



## Case report

## Brucellosis: A cause of meningitis not to neglect



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## ABSTRACT

Brucellosis is the most frequent bacteria zoonosis in the world, with more than half a million new cases each year [1]. It is also the most significant zoonosis in the edge of the Mediterranean Sea [2]. This zoonosis is capable of affecting humans and cause polymorphic clinical manifestations. In Morocco, the southern regions are the main affected areas [3].

We are reporting the observation of a 17-year-old male patient, who presented a febrile meningeal syndrome for 9 months without sensitive-motor deficit. Tuberculosis is frequently evoked in such clinical presentations because Morocco is an endemic country, brucellosis is therefore often forgotten. The results of lumbar puncture, magnetic resonance imaging (MRI) and especially serology aided to conclude to a neuro-brucellosis. The outcome was favourable with antibiotic therapy.

## Background

Brucellosis is a worldwide zoonosis. It is caused by a bacterium in the genus *brucella*. The WHO estimates that the infection is responsible for more than 500,000 cases per year across the world [4]. Although the disease has been reported in most countries, the exact number of people affected remains unknown, The WHO considers that the actual incidence is 10–25 times the declared cases [5]. It is endemic in North Africa and remains a public health problem in the Maghreb countries and often underestimated, his epidemiological situation remains unknown [6].

*Brucella melitensis* biovar 3 is the species responsible for human brucellosis and animal brucellosis mainly small ruminants.

In Morocco, seroprevalence in livestock is 1.5%. The most affected regions are the southern of Morocco with a rate between 2.8% to 3, 3% [5].

Brucellosis is characterised by its clinical polymorphism, the involvement of the Central Nervous System (CNS) remains rare and constitutes 4–13%; the meningeal infection is the most common presentation [7]. As tuberculous meningitis is the first diagnosis to be mentioned especially in an endemic country like Morocco, brucellosis is often missed. In Morocco, only a single case has been reported in the literature [5]. Here, we report a second documented case of neuro-brucellosis.

## Observation

A 17-year-old man, living in a metropolis in the south of the country, with no medical history, was admitted to the emergency ward with complaints of a chronic headache evolving for 9 months with some episodes of vomiting and intermittent fever. There had no visual deficit or limb weakness or balance impairment. He received empiric antibiotic in fever episodes without real improvement. On examination, the patient was conscious, febrile (39 °C) with stiff neck without limb deficit but some brisk reflexes on the lower limbs. Fundus examination was normal. Cerebrospinal fluid (CSF) was at high pressure and showed 90 cells (neutrophils 56%, lymphocytes 44%), proteins 4,11 g/l, glucose 3.06 mg/dl (blood glucose: 108.1 mg/dl).

Gram stain was normal. Soluble antigens screen using Wellcozyme Oxoid® eliminated other pathogens of meningitis. CSF GeneXpert investigation was negative excluding *mycobacterium tuberculosis* complex.

CSF culture in blood medium grew *brucella melitensis* while blood culture (BACTEC™ 960 BC system, Becton-Dickinson) remained negative after 3 weeks of incubation.

Blood formula showed haemoglobin of 10 g/dl with normal WBC and platelets, sedimentation rate, electrolytes, kidney and liver testing. CRP was mildly positive at 13.1 mg/l

Rose Bengal test (Brucellosis slide BioMerieux® France) was positive in the serum and CSF. CSF Wright test (brucella wright biorad®, France)

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was positive with a titer of 640. Other serological tests for syphilis, human immunodeficiency virus (HIV), hepatitis B and C virus and *Borrelia* were negative.

Magnetic resonance imaging (MRI) showed evocative signs of a leptomeningitis with meninges thickening especially in posterior cerebral fossa and spinal cone.

Thoraco-abdominal computed tomography (CT-Scan) showed lymph nodes in the stomachic coronary chains and the coeco-colo-appendicular regions, and discrete anterior vertebral collapse of the D11 without instability signs.

Electroencephalography showed slow spikes in the left temporal lobe. Ophthalmological examination was normal.

We concluded to neurobrucellosis diagnosis. The patient was given rifampicin 900 mg/d, doxycycline 200 mg/d for 3 months. Clinical and biological outcome was favourable.

## Discussion

We reported here what we consider the second case of neurobrucellosis in Morocco. But due to the underestimated incidence of the disease, the lack of reported cases, are likely due to non diagnosed nor declared and then not published ones.

Neurological impairment during brucellosis is a rare but serious complication. It occurs in 2–5% of cases [8]. Neurobrucellosis is characterised by a clinical polymorphism. It can mimic all neurological diseases [9]. Meningitis is the most frequent form; it can evolve in an acute or chronic mode [10]. In general, it is more likely to be chronic [11]. This is the case of our patient who presented chronic meningitis evolving for 9 months.

The neurological manifestations are various: encephalitis, meningo-encephalitis, meningo-myelorradiculitis or even a psychiatric form [12]. It can sometimes cause a pseudo-tumor with normal CSF. Uncommon cases of neurobrucellosis were described with demyelination in adults imitating multiple sclerosis. This form is frequent in adult and has not been seen in children or teenagers [8].

