Fiebre de malta: reporte de caso

Malta fever: Clinical case

Edward Jassir Rozo Ortiz [a], Javier Orlando Barón Barón [b], Daniela Rocío Castillo López [c], Ledmar Jovanny Vargas Rodríguez [d].

a. Internal Medicine Department. San Rafael hospital of Tunja, Colombia. Faculty of Health Sciences, Medicine. Tunja, Colombia. ORCID: https://orcid.org/0000-0002-3519-3645

b. Internal Medicine Department. San Rafael hospital of Tunja, Colombia. Faculty of Health Sciences, Medicine. Tunja, Colombia. ORCID: https://orcid.org/0000-0002-2268-7574

c. Medical student. San Rafael hospital of Tunja, Colombia. Faculty of Health Sciences, Medicine. Tunja, Colombia. ORCID: https://orcid.org/0000-0002-5547-8023

d. MD. Specialist in Epidemiology, Universidad de Boyacá, Tunja, Colombia. ORCID: https://orcid.org/0000-0001-6001-5720

DOI: 10.22517/25395203.24668

Abstract

Introduction: Malta fever (brucellosis) is a zoonotic infection produced by intracellular gram-negative coccobacilli, which is transmitted by the consumption of infected unpasteurized animal products, skin contact or mucous membranes with infected animal tissues and fluids, and inhalation of infected aerosolized particles.

Case: A 34-year-old man living in a rural area, who works in livestock, was admitted to the emergency department for presenting a clinical picture of 15 days of evolution of unquantified febrile peaks associated with symptoms such as chills, asthenia, adynamia and myalgia. The diagnosis of infection with Brucella Abortus was given through clinical-pathological correlation.

Conclusion: This pathology is more frequent in adult males. Serological studies (antibodies, agglutination and immunochromatographic assay) prove to have the highest sensitivity and diagnostic specificity in the clinical picture. The treatment is given with medication that acts on intracellular acidic environment (tetracyclines, aminoglycosides, fluoroquinolones), this in order to control the disease, and prevent complications and relapses.

Keywords: Brucellosis; Malta Fever; Brucella; Fever (MeSH)

Introduction

Brucellosis, also known as 'undulant fever', 'Mediterranean fever' or 'Malta fever' is a zoonotic infection produced by bacteria of the genus Brucella, which is found within the Alphaproteobacterial family (1).

Members of the genus Brucella are small, facultative intracellular, non-encapsulated, non-sporulated, and non-motile, aerobic gram-negative coccobacilli. Classically 6 species were recognized within the genus Brucella: B. melitensis, B. abortus, B. suis, B. canis, B. ovis and B. neotomae, where its name was seen according to the host (cattle, sheep, goats, camels, pigs or other animals) (2). Only the first three are harmful to humans and present their own pathogenicity that is transmitted to humans through the intake or ingestion of food products from infected animals (such as unpasteurized dairy products) or by contact with tissues or fluids (1) (2).

Currently, Brucellosis is considered a reemerging disease and represents a public health problem in many developing countries (3) (13), since the prevalence of brucellosis has increased due to increasing international tourism and migration (1).

Different endemic areas have been found for this infectious disease, in which are including countries in the Mediterranean basin, the Middle East, Central Asia, China, the Indian subcontinent, Sub-Saharan Africa, and parts of Mexico and Central and South America. (4) Worldwide, approximately 500,000 cases are reported annually, and an estimated 2.4 billion people are at risk (2), (5), (12).

The objective of the following paper is to present the clinical case of a patient with Malta fever (Brucellosis) treated at the San Rafael hospital of Tunja.

Clinical case.

34-year-old man living in the rural area of Sotaquirá (Boyacá). He was admitted to the emergency service of a second-level health center, due to a clinical picture of 15 days of evolution of unquantified fever peaks with associated symptoms like chills, asthenia, adynamia and myalgia; he reported having consumed amoxicillin 500 mg every 8 hours, chlorpheniramine 4 mg each 8 hours and ascorbic acid 500 mg per day for 7 days without showing improvement.

He reported important work history of contact with cattle and their fluids without adequate biosecurity elements. The admission vital signs were temperature 37.9 °C, heart rate 117 beats per minute, blood pressure of 110/70 mmHg, respiratory rate of 20 breaths per minute, it was highlight-

ing tachycardia and fever, in the general physical examination did not reveal alterations other than the described.

