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## Total knee prosthesis infection by *Brucella melitensis*: case report and review of the literature

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**Abstract** We refer a case of total knee prosthesis infected by *Brucella melitensis*: a 74-years-old woman, affected by knee arthritis and operated 9 years before in a different hospital with the implant of a total prosthesis to the left knee. The lapse of time between the joint implant and the onset of the general symptoms of infection was 36 months. The infection localized to the left knee 12 months later. The source was identified with the consumption of a dairy unpasteurized product. The first treatment was conservative by antibiotic cocktail, then the prosthetic implant removal has become necessary. To our knowledge, in the literature only 8 cases of brucellar prosthetic infec-

tion have been previously reported (5 knee and 3 hip prosthesis): in 7 cases *Brucella melitensis* was isolated, in one *Brucella abortus*.

**Key words** Brucellosis • Total knee arthroplasty

### Introduction

Brucellosis is a zoonosis caused by microorganisms of the *Brucella* type. It occurs worldwide, but mainly in the Arabic Gulf area, the Mediterranean zone and in Latin America [1]. In Italy, it is most commonly found in Sicily, with an incidence of 19 cases per 100 000 inhabitants [2].

Primarily, brucellosis is considered an animal disease with humans being a secondary host. Overall, 6 different gram-negative bacteria may be responsible for the infection: *B. melitensis*, *B. abortus*, *B. suis*, *B. canis*, *B. ovnis* and *B. neotomae*. The first four can cause the disease in humans, but *B. melitensis* is the most common pathogen [1]. In humans, there are 2 possible ways of transmission: one is related to professional activities that deal with ani-

mals (e.g. livestock breeding, veterinary medicine, butchery) and one that is related to the consumption of non-pasteurized milk and milk products [1, 2]. In only 15%–20% of all cases is the diagnosis of brucellosis confirmed by culture. Most cases are diagnosed by serology with the agglutination test of Wright [3].

The initial symptoms of a brucellosis infection are non-specific (recurrent fever, excessive sweating, migraine headaches, apathy and asthenia). The most frequent complications affect the osteoarticular complex and can include polyarthralgia, spondylitis, sacroiliitis, coxitis, osteomyelitis and aseptic arthritis. Because brucella organisms grow intracellularly, it is necessary to use an antibiotic that not only is active against the brucella bacteria but is also able to penetrate the cell membrane. Tetracycline, rifampicin, co-trimoxazole and ami-

noglycosides all respond to these two criteria. The combination of doxycycline, rifampicin and streptomycin is the therapy of choice, especially in patients with complications such as spondylitis. The total duration of therapy in order to totally eradicate the infection is not known, although 6 weeks of treatment is considered to be the absolute minimum [3, 4].

Here, we describe a rare case of brucellosis that localized in the left knee prosthesis. To our knowledge, only 8 other cases of this infection involving prosthetic hip and knee joints have been reported.