*Brucella* bacteria may affect the nervous system directly or indirectly, as a result of cytokine or endotoxin effect on the neural tissue. Activation of microglia and cytotoxic T lymphocytes are implicated in the path-physiology of this disease. Infection triggers the immune mechanism leading to demyelinating lesions of brain and spinal cord [13].

The radiological diagnosis of neurobrucellosis is based on the existence of a CNS images not explained by any other neurological disease [14]. Only 45 % of patients affected with neurobrucellosis present radiological abnormalities. The radiological findings can be grouped in 4 categories: (i) Inflammatory lesions: cerebral abscess, granulomas and arachnoiditis, leptomeningeal lesions, basal meningeal or cranial nerves impairments, (ii) White matter impairment with or without demyelinating lesions, (ii) Vascular lesions with chronic ischemic cerebral disease, (iv) Hydrocephalus, cerebral oedema [14].

In our case, brain and spinal cord MRI showed a leptomeningitis of posterior cerebral fossa and spinal cone. In addition, the electroencephalogram revealed a left hemispheric suffering with slow spikes in the left temporal lobe leading to the likely diagnosis of meningo-encephalitis. The impairment of spinal cone was subclinical as patient had no limbs weakness nor bowel or urinary complaints but brisk reflexes on the lower limb. The vertebrae collapse seen in MRI may be the hallmark of spondylitis though patient didn't complaint of any back pain but he also didn't report any history of back trauma. Hence, as the patient is young with no morbid conditions, spine involvement by *Brucella* is the most likely cause of this collapse [15].

In neurobrucellosis, CSF is normal in 84, 6% [12]. Our patient had a clear CSF with a mixed formula of cells, high level of proteins and a low glucose. These findings can fit to diagnosis of tuberculosis especially in our country where tuberculosis is endemic more than brucellosis. But the chronic presentation was against this hypothesis, CNS involvement in tuberculosis being a serious condition that can be lethal if treatment

is delayed. Moreover the geneXpert test was negative.

Taking into account the epidemiologic data of our patient, as people in south Morocco drink raw camel milk as a custom, and in the patient history, we found that the father has been treated for brucellosis, we had to consider this diagnosis at first and assessed for it. Rose Bengal and Wright's serum agglutination tests were positive in CSF. These results are in line with literature as serological test in the CSF may be positive in 77% of cases [12]. In addition, CSF culture grew *Brucella melitensis* but blood culture was negative.

Thoraco-abdominal CT-Scan showed lymph nodes in the stomachic coronary chains and appendicular coeco-colic region, which can suggest a digestive source of the contamination [5].

Differential diagnoses of the neurobrucellosis are numerous as the pathogen does not give a typical clinical syndrome or specific modification in the CSF. A large number of investigations usually used in the diagnosis of brucellosis often give negative results [11]. Indeed, false negative results in sero-agglutination tests (SAT) may be obtained in the presence of blocking antibodies or absence of agglutination in low serum dilutions as called prozone phenomenon; Coombs test increases the sensitivity of the SAT [16]. The specificity of blood culture in the diagnosis of brucellosis ranges between 17% and 85% [17]. It was negative in our patient although he had a multiple site involvement.

As consequence, the disease must be evoked in all patients who develop unexplained neurological symptoms particularly those who live in endemic areas. In our case, other aetiologies were evoked namely *Borrelia* and neurosyphilis that had been excluded by appropriate testing.

Treatment of this pathology relies on active antibiotics having good tissue and intracellular diffusion. This treatment must be early and include two to three synergistic and specific antibiotics. They are represented by, cyclines (doxycycline, minocycline), at a dose of 100 to 200 mg per day (adults) associated with Rifampicin at 20 mg/kg/day in children and 600 to 1200 mg/day in adults or an aminoglycoside (streptomycin in particular) for the first 6 weeks of treatment [18]. Other antibiotics such as Amphenicols, Penicillin A and Cotrimoxazole have a questionable activity in vivo. The duration of treatment for neurobrucellosis depends on the stage of the infection. In the secondary forms, notably neuromeningitis, the duration should not be less than 3 months. The rate of relapse is less than 5% [19]. Adding levofloxacin to cycline-rifampin therapy may increase its efficacy in terms of lowering the relapse rate of the disease [20].

Our patient was treated by rifampine 900 mg per day, doxycycline 200 mg per day. The progression was marked by a significant clinical improvement.

## Conclusion

Brucellosis is a multi-systemic infection, with a wide range of clinical presentations. Neurobrucellosis is among the most serious forms of the infection.

Its clinical symptoms and neuro-radiological signs are usually atypical and can be confused with other neurological diseases that explain the delayed diagnosis and late management. In endemic areas, neurobrucellosis should be considered for any unexplained neurological symptoms.