Due to the patient's work history and clinical picture, it was decided to perform paraclinical (Table 1), where the seroagglutination tests confirmed the diagnosis of brucellosis; due to this result, management with doxycycline 100 mg orally every 12 hours and rifampicin 300 mg orally every 8 hours for 6 weeks were given, with which an improvement was obtained, and the patient was indicated to be follow-up on an outpatient basis.

Table 1. Admission laboratories

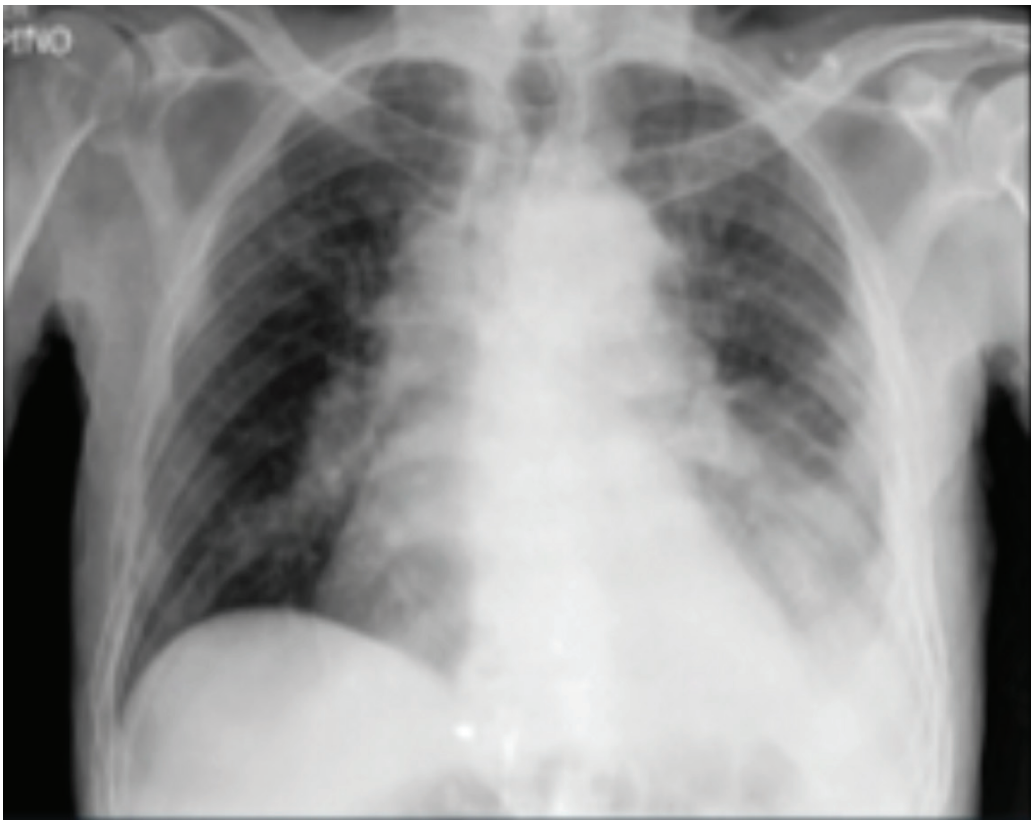
Tabla 1. Admission laboratories.

Laboratories	Results	Reference
Leukocytes	98600/mm3	4500 a 11000/mm3
Neutrophils	46.8%	40,0 a 65,0 %
Lymphocytes	41,40%	30,0 a 40,0%
Monocytes	11,60%	3,0 a 10,0%
Platelets	226000/mm3	150 a 350000/mm3
Hemoglobin	14,5 gr/dl	14,50 a 16,50 g/dl
C Reactive Protein	50,8 mg/l	0.5-10 mg/l
Blood Culture	Negative at 48 hours	Negative
Urine Culture	Negative at 48 hours	Negative
TGP/ALT	104 U/L	Hasta 42 UI/L
TGO/AST	70 U/L	Hasta 37 UI/L
Hepatitis B Surface antigen	Negative	Negative
Hepatitis C Antibodies	Negative	Negative
WIDAL Reaction	Negative	Negative
Salmonella Typhi O	Non-reactive	Non-reactive
Salmonella Typhi H	Negative	Negative
Salmonella Paratyphi A	Negative	Negative
Salmonella Paratyphi B	Negative	Negative
Weil Felix Reaction	Negative	Negative
Total anti-Brucella antibodies (rose bengal method)	100 UI/ml positive	Less than 25 UI/ml
Huddleson Reaction (*Brucella* Abortus)	Reactive (1/320)	Non-reactive

