

Case Report

Prepatellar bursitis: a rare manifestation of chronic brucellosis

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Introduction: Bursitis is a rare complication of brucellosis that has only once been described in a country where disease has been eradicated in domestic animals.

Case Presentation: A 63-year-old diabetic man presented with an 11-year history of painless swelling over his right knee. Magnetic resonance imaging (MRI) showed a large, multiloculated cyst overlying the knee joint. The patient underwent bursectomy which revealed caseous necrosis. Operative samples cultured *Brucella abortus*. The patient was treated with a combination of surgery and antimicrobials (doxycycline, rifampicin and gentamicin). His only risk factor for acquiring *Brucella* was drinking unpasteurized milk during childhood. Fifty eight cases of *Brucella* bursitis have been described in the English-language medical literature. Half have involved the prepatellar bursa. Only one case, from Australia, occurred in a country that has eradicated brucellosis in domestic animals. Although symptoms are often prolonged, local features of inflammation are usually absent. Diagnosis is primarily by bursal fluid culture. Treatment involves antimicrobials with or without aspiration or excision of the bursa. As the diagnosis was unexpected, several laboratory workers were exposed to the *Brucella* isolate before its identification. Follow up according to UK guidelines revealed no cases of occupationally acquired infection.

Conclusion: Bursitis is an unusual manifestation of brucellosis. It is extremely rare outside countries where the infection is endemic, but the chronicity of symptoms and increase in global travel mean that patients with the condition may present in non-endemic settings. Clinicians should therefore consider the diagnosis in cases of unexplained chronic bursitis.

Keywords: *Brucella*; brucellosis; bursectomy;; bursitis; doxycycline; gentamicin; prepatellar; rifampicin.

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Introduction

Brucellosis is a zoonotic infection which is classically characterized by undulating fever and constitutional upset (Corbel

& Beeching, 2011). Osteoarticular infection is common, occurring in 23–45 % of patients (Taşova *et al.*, 1999; Mousa *et al.*, 1987; Pourbagher *et al.*, 2006; González-Gay *et al.*, 1999; Colmenero *et al.*, 1996). Sacroiliitis, vertebral osteomyelitis, discitis and large joint inflammatory arthritis are the usual manifestations, whilst bursitis accounts for just

Abbreviation: MRI, magnetic resonance imaging.

Table 1. Cases of *Brucella* bursitis published in the English-language literature

Reference	Number of bursitis cases	Total number of patients in series	Site(s) of infected bursa(e)	Species (n)
Kennedy (1904)	1	1	Subdeltoid	Not reported (probable <i>B. melitensis</i>)
Johnson & Weed (1954)	4	4	Prepatellar	<i>B. abortus</i>
Rotés-Querol (1957)	3	174	Olecranon (two cases) Greater trochanter (1)	Not reported
Schirger <i>et al.</i> (1960)	3	224	Prepatellar	<i>B. abortus</i> (2) <i>B. suis</i> (1)
Kelly <i>et al.</i> (1960)	8*	36†	Prepatellar	<i>B. abortus</i> (6) <i>B. suis</i> (2)
Ariza <i>et al.</i> (1985)	3	331	Not reported	Not reported
Mousa <i>et al.</i> (1987)	1	452	Olecranon	Not reported
Colmenero <i>et al.</i> (1991)	2	263	Olecranon	Not reported
González-Alvaro <i>et al.</i> (1994)	1	2	Olecranon (bilateral)	<i>B. melitensis</i>
McDermott <i>et al.</i> (1994)	1	1	Suprapatellar	<i>B. abortus</i>
Solera <i>et al.</i> (1996)	2	64	Prepatellar ‡	Not reported
Davis & Broughton (1996)	1	1	Prepatellar	<i>B. abortus</i>
González-Gay <i>et al.</i> (1997)	1	1	Prepatellar	<i>B. abortus</i>
García-Porrúa <i>et al.</i> (1999)	3*	(75 cases of septic bursitis)	Not reported	<i>B. abortus</i>
González-Gay <i>et al.</i> (1999)	3	158	Prepatellar (2) Olecranon (1)	<i>B. abortus</i>
Taşova <i>et al.</i> (1999)	5	238	Prepatellar (3) Subacromial (2)	Not reported
Guiral <i>et al.</i> (1999)	1	1	Iliopsoas	<i>B. melitensis</i>
Pourbagher <i>et al.</i> (2006)	13§	251	Suprapatellar (6) Olecranon (3) Subacromial (3) Lateral malleolus (1)	Not reported
Traboulsi <i>et al.</i> (2007)	1	1	Prepatellar	<i>B. melitensis</i>
Wallach <i>et al.</i> (2010)	1	1	Prepatellar	<i>B. abortus</i>

