

Pyelonephritis due to *Brucella* species: true clinical entity or ghost disease?

N. G. Vallianou, E. Geladari, K. Trigkidis and E. Kokkinakis

First Department of Internal Medicine, Evangelismos General Hospital, Athens, Greece

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Corresponding author: N.G. Vallianou, 5 Pyramidon str, 19005, Municipality of Marathonas, Athens, Greece
E-mail: natalia.vallianou@hotmail.com

Brucellosis is a chronic granulomatous infection caused by intracellular Gram-negative bacteria belonging to *Brucella* species. While uncommon in the United States, northern Europe and Eastern Asia, it is common in the Middle East, southern Europe, and South America [1]. Human brucellosis is a potentially life-threatening multisystem disease which requires combined and prolonged treatment with antimicrobial agents.

Genitourinary system involvement occurs in 2 to 20% of patients with brucellosis and includes prostatitis, epididymo-orchitis, cystitis, pyelonephritis, interstitial nephritis, exudative glomerulonephritis and renal abscesses. Because of its nonspecific symptoms, infections of the urinary tract due to *Brucella* species often remain underdiagnosed and underreported [2]. Epididymis seems to be the most often affected organ of the genitalia and lower urinary tract. Epididymitis due to *Brucella* species may cause serious complications if left untreated, such as necrotizing orchitis, aspermia or oligospermia [3].

To our knowledge, genitourinary complications of brucellosis have rarely been reported in the medical literature, not to mention pyelonephritis due to *Brucella* species, which has barely been documented [4]. Specifically, only three cases of documented pyelonephritis due to *Brucella* species have been confirmed with a positive urine culture for *Brucella* species together with pyuria and/or urinary tract infection symptoms [4]. In the same study, which involved 390 patients with genitourinary brucellosis, pyelonephritis was diagnosed in another 30 female patients using extra laboratory tests, such as blood

cultures, bone marrow cultures and positive antibody titres of >1/160 for *Brucella* species (Wright test). Interestingly, pyelonephritis due to *Brucella* species (33/38, 86.8%) was significantly higher in female than in male patients (11/352, 3.1%) ($p < 0.0001$). Recently a case of pyelonephritis was documented that presented with fever, dysuria, flank pain and pyuria together with a positive Wright test and a positive blood culture; the case was confirmed by PCR [5].

We report a case of pyelonephritis due to *Brucella* species in a female patient who presented with a temperature of 39.1°C and left flank pain with tenderness on palpation, pyuria with >100 leukocytes in the microscopical urine examination, a negative urine culture but three blood cultures that grew *Brucella* species and a positive Wright test of $I > 1280$ titre. Although *Brucella* pyelonephritis has been reported to occur in conjunction with endocarditis, the transesophageal ultrasound was negative for vegetations in our patient. Nevertheless, because of imminent bacteraemia we performed magnetic resonance imaging, which revealed sacroiliitis, a finding that could explain the prominent bacteraemia. In addition, pyelonephritis due to *Brucella* species may not always be associated with endocarditis but just with bacteraemia from a usual site of involvement in brucellosis, such as spondylodiscitis, as occurred in our patient. The patient was first administered amikacin and cefuroxime intravenously, but this regimen changed after the correct diagnosis was established to gentamicin 5 mg/kg iv daily for 6 weeks combined with doxycycline 100 mg \times 2 and rifampin 600 mg daily by mouth for 6 months in total, the result of the occurrence of *Brucella* sacroiliitis apart from pyelonephritis. The patient remained well 1 year after the completion of the treatment.

The above-mentioned findings pose some questions regarding the diagnosis of pyelonephritis due to *Brucella* species. Firstly, in most cases the urine culture was negative. This phenomenon could be explained by the fact that urine cultures are routinely performed on MacConkey agar plates, where *Brucella* species cannot be grown. Secondly, even in 5% sheep's blood agar plates, where *Brucella* species can be grown, the sensitivity of a urine culture for *Brucella* species is very low. Thirdly, even in 5% sheep's blood agar plates, the sensitivity of a positive blood culture ranges from 15 to 70%. Also, the plates should be incubated and subcultures should be performed for 4 weeks [1]. Lastly, 5% sheep's blood agar plates should be incubated not only for 24 hours, as is routinely performed with urine cultures, but for a much longer time, as *Brucella* species are small, difficult-to-cultivate, Gram-negative coccobacilli which resemble fine grains of sand [1]. Therefore, routine urine cultures cannot yield *Brucella* species, and brucellosis should be suspected in every febrile disease with pyuria and negative urine

cultures, just as tuberculosis—also a granulomatous disease—should be included in the differential diagnosis, especially in endemic areas.

In conclusion, pyelonephritis due to *Brucella* species is difficult to diagnose, which could be the reason for the rarity of reports of this clinical entity. Clinicians should suspect brucellosis in cases of pyelonephritis with negative urine cultures, especially where the disease is endemic.

Conflict of Interest

None declared.

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