Once the treatment was completed, the patient was evaluated again for outpatient consultation by the infectious disease service who considered that the dual treatment (doxycycline and rifampicin) was suitable, however, the patient persisted with positive serology for infection by Brucella (Huddleson reaction -Brucella Abortus- positive plate agglutination technique), for which the handling indicated was modified as follows: ciprofloxacin 500mg tablet every 12 hours for 20 days, doxycycline 100 mg every 12 hours for 20 days and control laboratories.

The patient was admitted again to the emergency department 10 months after the last admission, due to similar clinical picture to the one previously presented, this time associated with myalgias and arthralgias, the laboratories showed a slight increase in transaminases, the abdominal ultrasound showed hepatosplenomegaly and chest X-ray did not show alterations, the trachea in a central position, at the level of the lung area no condensation or data suggestive of abnormal atelectasis were observed, cardiac silhouette within normal limits, free cardio and costophrenic angles, bone mineralization within normal parameters (figure 1).

Figure 1. Chest X-ray.



In view of the results obtained in the ultrasound and chest X-ray, it was decided to hospitalize the patient indicating management for suspected relapse by Brucella with Doxycycline 100mg every 12 hours plus gentamicin 240 mg intravenously per day. The patient completed 6 days of in-hospital antimicrobial management; he was presenting improvement in symptoms so discharge with outpatient follow-up was indicated.

Discussion

In Latin America, Mexico has the highest annual incidence of Brucellosis cases. In South America, Peru and Argentina have the highest incidences of 34.9 and 8.4 annual cases per million inhabitants. In Colombia, the incidence is 1.85 annual cases per million inhabitants. The disease in non-endemic areas is of occupational origin and the most affected population are male adults (6).

Table 2 lists the main clinical manifestations and most frequent laboratory findings and their prevalence (14).

Table 2. Clinical and paraclinical characteristics of Malta fever.

Table 2. Clinical and paraclinical characteristics of Malta fever (1).	
Clinical manifestation	**Prevalence (%)**
Fever	76%
Discomfort	68%
Night sweats	72%
Arthralgias	80%
Hepatomegaly	50%
Splenomegaly	29%
Paraclinical Findings	**Prevalence (%)**
Alanine aminotransferase increase	33%
Anemia	27%
Leukopenia	9%
leukocytosis	8%
Relative lymphocytosis	24%
Thrombocytopenia	12%
Pancytopenia	<1%

It is important to consider that for patients with fever of unknown origin, the panel of antifebrile antigens should be performed to rule out other infectious pathologies, within which blood cultures that have a low sensitivity

for brucellosis (15 to 60%) (1) can be performed; due to, for this case it was preferred to perform serological tests that allow the detection of antibodies against lipopolysaccharide or other antigens of bacteria such as the IgM and IgG ELISA (sensitivity 94%, specificity 97%), Rose Bengal agglutination test (sensitivity 87%, specificity 100%) and the immunochromatographic lateral flow assay (sensitivity 92%, specificity 97%) (1, 6, 7), which were positive in the case presented.

The goal of the treatment is to control the disease, prevent complications, relapses, and sequels (8) (15), which is why combined antibiotics with activity in acidic intracellular environments are included, at high doses with prolonged duration as it decreases the risk of relapse (7). Within the management regimens for the general population, doxycycline can be combined with an aminoglycoside (streptomycin or gentamicin) or the combination of doxycycline with rifampicin for 6 weeks; the first combination is being more effective and with lower risk of relapse (8). In cases of relapse or therapeutic failure, fluoroquinolones should be added (9).

For pregnant women the treatment is still uncertain, since tetracyclines are contraindicated (10), however in pregnancies of less than 36 weeks, it can be given management with trimethoprim sulfamethoxazole with rifampicin for six weeks, and in case of more than 36 weeks it is preferred to give rifampicin monotherapy until delivery due to the risk of neonatal kernicterus with the use of trimethoprim sulfamethoxazole. After delivery, it is given management with combination therapy as in non-pregnant adults (11).