* Number likely to include some previously reported cases.

† Cases of osteoarticular brucellosis only.

‡ Unclear if one or both cases involved the prepatellar bursa.

§ Bursitis diagnosed radiologically.

1–7 % of bone and joint disease. Only 58 cases have been described in the English language literature over the past 100 years (see Table 1) and this figure may have been inflated by repeated reporting of a number of cases (Johnson & Weed, 1954). Apart from one case from Australia (Davis & Broughton, 1996), all of the reports have come from countries where brucellosis remains endemic in domestic animals.

We describe the first case of *Brucella* bursitis in England, where brucellosis in domestic animals has been eradicated. As the cause was unexpected, the diagnosis was delayed and a number of laboratory staff were exposed to the isolate before it had been identified. By reporting this case and reviewing the associated literature to highlight common features of the condition, we hope that clinicians in non-endemic countries will consider brucellosis in any unexplained chronic bursitis. This should ensure that the diagnosis

is made earlier and that laboratory staff can take the necessary precautions when handling both clinical samples and unidentified bacterial isolates.

Case report

The patient was a 63-year-old Caucasian man with a history of non-insulin dependent diabetes mellitus and hypertension. He was a retired high school teacher who had consumed unpasteurized milk whilst holidaying in the Republic of Ireland during childhood. The patient holidayed annually at a hotel in Jersey from 2001 to 2011. His only travel outside the UK was to the Pyrenees in 1989. In 2000, he noted a painless swelling over his right knee. It slowly enlarged over the following years, until he was seen by an orthopaedic surgeon in 2005. A diagnosis of a simple cyst was made on the basis of clinical examination and magnetic resonance imaging

(MRI). The patient declined an offer of surgical excision. Following this, the lesion continued to enlarge, eventually causing minor restriction of knee flexion. The patient reported experiencing night sweats approximately once per month during this period but no other constitutional symptoms.

In March 2011 he experienced an episode of cellulitis over the knee, precipitated by a carpet burn sustained when he fell at home. The cellulitis was treated with oral flucloxacillin and he was referred back to the orthopaedic surgeon. MRI in April showed a 15 cm multiloculated cyst encasing the anterior aspect and sides of the knee, lying in the soft tissue over the quadriceps muscles and patellar tendon (Fig. 1). The radiological impression was of severe chronic bursitis. Three months later, the patient again developed cellulitis of the skin overlying the lesion. Clinical examination at that time revealed an associated sinus. A superficial swab isolated *Streptococcus agalactiae* (Lancefield group B). Again, the cellulitis responded to flucloxacillin. In August 2011, a biopsy was taken for histological examination. This showed necrosis with areas of both acute and chronic inflammation, consistent with an infected prepatellar bursa. No sample was sent for culture. One month later, the patient underwent complete excision of the lesion. At surgery, there was extensive caseous necrosis.

Investigations

Three samples of tissue and one of pus were negative on Gram and auramine staining. They were cultured on

chocolate, Columbia blood and cysteine lactose electrolyte deficient agar (all from Oxoid) at 36 °C in aerobic conditions (supplemented with carbon dioxide for the chocolate and blood agar). They were also cultured on fastidious anaerobe agar (FAA; E&O Laboratories) at 36 °C in anaerobic conditions. For each tissue sample, an anaerobic broth culture was set up which was subcultured to chocolate, FAA and neomycin agar on 3 consecutive days, after 5 days incubation. All of the tissue samples isolated *Serratia marsecens* and a coagulase-negative *Staphylococcus*.

