

Brucellosis mimicking Henoch–Schönlein purpura

David Massasso and Kathryn Gibson

A young male immigrant from Syria with a vasculitic-appearing leg rash, asymmetrical polyarthritis, microscopic haematuria, and raised inflammatory markers was provisionally diagnosed with Henoch–Schönlein purpura. Skin biopsy showed leukocytoclastic vasculitis. Low-grade fevers persisted despite non-steroidal anti-inflammatory therapy, and Brucella sp. was subsequently grown from both blood and synovial fluid aspirates. Further tests gave positive results for B. abortus, and triple antibiotic therapy produced a rapid clinical response. Cutaneous vasculitis has rarely been described in brucellosis, and this is the first report in the English medical literature of brucellosis mimicking Henoch–Schönlein purpura. (MJA 2007; 186: 602-603)

Clinical record

A 22-year-old man presented with arthralgia, fevers, weight loss and a leg rash. His medical history was unremarkable, and he was taking no medications. He had emigrated from Syria 2 months before to be with his family in Australia. He had been sexually active before emigration, but did not describe any illness consistent with a sexually transmitted disease.

One month before presentation, the patient had left elbow pain and swelling, with subsequent involvement of the left knee, right ankle and foot. One week later, he developed a dry cough and night sweats. The non-pruritic leg rash started 1 week before presentation, ascending gradually to his knees. He had lost 8 kg in weight over the preceding weeks. Blood tests performed 2 weeks before admission showed: C-reactive protein (CRP) level, 18 mg/L (reference range [RR], 0–8 mg/L); erythrocyte sedimentation rate (ESR), 32 mm/h (RR, 1–20 mm/h); and a raised rheumatoid factor of 50 IU/mL (RR, < 40 IU/mL).

The patient presented to the emergency department with progressive leg rash and difficulty walking because of knee pain. At initial examination he had a temperature of 38°C, and an erythematous maculopapular rash with a vasculitic appearance on his feet, with discrete lesions on the leg distally and a more confluent appearance around both knees. There was an oligoarthritis involving the left elbow, both knees, right ankle and right metatarsophalangeal joints, as well as axillary lymphadenopathy. Urinalysis showed a large amount of blood, with no dysmorphic cells or casts.

The provisional diagnosis was Henoch–Schönlein purpura. Laboratory investigations showed a CRP level of 91 mg/L, an ESR of 78 mm/h, and a γ -glutamyl transferase (GGT) level of 118 U/L (RR, < 61 U/L), with other liver tests, a full blood count and renal function tests giving normal results. A blood and urinary vasculitic screen, including antinuclear antibody and serum complement tests, gave negative results, apart from high levels of anti-dsDNA antibodies (> 100 IU/mL; RR, 0–7 IU/mL). Other tests for an infectious cause including HIV, hepatitis B, hepatitis C, Epstein–Barr virus, cytomegalovirus, syphilis and streptococcal antigens gave negative results. His serum angiotensinogen-converting enzyme level was not raised. A 3 mL aspirate of blood-stained synovial fluid from the right knee was non-inflammatory. Skin biopsy from the leg showed leukocytoclastic vasculitis with IgA immunofluorescence of dermal vessels, consistent with Henoch–Schönlein purpura, and a Gram stain gave negative results.

Over the next few days, the oligoarthritis improved with non-steroidal anti-inflammatory therapy, but low-grade fevers contin-

ued and a repeat test of his CRP level showed it was still raised (37 mg/L). The haematuria had resolved. Subsequently, microscopy and culture of both blood (aerobic bottle) and synovial fluid samples showed gram-negative rods, which were identified as belonging to the genus *Brucella*. Antibody testing for *Brucella abortus* was highly positive (agglutinins, > 1280). Computed tomography scanning of the thorax and abdomen revealed axillary, mesenteric and para-aortic lymphadenopathy, and a radionuclide bone scan showed peripheral arthritis in several sites with no spinal involvement. Transoesophageal echocardiogram showed no evidence of endocarditis.

On further questioning, the source of *Brucella* organisms was thought to be cheese or yoghurt made from unpasteurised milk, consumed before emigrating to Australia. There were no close contacts of the patient who were unwell. Both the hospital's Infection Control Team and the Sydney South West Public Health Unit (Liverpool Hospital) were notified of the case.

The patient was given triple antibiotic therapy of gentamicin, doxycycline and rifampicin, which led to further improvement, and he was discharged after 2 weeks. At discharge, he was fully ambulant, with resolution of joint pain, fevers and rash. He completed a course of gentamicin for 3 weeks and oral antibiotics for 6 weeks. After taking antibiotics for 3 weeks, the CRP level had normalised and the GGT level was still raised at 126 U/L. Repeat tests for anti-dsDNA antibodies at 6 months gave normal results (3 kIU/L).

Discussion

Brucella melitensis was first isolated in 1887 by the Australian-born microbiologist, David Bruce, from human spleens of patients suffering from Malta fever or undulant fever. Brucellae are gram-negative, facultative intracellular bacteria, which represent a major global zoonosis.¹ Brucellosis is a systemic infection that can involve any organ.²

The different *Brucella* species are named for their preferred animal hosts. *B. melitensis* (principally goats and sheep) and to a lesser extent *B. abortus* (particularly cows) are the two species most closely associated with human infection because of higher virulence compared with other species.³ High-risk foods associated with acquisition of *Brucella* spp. include unpasteurised dairy products, particularly raw milk, soft cheese, butter and ice cream.³ Brucellosis is rarely transmissible by humans, and the major infectious risk relates to infection from a common food or animal tissue source.²

Brucellosis remains a significant global disease affecting the Middle East, Africa, the Indian subcontinent, Mexico and Central America, as well as parts of Europe including Spain, Greece and Turkey. However, eradication of brucellosis has been effective in certain countries such as Australia, New Zealand and the United Kingdom through stringent agricultural practice.²⁻⁴ While animal vaccines are available, there is no human vaccine.

