Acute Brucellosis Presenting as Cellulitis

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Sir,

Brucellosis, a worldwide anthropozoonosis, is an infectious disease caused by bacteria of the genus *Brucella*, a Gram-negative, facultative intracellular pathogen affecting a wide range of mammals, including domestic animals and humans. The heaviest burden of this disease lies in countries of the Mediterranean basin and Arabian Peninsula, northern and eastern Africa, Near Eastern countries, central Asia, Mexico, and Central and South America. It is transmitted to humans mainly through ingestion of infected unpasteurized raw milk or dairy products, but also subsequent to direct contact with infected animals or, rarely, humans, and through the inhalation of contaminated particles. Human brucellosis is a systemic disorder with protean clinical manifestations, the diagnosis of which represents a great challenge to physicians and is definitely established through the isolation of *Brucella spp*. from clinical specimens and the detection of specific antibodies (1).

The purpose of this paper is to draw attention to the presentation of acute brucellosis as cellulitis, which to the best of our knowledge, has not been reported previously.

CASE REPORT

A 43-year-old woman with a 4-week history of malaise and fever was admitted to the Department of Dermatology at the University of Patras Medical Center for a painful skin lesion on her lower left leg that had developed one week prior to her admission without any preceding trauma. Her personal and family medical history was unremarkable. During the preceding months she had received no systemic or topical drugs and had not been treated with either phototherapy or photochemotherapy. On admission the patient appeared well, her temperature was 38ºC, her blood pressure was 110/70 mmHg and her heart rate was 96 beats/min. Physical examination revealed an erythematous, oedematous, tender and painful area of her left distal calf, the borders of which were neither sharply defined nor elevated. Lymph nodes were not palpable and no portal of entry could be found. Blood was drawn for cultures and a skin biopsy was scheduled but refused by the patient. Laboratory tests showed the following: haematocrit 37.7%; haemoglobin 13.4 g/dl; white blood cells 4520 cells/mm^3; neutrophils 47.5%; lymphocytes 34.8%; monocytes 15.9%; platelets 245000/mm^3; erythrocyte sedimentation rate 30 mm/h. C-reactive protein, anti-streptolysin titre, rheumatoid factor, prothrombin time, partial thromboplastin time, international normalized ratio and fibrinogen were negative or within normal limits. Apart from a slight increase in alanine aminotransferase (53 U/l; normal: 5–40 U/l), all biochemical parameters and urinalysis were normal. Serum autoantibodies, immunoglobulins, C_3 and C_4 components of complement and immunophenotype of peripheral lymphocytes showed no abnormalities. Serological tests for syphilis, HIV 1 and 2, hepatitis B and C, cytomegalovirus, *Borrelia burgdorferi* and tuberculin skin test were negative, chest and left leg X-ray and electrocardiogram were unremarkable. Ultrasound scan of the abdomen and the left leg revealed no abnormalities.

Initially, an empirical therapeutic regimen comprising intravenous ciprofloxacin (400 mg twice daily) and clindamycin (600 mg 4 times daily) was administered that led to a slight clinical improvement. On day 3 blood cultures performed on specimens obtained at the time of admission and incubated in blood agar (in CO_2 atmosphere at 37ºC) yielded a coccobacillus identified as *Brucella melitensis* on the basis of Gram's stain, colonial morphology, positive oxidase, catalase and urease tests and negative hydrogen sulphide production test. Additionally, *Brucella agglutinin* titre was found to be positive at 1:1280. Thus, the diagnosis of brucellosis was established. Interestingly, upon repeated questioning the patient conceded to consumption of unpasteurized goat cheese about 5–6 weeks prior to the onset of her symptoms. Administration of clindamycin was discontinued. Since the patient expressed serious concerns about the possible adverse reactions of first-line drugs such as streptomycin, gentamicin, trimethoprim-sulphamethoxazole and rifampin, intravenous application of ciprofloxacin (400 mg twice daily) combined with oral doxycycline (100 mg twice daily) was initiated and resulted in a rapid and dramatic clinical response. By 7 days after onset of this treatment both the patient's symptoms and her skin lesions had completely resolved. Drug administration was discontinued on completion of 6 weeks of treatment. Six weeks after completion of therapy the *Brucella agglutinin* titre became negative.

DISCUSSION

Since the first description of the cutaneous lesions occurring in patients with brucellosis by Hughes in 1897

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(2), a considerable amount of clinical information has emerged indicating that a wide spectrum of solitary, multiple or generalized cutaneous manifestations (Table I) can develop either during the first outbreak of the disease or in the course of its relapse in 5–14% of infected patients (3–7). However, due to the non-specific and mostly transient nature of the skin lesions, which respond readily to antibiotic treatment, their diagnosis is often missed; it seems reasonable, therefore, to suggest that their prevalence in patients with brucellosis is higher than presently assumed. Cutaneous manifestations of brucellosis are caused, subsequent to haematogenous spread of *Brucella* or direct inoculation of the skin, by mostly immunological mechanisms that are far from being clearly understood. However, in view of the paramount importance of dendritic cells in cutaneous immunological potential, it is possible that these cells, apart from serving as a highly permissive host for *Brucella* development and dissemination (8), may be also implicated in the pathogenesis of cutaneous lesions associated with brucellosis.

Cellulitis is a commonly occurring infection of the skin and the subcutaneous tissues that, if not treated appropriately, has the potential to cause life-threatening complications. To the best of our knowledge, this is the first reported case of acute brucellosis presenting as cellulitis; it merits particular attention since it represents a new and severe form of cutaneous manifestation of this disorder due to the haematogenous spread of the causative bacteria. Due to the severity of the clinical picture and the lack of available microbiological culture data on admission we initially administered an empirical antibiotic therapy, comprising intravenous ciprofloxacin and clindamycin, in order to ensure adequate eradication of a wide spectrum of possible causative pathogens.

Table I. *Cutaneous manifestations of brucellosis*

Primary inoculation abscess
Brucellar dermatitis
Leukocytoclastic, granulomatous or necrotizing vasculitis
Thrombophlebitis, thrombotic microangiopathy
Livedo reticularis, purpura and petechiae
Contact urticaria
Erythema nodosum and erythema nodosum-like lesions
Fasciitis-panniculitis, liquefactive panniculitis
Multiple cutaneous and subcutaneous abscesses, ulcers and scars
Diffuse maculopapular and papulonodular eruption
Malar erythema, oedema
Pityriasis rosea-like eruption
Eczematous, psoriasiform or impetiginous lesions
Recurrent epidermal cyst

Since our patient refused the proposed biopsy from the lesional skin for tissue culture, the possibility that her cellulitis might have been caused by another pathogen that favourably responded to the administered broad-spectrum antibiotic regimen cannot definitely be ruled out; however, this hypothesis seems very unlikely, in view of the absence of portal of entry and preceding trauma, the isolation of *Brucella* from blood culture, the initially high *Brucella agglutinin* titre and its rapid decline after successful treatment and the rapid and dramatic therapeutic response to the combined administration of doxycycline and ciprofloxacin. This response supports the results of previous reports, indicating that combinations that incorporate ciprofloxacin may yield therapeutic efficacy in the management of brucellosis comparable to that of the classical regimens (9). In conclusion, the case described here indicates that brucellosis should be considered in the differential diagnosis of cellulitis, particularly in patients from *B. melitensis* endemic areas.

The authors declare no conflicts of interest.

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