After 72 h incubation, colonies of a small Gram-negative coccobacillus were noted on the blood and chocolate agar plates from all samples. The organism was identified by using a VITEK 2 system (Bio Merieux) as *Brucella melitensis* (98 % probability). Subsequent PCR of the 16S rRNA gene generated a 609 bp sequence that had 100 % similarity with *Brucella* spp. sequences published on the BLAST database. The Animal and Plant Health Agency Reference Laboratory (Weybridge, England) identified the organism as *Brucella abortus* biovar five. Serological testing of the patient's blood at the *Brucella* Reference Unit (Liverpool, England) showed a *Brucella* IgG titre of >1 : 2560 and IgM titre of <1 : 20. No follow up testing was performed.

Treatment

The patient was initially given oral ciprofloxacin, 500 mg twice daily, to treat the *Serratia* superinfection. Following the identification of *Brucella*, this was switched to oral

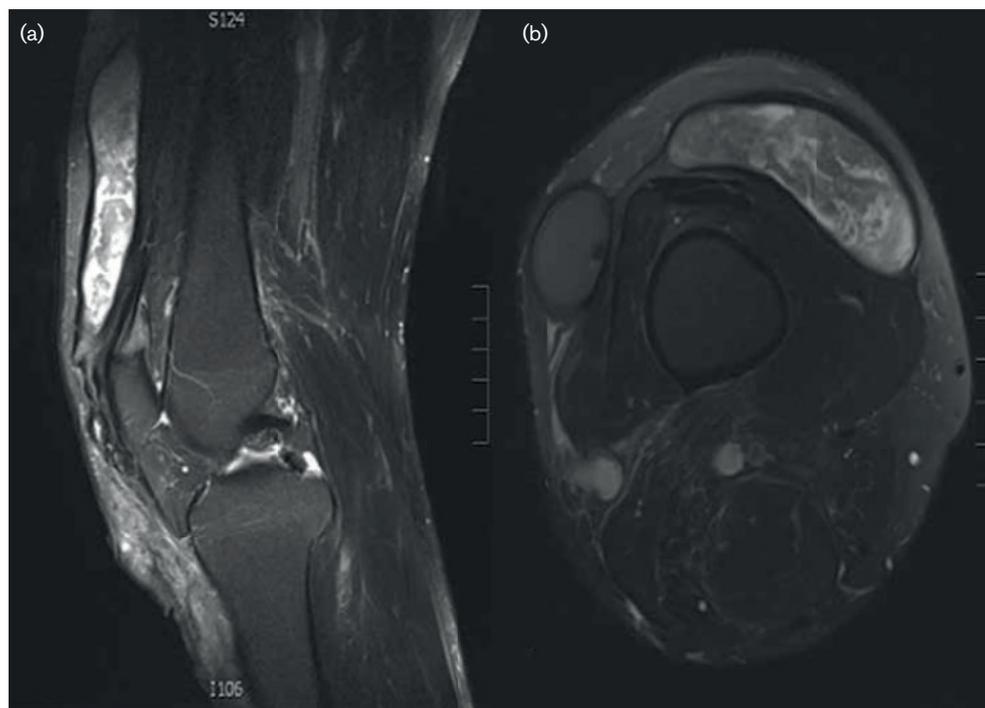


Fig. 1. T2-weighted sagittal (a) and coronal (b) MRIs of the right knee, showing a large cystic lesion overlying the quadriceps muscles and patellar tendon.

doxycycline 100 mg twice daily, oral rifampicin 600 mg once daily and intravenous gentamicin 7 mg kg⁻¹ body weight once daily. After 19 days of antimicrobial therapy, the patient underwent split skin grafting. The gentamicin was stopped at 2 weeks. The original plan was to give the patient a total of 12 weeks oral antibiotics, but treatment was stopped after 6 weeks due to persistent nausea.

Outcome and follow-up

The patient was discharged from follow-up after 11 months, and at 3 years has had no evidence of relapse.