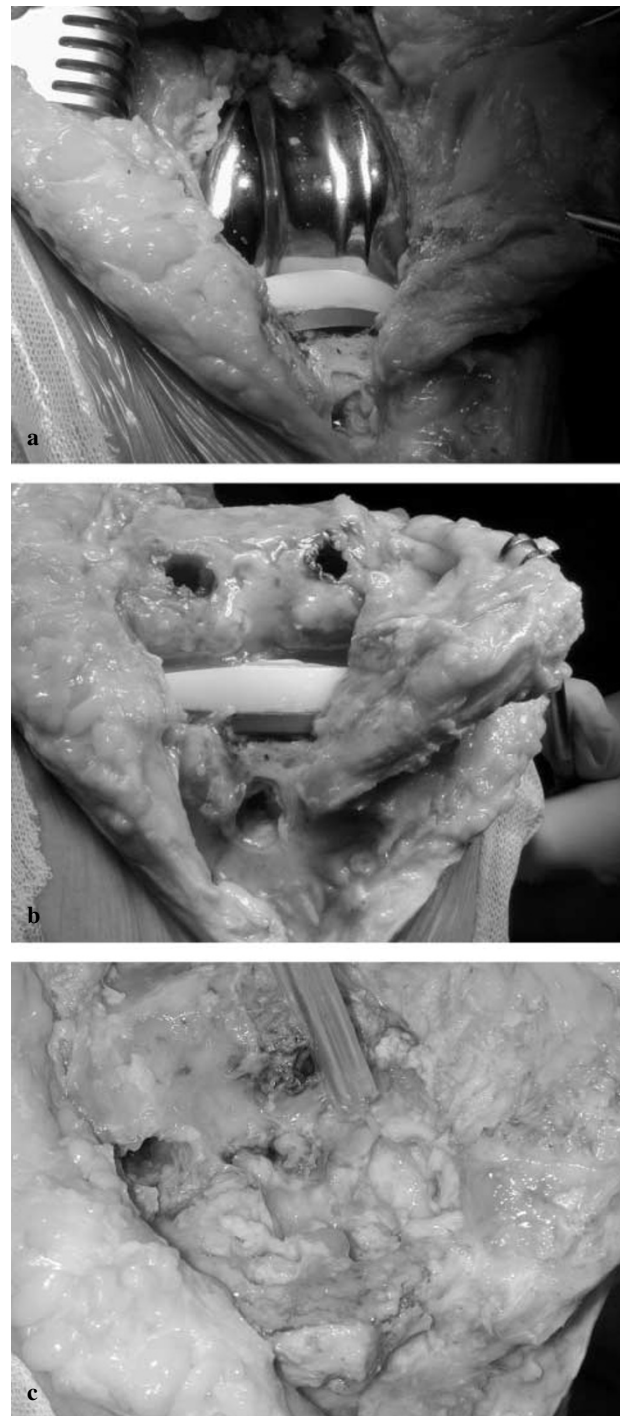
### Case report

In 1993, a 65-year-old Sicilian woman suffering from arthrosis of the left knee underwent total knee arthroplasty. In March 1996, she complained of recurrent febrile attacks, apathy and astenia for which she became hospitalised and subsequently diagnosed of having a *Brucella melitensis* infection. She reported having consumed fresh non-pasteurized milk products 2 months previously. Three weeks after dismissal from hospital, she represented with the same symptoms and needed another recovery in hospital.

In 1997, the brucella infection was localized in the left knee prosthesis and presented with all the signs of acute arthritis: cutaneous redness, swelling, pain, functional impairment and fever up to 40° C. The patient was again hospitalized. After therapy with antibiotics, her general and local conditions improved. A cultural exam of intra-articular fluid did not isolate any pathogenic microorganisms. In the next couple of years, the patient did relatively well.

Only in April 2002, at the age of 74 years, she presented again with a severe left gonalgia with cutaneous redness, edema and functional impairment. The indicators of inflammation, i.e. erythrocyte sedimentation rate (ESR = 105) and C-reactive protein (CRP = 434), were raised and the agglutination test of Wright was positive (titres >1:160). Radiographs and an osseous scintiscan with gallium Ga 67 citrate (74 MBq) confirmed the septic mobilisation of the prosthesis. Therefore, the prosthesis was removed and a layer of antibiotic-containing cement (poly-methyl-methacrylate and gentamicin) was added.

Surgical revision revealed the presence of abundant necrotic tissue and exudate, responsible for the septic mobilisation (Fig. 1). Culture from an intra-operative specimen revealed the presence of *B. melitensis*. Consequently, antibiotic therapy was started using streptomycin sulphate (1 g/day intramuscularly) and doxycycline hyclate (100 mg per os twice daily). After 30 days, serodiagnosis was negative (ESR, 57 mm/h; CRP, 44.4 mg/l) and the patient was dismissed from hospital.



**Fig. 1a-c** Surgical revision of a knee prosthesis infected with *Brucella melitensis*. **a** Arthrotomy and exposition of the prosthesis. **b** After removal of the femoral prosthesis, metallosis, bone necrosis and loss of bone matter on the tibial section communicating with purulent harvest were observed. **c** The tibial and femoral ends as they appeared below the prosthetic components

In June 2002, the patient had another check-up which revealed an infrapatellar fluctuating swelling covered by discoloured skin and antalgic flexion of the knee at 30°.

A surgical toilet was performed with subsequent continuous drainage. A different combination of antibiotics was administered: doxycycline hyclate (100 mg per os twice daily), rifampicin (900 mg/day iv) and levofloxacin (500 mg/day iv). After 7 days, the drain was removed and the patient was dismissed. A further decline in the parameters of infection (ESR, 16 mm/h; CRP, 7.4 mg/l) and negativity of the serodiagnosis of Wright were observed. Antibiotic therapy was continued for another 6 months. During a check-up in the beginning of 2003, the patient was proposed a new prosthesis which she refused.

## Discussion

The incidence of infection of total hip and knee prostheses during the first 2–10 years after operation is 5.9 and 2.3 per 1000, respectively [5].