## References

- [1] Hellenic. Center for disease control and prevention (HCDCP). ministry of health Greece. Brucellosis in the world today. 2017 Available: <http://www2.keelpno.gr/blog/?p=2033&lang=en>.
- [2] Aggad H, Boukraa L. Prevalence of bovine and human brucellosis in western Algeria: comparison of screening tests. *East Mediterr Health J* 2006;12. Nos1/2 3- Institut de veille sanitaire.
- [3] Directorate of Epidemiology. Directorate of Epidemiology and Disease Control DELM-Ministry of Health, Kingdom of Morocco. Data from the zoonotic surveillance system. 2013.
- [4] WHO/UK. Department for international development animal health programme;

- food and agriculture organization of the united nations; world organisation for animal health. The control of neglected zoonotic diseases: A route to poverty alleviation. Report of a joint WHO/DFID-AHP meeting; September 20 and 21, 2005. Geneva: WHO headquarters; 2006 WHO; Available) with the participation of FAO and OIE. Geneva. [http://www.who.int/zoonoses/Report\\_Sept06.pdf](http://www.who.int/zoonoses/Report_Sept06.pdf). Accessed 2014 May 13.
- [5] Ducrotoy MJ, Ammary K, Ait Lbacha H, Zouagui Z, Mick V, Prevost L, et al. Narrative overview of animal and human brucellosis in Morocco: intensification of livestock production as a driver for emergence? *Inf Dis Poverty* 2015;4:57.
- [6] Lounes N, Cherfa MA, Le Carrou G, Bouyoucef A, Jay M, Garin-Bastuji B, et al. Human brucellosis in Maghreb: existence of a lineage related to socio-historical connections with Europe. *PLoS One* 2014;9(December (12)).
- [7] Türel O1, Sanli K, Hatipoğlu N, Aydoğmuş C, Hatipoğlu H, Siraneci R. Acute meningoencephalitis due to Brucella: case report and review of neurobrucellosis in children. *Turk J Pediatr* 2010;52(July-August (4)):426–9.
- [8] Bektaş O1, Ozdemir H, Yılmaz A, Fitöz S, Ciftçi E, Ince E, et al. An unusual case of neurobrucellosis presenting as demyelination disorder. *Turk J Pediatr* 2013;55(March-April (2)):210–3.
- [9] Panagariya A, Sharma B, Mathew V. Pseudotumor-like presentation of neurobrucellosis. *J Assoc Physicians India* 2007;55(April):301–402.
- [10] Ceran N, Turkoglu R, Erdem I, Inan A, Engin D, Tireli H, et al. Neurobrucellosis: clinical, diagnostic, therapeutic features and outcome. Unusual clinical presentations in an endemic region. *Braz J Infect Dis* 2011;15(January-February(1)):52–9.
- [11] Haji-Abdolbagi M, Rasooli-Nejad M, Jafari S, Hasibi M, Soudbakhsh A. Clinical and laboratory findings in neurobrucellosis: review of 31 cases. *Arch Iran Med* 2008;11(January (1)):21–5.
- [12] Oueslati I, Berriche A, Ammari L, Abdelmalek R, Kanoun F, Kilani B, et al. Epidemiological and clinical characteristics of neurobrucellosis case patients in Tunisia. *Med Mal Infect* 2016;46(3):123–30.
- [13] Raina S, Sharma A, Sharma R, Bhardwaj A. Neurobrucellosis: a case report from himachal pradesh, India, and review of the literature. *Case Rep Infect Dis* 2016:2019535. Epub 2016 Oct 13.
- [14] Erdem H, Senbayrak S, Meriç K, Batirel A, Karahocagil MK, Hasbun R, et al. Cranial imaging findings in neurobrucellosis: results of Istanbul-3 study. *Infection* 2016;44(October (5)):623–31. <http://dx.doi.org/10.1007/s15010-016-0901-3>. Epub 2016 May 2.
- [15] Baradaran Bagheri A, Ahmadi K, Jafari Chokan NM, Abbasi B, Akhavan R, Bolvardi E, et al. The diagnostic value of MRI in brucella spondylitis with comparison to clinical and laboratory findings. *Acta Inform Med* 2016;24(April (2)):107–10.
- [16] Guven GS, Cakir B, Oz G, Tanriover MD, Turkmen E, Sozen T. Could remembering the prozone phenomenon shorten our diagnostic journey in brucellosis? A case of Brucella spondylodiscitis. *Rheumatol Int* 2006;26:933–5.
- [17] Chelli Bouaziz M, Ladeb MF, Chakroun M, Chaabane S. Spinal brucellosis: a review. *Skeletal Radiol* 2008;37:785–90.
- [18] World Health Organization. Brucellosis in humans and animals. Treatment of brucellosis in humans 7. WHO/CDS/EPR; 2006. p. 36–8.
- [19] Ben Hamouda I, Gouider R, Mrabet A. EMC Neurobrucellose 2007:50. [http://dx.doi.org/10.1016/S0246-0378\(07\)43860-X](http://dx.doi.org/10.1016/S0246-0378(07)43860-X).
- [20] Hasanain A, Mahdy R, Mohamed A, Ali M. A randomized, comparative study of dual therapy (doxycycline-rifampin) versus triple therapy (doxycycline-rifampin-levofloxacin) for treating acute/subacute brucellosis. *Braz J Infect Dis* 2016(June (3)):14. <http://dx.doi.org/10.1016/j.bjid.2016.02.004>. Epub 2016 Apr 14.