Discussion

Brucella bursitis was first described in 1904 by Kennedy (1904). The condition has parallels with fistulous withers in horses (Cohen *et al.*, 1992). Early published cases are mostly from the USA (Johnson & Weed, 1954; Schirger *et al.*, 1960; Kelly *et al.*, 1960). More recent reports come from northern Spain, Turkey and Kuwait (Taşova *et al.*, 1999; Mousa *et al.*, 1987; Pourbagher *et al.*, 2006; González-Gay *et al.*, 1999). This is consistent with the current global epidemiology of brucellosis, which remains endemic in parts of the Mediterranean and the Middle East (Corbel & Beeching, 2011).

Brucellosis has been described involving a number of bursae (Table 1). Previous reviewers have suggested that the olecranon bursa is the most common site (Akhvlediani *et al.*, 2011) but our review of the literature has revealed more cases of prepatellar bursitis.

In 1954, Johnson & Weed (1954) published the first comprehensive description of four cases of prepatellar bursitis. Six years later, the same group included eight cases in a series of osteoarticular brucellosis (Kelly *et al.*, 1960). It is unclear if the patients from the original report were included in this number. Since that paper, there have been a further four single case reports (Davis & Broughton, 1996; González-Gay *et al.*, 1997; Traboulsi *et al.*; 2007; Wallach *et al.*, 2010). All of these patients have had prepatellar bursitis as the only or main manifestation of *Brucella* infection. All but one of the cases occurred in men, perhaps reflecting an increased risk of exposure through occupation. In the majority of cases (6/8) the patients were farmers, in whom local inoculation with *Brucella* may have occurred during recurrent trauma from kneeling (Johnson & Weed, 1954). However, in one case, the route of infection was the consumption of cheese made with unpasteurized milk, suggesting haematogenous seeding of the bursa (Traboulsi *et al.*, 2007). We believe this is the mechanism by which our patient acquired *Brucella* infection.

Despite the small number of cases of prepatellar bursitis due to *Brucella*, several common features are evident (Table 2). The first is the duration of symptoms before diagnosis. Although cases are occasionally described as presenting acutely (Akhvlediani *et al.*, 2011), the majority of patients with bursitis are symptomatic for much longer. Amongst the cases of prepatellar infection, the duration of illness ranges from 2 months to 14 years. This is consistent with the observation in several case series that symptoms are more prolonged in patients with osteoarticular forms of brucellosis, compared to those without focal disease (González-Gay *et al.*, 1999; Schirger *et al.*, 1960; Ariza *et al.*; 1985).

Table 2. Clinical features and treatment of prepatellar *Brucella* bursitis from case reports

Reference	Gender	Occupation	Duration of symptoms	Systemic features	Local inflammation	Treatment
Johnson & Weed (1954)	Male (four cases)	Farmers	8 months – 14 years	No	No	Bursectomy in all cases; aureomycin 3 g and streptomycin 1 g daily for 6–30 days in three cases
Davis & Broughton (1996)	Male	Retired farm worker	2 months	Yes	N/K	Doxycycline for 22 weeks and rifampicin for the first 6 weeks (doses not stated)
González-Gay <i>et al.</i> (1997)	Male	Farmer	10 years	No	Yes*	Streptomycin 1 g once daily for 3 weeks and doxycycline 100 mg twice daily for 6 weeks plus bursectomy
Traboulsi <i>et al.</i> (2007)	Female	Housewife	1 year	No	No	Streptomycin 1 g daily and doxycycline 100 mg twice daily for 2 weeks, then doxycycline 100 mg and rifampicin 600 mg one daily for 8 weeks, with recurrent aspiration
Wallach <i>et al.</i> (2010)	Male	Former abattoir worker	5 years	Yes	Yes	Doxycycline 100 mg twice daily and rifampicin 300 mg twice daily (both for 6 weeks)

* Patient had coinfection with *S. agalactiae* at presentation

Fever and other constitutional symptoms are common in brucellosis, both with and without osteoarticular involvement (Taşova *et al.*, 1999; Mousa *et al.*, 1987). In contrast, in six of the eight detailed case reports of pre-patellar bursitis, there was no history of fever or other systemic upset (Johnson & Weed, 1954; González-Gay *et al.*, 1997; Traboulsi *et al.*; 2007). Infrequent night sweats was the only systemic symptom our patient described. In addition, local signs of inflammation are usually mild or absent, except when secondary infection is present (González-Gay *et al.*, 1997). The indolent nature of the *Brucella* bursitis may relate to the fact that *B. abortus* is the commonest infecting organism (Table 1). This species is classically said to be less virulent than *B. melitensis* (Corbel & Beeching, 2011).

