-------------------------------|------------------|-------------------|---------------------|------------------------|---------|----------------|-------------------------------|-----------------|----------------|---------|
| Carothers et al., 2015 [21] | 67 | F | USA or Mexico | No | NR | R THR | 24 | NR | Loosening | NR | NR | B. abortus | Doxycycline 100 mg BID Rifampicin 300 mg BID | 20 | Two-stage revision | 24 | Well, no evidence of infection |
| Present case | 51 | M | Thailand | Yes | Company director | L TKR | 60 | >2500 | No loosening | Yes | Yes | B. melitensis | Gentamicin 200 mg QD Rifampicin 600 mg QD Gentamicin 400 mg QD | 24 | Gentamicin in first 2 weeks only | None | 12 | Well, pain free, fully mobile, no radiographic changes |

M = male, F = female, L = left, R = right, NR = not reported, SAT = Standard agglutination test, QD = quaque die [once daily], BID = bis in die [twice daily], TID = ter in die [thrice daily], QID = quater in die [four times daily], THR = total hip replacement, TKR = total knee replacement. Where dose and/or dosing interval are given in original report, they are reproduced here.

It is possible to draw several conclusions from these reports. First, Brucella-related prosthetic joint infections are rare but can be serious. Second, Brucella infection can be difficult to diagnose, and patients may present with symptoms similar to those of other joint infections. Third, the effectiveness of treatment varies depending on the stage of infection and the type of bacteria involved. Fourth, surgical intervention may be necessary to remove infected tissue and prevent further spread of the infection. Finally, healthcare workers should follow strict infection control measures when performing joint aspirations or surgeries to prevent the transmission of Brucella bacteria.
Brucellosis is not a diagnosis that would usually be considered in a traveller returning from Thailand [24]. Two cases acquired in Thailand have been mentioned in passing in reviews of children [25] and adult [26] travellers returning to North America and Europe respectively. Foci in China, Mongolia and Central Eurasia are well recognised but the range of other countries newly affected by brucellosis continues to expand [2,27–30]. Human infections are under-reported compared to the patchy knowledge of its increasing incidence in livestock in South Asia [31]. A boy acquired brucellosis from raw goat’s milk in Penang, Malaysia in 2010 and a German visitor acquired brucellosis in Myanmar from drinking lassi [32]. An outbreak of caprine and human brucellosis in Ratchaburi Province in Thailand was investigated in 2003 [33] and there have been sporadic case reports and more recent reviews of emerging brucellosis endemicity in Thailand over the past decade [34–36]. As demonstrated by our patient, the highest risk to humans in Thailand is exposure to parturient goats (B. melitensis) but there is a separate risk of B. abortus transmission from buffaloes. Diagnosis of illness in travellers can highlight the presence of locally unrecognised infections, as shown by this patient and his contacts.

4. Conclusion

In conclusion, we report the first detailed case report of brucellosis in a traveller returning from Thailand. Clinicians should consider brucellosis as well as the more commonly encountered causes of fever in returnees from this area. Brucellosis should be included in the list of possible causes of an infected prosthetic joint in patients who have an appropriate epidemiological risk and PPE, including fit-tested masks, should be used by operators undertaking joint aspiration or surgery in such cases. Though the small number of cases identified in this review warrants caution about drawing any firm conclusions regarding optimal treatment, in the absence of implant loosening, treatment with antibiotics may be appropriate in the first instance. There are no specific strategies for avoidance of Brucella spp. PJIs beyond those needed by all travellers to prevent brucellosis. These include the avoidance of unpasteurised dairy products (including lassi and buffalo milk or cheese) and animal contact (particularly in farms or abattoirs) in endemic areas. Travellers (with or without prosthetic joints) should be made aware of these risks as part of their standard pre-travel assessment.

Conflict of interest

Nil.

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Preliminary data about this patient were published on-line in May 2015 [32], and reported through the GeoSentinel network (of which LSTM is a contributing centre). We thank the patient for consenting to his details being published.

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