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Original article

Epidemiological and clinical characteristics of neurobrucellosis case patients in Tunisia

Caractéristiques épidémiologiques et cliniques des cas de neurobrucellose en Tunisie

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Abstract

Objective. – We aimed to identify epidemiological, clinical, therapeutic, diagnostic, and outcome characteristics of neurobrucellosis case patients in Tunisia.

Patients and methods. – We conducted a retrospective and descriptive study over a 17-year period (January 1997–December 2013). We included all neurobrucellosis patients hospitalized in the infectious disease department of La Rabta Hospital of Tunis during the study period.

Results. – A total of 13 patients were included in the study: 9 men and 4 women. Mean age was 31.6 years. Six patients presented with meningitis, three with encephalitis, two with meningoencephalitis, and two with meningo-myeloradiculitis. All patients had a lumbar puncture performed. Eleven patients had an abnormal cerebrospinal fluid (CSF) (84.6%): lymphocytic pleocytosis in seven patients, high level of CSF proteins in 11, and low level of CSF glucose in seven. All patients had a positive *Brucella* serological test in blood. A *Brucella* serological test was also performed in CSF and was positive for 10 patients (77%). A total of nine patients had a cerebral CT scan and/or MRI performed and abnormalities were observed in six patients. Antibiotic therapy was prescribed to all patients: a combination of rifampicin and co-trimoxazole ($n=9$) or doxycycline ($n=4$) for an average duration of eight months. Two patients also received steroids. A positive outcome was observed in 10 patients. Three patients were lost to follow up.

Conclusion. – Brucellosis may be severe when neurological involvement occurs. Brucellosis should be considered in the event of any neurological involvement associated with suggestive epidemiological features.

Keywords: Neurobrucellosis; Rifampicin; Co-trimoxazole

Résumé

Objectif. – Relever les caractéristiques épidémiologiques, cliniques, diagnostiques, thérapeutiques et évolutives de la neurobrucellose en Tunisie.

Patients et méthodes. – Étude rétrospective et descriptive menée dans le service des maladies infectieuses de l'hôpital la Rabta de Tunis pendant 17 ans (janvier 1997–décembre 2013). Nous avons inclus tous les patients hospitalisés pour neurobrucellose.

Résultats. – Treize cas ont été colligés : 9 hommes et 4 femmes. L'âge moyen était de 31,6 ans. Six patients avaient une méningite, trois une encéphalite, deux une méningo-encéphalite et deux une méningo-radiculo-myélite. Tous les patients avaient eu une ponction lombaire. Le liquide cérébro-spinal (LCS) était pathologique dans 11 cas (84,6 %) : une pléiocytose à prédominance lymphocytaire a été observée chez sept patients, une hyperprotéinorachie chez 11 et une hypoglycorachie chez sept. Tous les patients avaient une sérologie pour la brucellose positive dans le sang. Elle a aussi été pratiquée dans le LCS pour tous les patients et était positive chez 10 patients (77 %). Neuf patients ont eu un scanner cérébral et/ou une IRM et six étaient pathologiques. Tous les patients ont reçu une antibiothérapie spécifique associant la rifampicine au co-trimoxazole ($n=9$) ou à la doxycycline ($n=4$) pour une durée moyenne de huit mois. Deux patients ont reçu une corticothérapie associée. Une évolution favorable a été observée chez 10 patients et trois ont été perdus de vue.

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Conclusion. – La brucellose peut être grave en cas de focalisation, en l'occurrence neurologique, et doit être évoquée devant tout tableau neurologique associé à un contexte épidémiologique évocateur.