Diagnosis is usually achieved by culturing *Brucella* in synovial fluid aspirated from the bursa (González-Gay *et al.*, 1999), though it is not always positive (Pourbagher *et al.*, 2006). In some cases of bursitis, the organism can also be recovered from blood cultures (García-Porrúa *et al.*, 1999). Serology is almost always positive at high titres in patients with bursitis, as well as other osteoarticular complications (Mousa *et al.*, 1987; Colmenero *et al.*, 1991). In our case, the diagnosis was not expected, and precautions to limit the risk of exposing laboratory workers to *Brucella* (a category 3 pathogen) were not taken during microbiology processing of samples. Laboratory staff who were exposed to this isolate of *B. abortus* were followed up in line with UK guidance (Brucella Reference Laboratory, 2013). This did not reveal any evidence of occupationally acquired infection.

Treatment of *Brucella* bursitis involves antimicrobial therapy with or without aspiration or bursectomy. Early authors favoured surgical resection (Johnson & Weed, 1954; Kelly *et al.*, 1960), but in more recent reports medical treatment alone, sometimes with aspiration, has been successful (González-Alvaro *et al.*, 1994; Traboulsi *et al.*, 2007; Wallach *et al.*, 2010). This most likely reflects improvements in antimicrobial treatment for brucellosis. Our patient underwent complete excision of the lesion before the diagnosis had been made. Subsequent treatment was with 6 weeks of oral doxycycline and rifampicin, with intravenous gentamicin for the first 2 weeks. This combination was chosen in the basis of its efficacy in a meta-analysis of brucellosis treatment trials (Skalsky *et al.*, 2008). Twelve weeks of therapy is advised when focal disease is present (Corbel & Beeching, 2011), but a variety of both agents and treatment durations have been used for bursitis (Table 2).

Bursitis is a rare but well-described complication of brucellosis. This case and review of the literature shows that the diagnosis requires a high index of suspicion as clinical features are often non-specific. The diagnosis should be considered in cases of unexplained chronic bursitis, even in countries where brucellosis has been eradicated in domestic animals. Samples for microbiological analysis

should be collected and processed using appropriate precautions to prevent exposure of laboratory staff to the pathogen.

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References

- Akhvlediani, T., Ellis, M. W., Rivard, R., Zenaishvili, O., Battafarano, D. J. & Hepburn, M. J. (2011). A review of the English and Russian language literature on the osteoarticular manifestations of brucellosis infection. *Curr Rheumatol Rev* 7, 263–271.
- Ariza, J., Gudiol, F., Valverde, J., Pallarés, R., Fernández-Viladrich, P., Rufi, G., Espadaler, L. & Fernández-Nogues, F. (1985). Brucellar spondylitis: a detailed analysis based on current findings. *Rev Infect Dis* 7, 656–664.
- Brucella Reference Laboratory (2013)**. Procedural checklist to follow after a laboratory exposure to *Brucella* spp. Distributed by Public Health England https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/348922/BRU_procedural_checklist.pdf
- Cohen, N. D., Carter, G. K. & McMullan, W. C. (1992). Fistulous withers in horses: 24 cases (1984-1990). *J Am Vet Med Assoc* 201, 121–124.
- Colmenero, J. D., Reguera, J. M., Fernández-Nebro, A. & Cabrera-Franquelo, F. (1991). Osteoarticular complications of brucellosis. *Ann Rheum Dis* 50, 23–26.
- Corbel, M. J. & Beeching, N. J. (2011). Brucellosis. In *Harrison's principles of internal medicine*, 18th edn., pp. 1296–1300. Edited by D. L. Longo, A. S. Fauci, D. L. Kasper, S. L. Hauser, J. L. Jameson & J. Loscalzo. New York: McGraw Hill.
- Davis, J. M. & Broughton, S. J. (1996). Prepatellar bursitis caused by *Brucella abortus*. *Med J Aust* 165, 460.
- García-Porrúa, C., González-Gay, M. A., Ibañez, D. & García-País, M. J. (1999). The clinical spectrum of severe septic bursitis in north-western Spain: a 10 year study. *J Rheumatol* 26, 663–667.
- González-Alvaro, I., Estévez, M., Carmona-Ortels, L., Alvaro-Gracia, J. M., López-Bote, J. P. & Humberia, A. (1994). Osteoarticular brucellosis resembling microcrystalline arthropathy. *J Rheumatol* 21, 1783–1785.
- González-Gay, M. A., Blanco, R., García-País, M. J., Alonso, P., Rodríguez, A., Coira, A. & Mayo, J. (1997). Polymicrobial prepatellar septic bursitis caused by *Brucella abortus* and *Streptococcus agalactiae*. *J Clin Rheumatol* 3, 120.