Between 5 to 15% of patients after treatment may relapse, it even may occur up to 12 months later (1), among the factors that can predict relapse are temperature ≥38.3 ° C, symptoms duration <10 days before treatment and positive blood cultures at the beginning of the study. Causes of relapse include inadequate antibiotic regimen, inadequate duration of antibiotic therapy, lack of adherence, or localized outbreak of infection (1) (7).

Conflicts of interests: None

Funding: None

E-mail Address: drcastillo@uniboyaca.edu.co

References

1. Bosilkovski M. Brucellosis : epidemiology , microbiology , clinical manifestations , and diagnosis. [Internet] 2019 [citado el 8 de agosto 2021] Disponible en: file:///D:/CARDIOLOGIA/ARTICULOS DE BRUCELOSIS/brucellosis - UpToDate.pdf Eng (3).pdf
2. Facciolà A, Palamara M, D'Andrea G, Marano F, Magliarditi D, Puglisi G, et al. Brucellosis is a public health problem in southern Italy: Burden and epidemiological trend of human and animal disease. J Infect Public Health [Internet]. 2018;11(6):861–6. Available from: https://doi.org/10.1016/j.jiph.2018.07.007
3. Colmenero JD. Chronic bacterial infections (II). Brucellosis. Med [Internet]. 2018;12(53):3124–31. Available from: https://doi.org/10.1016/j.med.2018.03.021
4. Sánchez Ramos A, Arteaga Lira MÁ. Brucelosis: Un problema de salud no reportado en Hidalgo. TEPEXI Boletín Científico la Esc Super Tepeji del Río. 2019;6(12):34–7.
5. Abdelbaset AE, Abushahba MFN, Hamed MI, Rawy MS. Sero-diagnosis of brucellosis in sheep and humans in Assiut and El-Minya governorates, Egypt. Int J Vet Sci Med [Internet] 2018;6(sup1):S63–7. Available from: http://dx.doi.org/10.1016/j.ijvsm.2018.01.007
6. Rodríguez Y, Torres SN, Mora JFJ, Charry JCV. Brucelosis recurrente. [Internet]. 2014;47(1–2):32–5. Available from: http://dx.doi.org/10.1016/S0120-4912(15)30129-4
7. Dadar M, Shahali Y, Whatmore AM. Human brucellosis caused by raw dairy products: A review on the occurrence, major risk factors and prevention. Int J Food Microbiol [Internet]. 2019;292(November 2018):39–47. Available from: https://doi.org/10.1016/j.ijfoodmicro.2018.12.009
8. Yousefi-Nooraie R, Mortaz-Hejri S, Mehrani M SP. Antibiotics for treating human brucellosis (Review) SUMMARY OF FINDINGS FOR THE MAIN COMPARISON. Cochrane Libr. 2012;(10):1–89.
9. Center for Disease Control and Prevention. Brucellosis Reference Guide: Exposures, Testing and Prevention. 2017;1–35. Available from: https://www.cdc.gov/brucellosis/pdf/brucellosi-reference-guide.pdf
10. Vilchez G, Espinoza M, D'Onadio G, Saona P, Gotuzzo E. Brucellosis in pregnancy: Clinical aspects and obstetric outcomes. Int J Infect Dis [Internet]. 2015;38:95–100. Available from: http://dx.doi.org/10.1016/j.ijid.2015.06.027
11. Gulsun S, Aslan S, Satici O, Gul T. Brucellosis in pregnancy. Trop Doct. 2011;41(2):82–4.
12. Harrison ER, Posada R. Brucellosis. Pediatr Rev. 2018;39(4):222–4.
13. Ortiz-reynoso MDM. Medicina e Investigación. 2015;3(2):2–6.
14. Dean AS, Crump L, Greter H, Hattendorf J, Schelling E, Zinsstag J. Clinical Manifestations of Human Brucellosis: A Systematic Review and Meta-Analysis. PLoS Negl Trop Dis. 2012;6(12).
15. Guzmán-Hernández RL, Contreras-Rodríguez A, Ávila-Calderón ED, Morales-García MR. Brucelosis: Zoonosis de importancia en México. Rev Chil Infectol. 2016;33(6):656–62.