The majority (65%) is caused by aerobic gram-positive cocci, most frequently by *S. aureus*, coagulase-positive

staphylococci and enterococci. The aerobic gram-negative bacilli *Escherichia coli*, *Proteus mirabilis* and *Pseudomonas aeruginosa* are less commonly the causative agent (6%). Anaerobic organisms account for 4% of all infections, while infections by fungi and microbacteria are absolutely unusual [4]. Brucellosis is a disease that causes both acute and chronic manifestations. It is a systemic disease in which every organ can be affected [1]. Osteoarticular complications are common (up to 10%–85% of all cases) and can manifest as sacroiliitis, arthritis, spondylitis, osteomyelitis, tenosynovitis and borsitis [6–8].

In the literature, we found only 8 other cases of prostheses infected by *Brucella sp* (Table 1). Including the present case of a total of 9 patients, there were 7 males and 2 females. Median age was 57.5 years. All patients had consumed fresh unpasteurized milk or goat cheese or had been exposed professionally; 8 patients originated from an endemic area [3, 4, 9, 10]. In 6 cases there was infection of the knee prosthesis; in 3 cases the hip prosthesis was affected. The average time from implantation to manifestation of the infection was 42.1 months. In our

**Table 1** Characteristics of patients with prosthetic brucellosis

Reference	Age, years	Gender	Profession	Country	Implant site	Risk factor of comorbidity	Time from implantation to infection	Symptomatology
Jones et al. [9]	54	M	Farmer	USA	Hip	-	5 months	Systemic
Agarwal et al. [3]	24	F	NG	Saudi Arabia	Knee	Juvenile rheumatoid arthritis	2 months	Local
Malizos et al. [10]	74	M	Shepherd	Greece	Knee	-	4 months	Local
Ortì et al. [8]	60	M	Sheep farmer	Spain	Knee	Idiopathic osteonecrosis (medial femoral condyle)	14 months	Local
Weil et al. [4]	38	M	Artist	Israel	Hip	Psoriatic arthritis	4 years	Local
	64	M	Retiree	Israel	Knee	Hip arthrodesis Previous prosthetic infection <sup>a</sup>	2.5 years	Local
	67	M	Retiree	Israel	Knee	Arthrosis	14 years	Systemic
Ortega-Andreu et al.	63	M	Cattle farmer	Spain	Hip	-	5 years	Local
Present case	74	F	Retiree	Italy	Knee	Arthrosis	4 years	Systemic

<sup>a</sup> Popliteal abscess and septic arthritis from *Acinetobacter sp*; NG, not given

case, general symptoms started 3 years after the intervention and the knee was affected another year later.

The biggest problem in diagnosing prosthetic brucella infections is the aspecific and confounding character of the symptoms and clinical signs. Cultural examination of the synovial fluid performed in another hospital during the first arthrocentesis (1997) was negative. When the patient was recovered in our hospital in 2002, laboratory results were slightly changed but non-specific. Once the septic mobilisation of the prosthesis with osseous deficit was proven by radiography and scintigraphy, a revision operation was performed (9 years after implantation, 6 years after the systemic brucella infection, and 5 years after the operated knee was affected). Only then was the brucella infection confirmed by cultural examination of intra-operative synovial fluid.

As a fact, isolation of brucella from the synovial fluid obtained preoperatively through arthrocentesis is only possible in 50% of all cases [7], but a negative test does not exclude osteoarticular brucella infection. In these patients, there is always a high titre of specific antibodies (>1:160). There is much controversy about how osteomyelitis and arthritis caused by brucella should be treated, especially regarding the choice of antibiotics, the duration of therapy and the role of surgery [4]. In 1986, the WHO recommended the combination of doxycycline and rifampicin (600–900 mg/day) for a period of 6 weeks. Further

studies that compared the combination doxycycline + rifampicin to doxycycline + streptomycin favoured the second combination, especially in patients with complications such as spondylitis [11, 12]. Similarly, the use of quinolones was disappointing despite a good reaction in vitro and a good cellular penetration [11]. As a consequence, the quinolones are more often recommended as additional therapy [11].

The total duration of treatment is not well known yet. Generally, 6 weeks of treatment is seen as a minimum in order to suppress the infection which has to be proven by cultural exam [4, 12]. Our case was treated for 8 weeks. On the contrary, the surgical approach to brucella infection of a prosthesis is not well-defined, because of the lack of randomized controlled studies on large scale [4]. It seems reasonable to save the prosthesis only in absence of aseptic mobilisation or in patients with a relatively acute onset of infection [9]. If reimplantation is the option, the optimal timing for surgery is not known. The disease is indolent and there are no accurate tests to show that infection is taking place. In the literature, it is recommended to wait for a longer time than one should wait in the case of more common microorganisms [10]. The 'two-stage' procedure which we use in cases of prosthesis infection allows preparation of the surgical equipment and provision of special revision prostheses. In the present case, reimplantation of the prosthesis was not performed because the patient refused.

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