- González-Gay, M. A., García-Porrúa, C., Ibañez, D. & García-País, M. J. (1999).** Osteoarticular complications of brucellosis in an Atlantic area of Spain. *J Rheumatol* **26**, 141–145.
- Guiral, J., Reverte, D. & Carrero, P. (1999).** Iliopsoas bursitis due to *Brucella melitensis* infection—a case report. *Acta Orthop Scand* **70**, 523–524.
- Johnson, E. W. Jr & Weed, L. A. (1954).** Brucellar bursitis. *J Bone Joint Surg Am* **36**, 133–139.
- Kelly, P. J., Martin, W. J., Schirger, A. & Weed, L. A. (1960).** Brucellosis of the bones and joints. *Experience with thirty-six patients. JAMA* **174**, 347–353.
- Kennedy, J. C. (1904).** Notes on a case of chronic synovitis, or bursitis, due to organism of the Mediterranean fever. *J R Army Med Corps* **2**, 178–180.
- Mousa, A. R., Muhtaseb, S. A., Almudallal, D. S., Khodeir, S. M. & Marafie, A. A. (1987).** Osteoarticular complications of brucellosis: a study of 169 cases. *Rev Infect Dis* **9**, 531–543.
- Pourbagher, A., Pourbagher, M. A., Savas, L., Turunc, T., Demiroglu, Y. Z., Erol, I. & Yalcintas, D. (2006).** Epidemiological, clinical and imaging findings in brucellosis patients with osteoarticular involvement. *AJR Am J Roentgenol* **187**, W191–W194.
- Rotés-Querol, J. (1957).** Osteo-articular sites of brucellosis. *Ann Rheum Dis* **16**, 63–68.
- Schirger, A., Nichols, D. R., Martin, W. J., Wellman, W. E. & Weed, L. A. (1960).** Brucellosis: experiences with 224 patients. *Ann Intern Med* **52**, 827–837.
- Skalsky, K., Yahav, D., Bishara, J., Pitlik, S., Leibovici, L. & Paul, M. (2008).** Treatment of human brucellosis: systematic review and meta-analysis of randomised controlled trials. *BMJ* **336**, 701–704.
- Solera, J., Espinosa, A., Geijo, P., Martínez-Alfaro, E., Sáez, L., Sepúlveda, M. A. & Ruiz-Ribó, M. D. (1996).** Treatment of human brucellosis with netilmicin and doxycycline. *Clin Infect Dis* **22**, 441–445.
- Taşova, Y., Saltoğlu, N., Sahin, G. & Aksu, H. S. (1999).** Osteoarthricular involvement of brucellosis in Turkey. *Clin Rheumatol* **18**, 214–219.
- Traboulsi, R., Uthman, I. & Kanj, S. S. (2007).** Prepatellar *Brucella melitensis* bursitis: case report and literature review. *Clin Rheumatol* **26**, 1941–1942.
- Wallach, J. C., Delpino, M. V., Scian, R., Deodato, B., Fossati, C. A. & Baldi, P. C. (2010).** Prepatellar bursitis due to *Brucella abortus*: case report and analysis of the local immune response. *J Med Microbiol* **59**, 1514–1518.