Mots clés : Neurobrucellose ; Rifampicine ; Co-trimoxazole

1. Introduction

Brucellosis is a common anthropozoonosis [1]. Several designations have been suggested for the disease such as Mediterranean fever, Malta fever, or undulant fever [2]. Brucellosis is a notifiable occupational disease. Transmission to humans occurs through direct or indirect route. Three species are responsible for the human infection: *Brucella melitensis*, *Brucella abortus*, and *Brucella suis* [3,4]. Brucellosis monitoring in Tunisia is carried out by the national epidemiological institute and falls under the responsibility of the Ministry of Health. Before 1989 brucellosis was a low endemic disease in Tunisia. This might have been due to an under-reporting as the average number of brucellosis case patients reported every year was five. An epidemic broke out in 1991–1992 due to the lack of preventive measures and to the introduction of infected animals coming from neighboring countries. More than 500 case patients were reported in the South-West regions of the country. Brucellosis is now a rare disease in Tunisia as ovine and bovine animals are systematically vaccinated. The disease incidence is estimated at 0.99/100,000 population. The incidence is, however, higher in some localized areas of South Tunisia and a second epidemic broke out in 2006 [5]. Neurobrucellosis is the second most frequent presentation of the disease after bone and joint involvement. It can be severe as the disease clinical presentations are quite varied, resulting in diagnostic and treatment delays [2].

We aimed to describe the epidemiological, clinical, diagnostic, therapeutic, and outcome characteristics of neurobrucellosis case patients in Tunisia.

2. Material and methods

We conducted a retrospective and descriptive study at the infectious disease department of La Rabta Hospital in Tunis over a 17-year period (January 1997–December 2013). We included all patients hospitalized for neurobrucellosis during the study period. Neurobrucellosis was defined by the association of epidemiological factors (patients at risk of brucellosis) with neurological symptoms of meningitis or encephalitis symptoms with a bacteriological and/or serological confirmation of brucellosis in blood and/or cerebrospinal fluid (CSF). Data was collected from the patients' charts: epidemiological data (age, sex, geographical origin, occupation, likely transmission route), clinical data (functional and physical symptoms), paraclinical data (blood and CSF serological test, bacteriological test in CSF and blood, and radiological features), therapeutic, and outcome data. The neurobrucellosis diagnosis was made on the basis of epidemiological, clinical, and microbiological factors: Wright's serum agglutination test > 1/80 in blood and/or > 1/32 in CSF, or detection of *Brucella* spp. in blood and/or CSF.

3. Results

We identified 13 neurobrucellosis case patients out of 197 patients hospitalized for brucellosis during the study period (6.5% prevalence): nine men and four women with a sex ratio of 2.25. Mean age was 31.6 years (range 20–72 years). No patient presented with comorbidities. Eight patients came from rural areas (61.5%). Seven patients had been exposed to the disease at work: three agricultural workers (helped animals give birth without any protection), two shepherds, one slaughterhouse employee, and one traditional dairy shop employee who ate and handled unpasteurized dairy products. A total of 10 patients (77%) were most likely indirectly contaminated: consumption of unpasteurized milk and/or by-products. A direct transcutaneous contamination was probably the cause of the infection for one patient as he helped animals give birth without any protection and two patients were most likely directly and indirectly contaminated.

Progressive clinical symptoms could initially be observed in 10 patients (77%). Mean time to consultation was 65 days (range 1–210 days). Clinical symptoms varied but patients mostly presented with fever ($n = 12$), headache ($n = 10$), vomiting ($n = 7$), and asthenia ($n = 8$). Neurological symptoms included behavior and mood disorders ($n = 3$), delirium ($n = 1$), convulsions ($n = 1$), and hallucinations ($n = 1$). A total of five patients presented with blurred vision, three with diplopia, and two with hearing loss. Three patients presented with concomitant neurological and not specific symptoms. Mean time to neurological symptom onset for patients with no neurological presentation at onset was 91 days (range 20 days–1 year).

Fever was observed at physical examination in 11 patients (84.6%): mean temperature was 39.1 °C. Both afebrile patients had consulted five and seven months after symptom onset, respectively. Symptoms of meningitis were observed in 11 patients and six patients presented with cranial nerve involvement.

Neurological and not specific symptoms, CSF cytochemical data, serological and radiological data, and clinical presentations are detailed in Table 1.

With regard to biological results, five patients presented with thrombopenia, four with anemia, and two with leucopenia. One patient presented with pancytopenia. A total of six patients presented with an inflammatory syndrome (46.1%).