As seen in our patient, brucellosis most commonly affects adolescents and young adults. The onset of symptoms is generally 2–4 weeks after inoculation, although with chronic infection a pattern of undulant fever is described.²

Clinical manifestations of brucellosis are protean. Cutaneous lesions in brucellosis are unusual,⁵ and cutaneous vasculitis has only rarely been reported.^{6,7} Although dermal IgA deposits have been rarely described in association with *Brucella*-associated vasculitic rash,⁶ this is the first case of brucellosis mimicking Henoch–Schönlein purpura. Skin lesions are usually sterile,^{6,7} but *B. melitensis* has been cultured from a skin biopsy in a patient with arthritis and papulonodular rash.⁵

In contrast to skin disease, osteoarticular involvement is common.⁴ The major osteoarticular manifestations include peripheral arthritis, sacroiliitis and spondylitis. Most frequently involved are the hip, knee and ankle joints. Although a large-joint monoarthritis is the usual presentation of peripheral arthritis, both oligoarthritis and a rheumatoid-like pattern occur.⁴ In many cases of monoarthritis, *Brucella* spp. is not cultured from synovial fluid.⁸ In polyarthritis, the frequency of bacterial isolation from synovial fluid is unclear.^{9,10}

Diagnosis of brucellosis is based on tissue-specific and serological tests. Definitive diagnosis of brucellosis is by isolation of bacteria from body tissue, including blood, bone marrow or synovial fluid. Presumptive diagnosis can be made by specific antibody tests against bacterial lipopolysaccharide or other bacterial antigens. Both high or rising titres of antibodies may aid in the diagnosis.²

Treatment of brucellosis is most effective with combination antibiotic therapy, as monotherapy often results in relapse. Effective antibiotics are those that can penetrate macrophages and work in an acidic environment. Antibiotics generally employed include: gentamicin, doxycycline, rifampicin, co-trimoxazole, quinolones and streptomycin.³ Oral treatment regimens are often based around doxycycline, and the duration of oral therapy is usually 6 weeks. Neurobrucellosis and endocarditis usually require longer treatment periods. Incomplete duration of therapy or an inade-

quate treatment regimen can result in disease relapse, and chronic infections are usually associated with deep foci of infection.²

This case highlights the diagnostic variability of the presentation of brucellosis and its ability to mimic systemic vasculitic disease, in particular Henoch–Schönlein purpura. This is of particular importance in patients who have recently emigrated from or travelled to high prevalence areas, especially with exposure to unpasteurised animal products.

Competing interests

None identified.

Author details

David Massasso, MB BS, BSc, FRACP, Rheumatologist
Kathryn Gibson, BM BCh, FRACP, PhD, Director, Department of Rheumatology
Liverpool Hospital, Sydney, NSW.
Correspondence: david.massasso@dr.nswama.com.au

References

- Cutler SJ, Whatmore AM, Commander NJ. Brucellosis — new aspects of an old disease. *J Appl Microbiol* 2005; 98: 1270-1281.
- Young EJ. *Brucella* species. Chapter 223. In: Mandell GL, Bennett JE, Dolin R, editors. Principles and practice of infectious diseases. 6th ed. Philadelphia: Churchill Livingstone, 2005: 2269-2272.
- Pappas G, Akritidis N, Bosilkovski M, Tsianos E. Brucellosis. *N Engl J Med* 2005; 352: 2325-2336.
- McGill PE. Geographically specific infections and arthritis, including rheumatic syndromes associated with certain fungi and parasites, *Brucella* species and *Mycobacterium leprae*. *Best Pract Res Clin Rheumatol* 2003; 17: 289-307.
- Ariza J, Servitje O, Pallares R, et al. Characteristic cutaneous lesions in patients with brucellosis. *Arch Dermatol* 1989; 125: 380-383.
- Perez C, Hernandez R, Murie M, et al. Relapsing leucocytoclastic vasculitis as the initial manifestation of acute brucellosis. *Br J Dermatol* 1999; 140: 1177-1178.
- Nagore E, Sanchez-Motilla JM, Navarro V, et al. Leukocytoclastic vasculitis as a cutaneous manifestation of systemic infection caused by *Brucella melitensis*. *Cutis* 1999; 63: 25-27.
- Khateeb MI, Araj GF, Majeed SA, Lulu AR. Brucella arthritis: a study of 96 cases in Kuwait. *Ann Rheum Dis* 1990; 49: 994-998.
- Bosilovski M, Krteva L, Caparoska S, Dimzova M. Osteoarticular involvement in brucellosis: study of 196 cases in the Republic of Macedonia. *Croat Med J* 2004; 45: 727-733.
- Geyik MF, Gur A, Nas K, et al. Musculoskeletal involvement of brucellosis in different age groups: a study of 195 cases. *Swiss Med Wkly* 2002; 132: 98-105.

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