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Case Report

Esophageal brucellosis? Straight to the goat

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ABSTRACT

We report the case of a 58-year-old immunocompetent man from Algeria, who presented to the hospital with fever and hepatic cytolysis. Abdominal computed tomography scan showed a homogeneous splenomegaly and a hypodense 12-mm mass on the posterior wall of the esophagus. After ruling out tuberculosis, the patient was diagnosed with brucellosis. Patient was cured after receiving 6 weeks of oral doxycycline and intravenous gentamicin during the 7 first days of therapy. Such treatment was considered as an acceptable alternative of the recommended first-line therapy. This case illustrates the diagnostic issues in the context of an authentic brucellosis presenting as upper gastrointestinal symptoms, with impaired general condition.

Case presentation

A 58-year-old Algerian male was admitted to the hospital due to persistent fever (38°C), chills and night sweats. Patient history revealed that he was returning from his home village (El Oued, Algeria), where he spent 3 months (from November 2021 until early February 2022). He is a nonsmoker, with no habits of alcohol drinking or any medical history. One month before admission, he complained of sleep loss and weight loss (8-10 kg), which made him consult his general practitioner who performed biological tests. Blood tests revealed an elevated C-reactive protein level of 62 mg/l, with normal white blood cell but abnormal liver enzymes (6-times above the normal values (aspartate aminotransferase [ASAT] = 191 U/l, alanine aminotransferase [ALAT] = 200 U/l, alkaline phosphatases [ALP] = 447 U/l, and gamma-glutamyl transferase [GGT] = 546 U/l), despite the fact that the patient took no medication.

In the hypothesis of tuberculosis, considering the clinical picture and the ethnical origin of the present case, the patient was admitted in our department for further investigation. Physical examination was unremarkable and only revealed hepatosplenomegaly, leading to abdominal CT (computed tomography) scan at day 1 of admission. CT scan showed homogeneous splenomegaly, no dilatation of biliary tracts, and no intra-abdominal effusion but revealed a small and hypodense 12-mm mass on the posterior wall of the esophagus, compatible with cancer (Fig. 1). In addition, a complementary pulmonary CT scan revealed no radiologic evidence of tuberculosis.

Further investigations with serologies for hepatitis A, B, C, and E viruses, HIV, and syphilis were negative. Interferon-gamma with sputum cultures for 3 days were also negative for tuberculosis (cultures were maintained for one month on Lowenstein's medium). During hospitalization, patient remained febrile, with fatigue and insomnia and reported eructation with nausea without any true dysphagia. Simultaneously, the patient benefited from an upper gastrointestinal endoscopy on the third day after admission to rule out an esophageal cancer. Endoscopy showed an inflamed mucosa, with an aspect of antral atrophy and a hiatus hernia of 3 cm, without any lesion to guide a biopsy. The esophageal mass observed on the CT scan was ultimately considered as extramural.

Recent medical history revealed that while the patient was abroad, he often consumed unpasteurized goat milk. However, he was not in direct contact with the animals during his stay. Although the patient presented with atypical digestive symptoms, we hypothesized that the patient could be suffering from brucellosis or Q fever, considering his recent stay in an endemic country

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Fig. 1. Axial (A) and coronal (B) contrast-enhanced abdominal CT images demonstrated a small nodular hypodense lesion of the distal esophagus.

with acute hepatitis and persistent fever. *Coxiella burnetti* serology came back negative. On day 5 of admission, 2 pairs of blood cultures returned retrospectively positive for *Brucella melitensis* after 48 hours of growth culture, confirmed by the national reference center for brucellosis. Indeed, direct examination revealed gram-negative coccobacilli (Supplementary data), which was falsely confirmed by Matrix-Assisted Laser Desorption/Ionization - Time of Flight mass spectrum identification to be an *Ochrobactrum* spp, as commonly described for *B. melitensis* (Khaliulina Ushakova et al., 2020). In addition, the Rose Bengal test was also positive, supporting treatment initiation with doxycycline 100 mg twice per day for 6 weeks and gentamicin 5 mg/kg per day during the first 7 days of therapy. Subsequent test for brucellosis with a Wright serology (BioRad, Marnes-La Coquette, France) confirmed the diagnosis of brucellosis with a titer of 1/1280, with positive IgM antibodies and negative IgG against *B. melitensis*. Complementary transthoracic echocardiography ruled out infective endocarditis associated with brucellosis. Considering clinical and biological resolution under treatment (ASAT = 58 U/l, ALAT = 75 U/l, ALP = 148 U/l, GGT = 217 U/l, and C-reactive protein level at 1 mg/l), the patient was discharged after 10 days of hospitalization.

The patient was followed up after one month. He was considered cured, with no signs of infection, with weight gain (+ 2 kg), and liver enzymes were back to normal. Moreover, no adverse effect related to the antimicrobial therapy was reported; in particular, there were no complaints of esophageal symptoms caused by doxycycline or nephrotoxicity due to gentamicin.

Discussion

In the current case, the atypical clinical presentation, associated with the recent history of consumption of goat milk in a high-risk outbreak area (Ariza et al., 2007; Khezzani et al., 2021), was very likely to be brucellosis. However, the systematic review of cases with esophageal brucellosis and its involvement has only been reported once in the literature (Laso et al., 1994). Physician should be wary of this so-called entity in a context where imaging plays a major role in the diagnosis of a persistent fever.

Indeed, *Brucella melitensis* is a gram-negative coccobacillus that affects sheep and goats and their byproducts, especially dairy products. Humans can get infected by direct contact or inhalation of the bacteria after a 3–4-week incubation period. The disease is subject to mandatory reporting in France. Typically, acute brucellosis yields undulant fever, night sweats, myalgia, and fatigue. Secondary localizations are rare but possible, such as spondylitis, endocarditis, or neurobrucellosis (Alton and Forsyth, 1996). Although Laso et al (1994) reported a submucous tumor, located at the lower third part of the esophageal during the endoscopy, we did not find any abnormality attesting the extramural involvement of our present case. Various hypotheses have been raised to explain the atypical esophageal localization of brucellosis, which is caused either by direct inoculation, extension of adjacent structures, or a retrgrade dissemination from lymph nodes (Laso et al., 1994). We retained in the current case a potential lymph node involvement that is responsible for an extramural noncompressive mass, which is not visible during endoscopy.

Brucellosis is commonly diagnosed by positive blood cultures on enrichment broths during the acute phase of the disease (first 10–15 days). The laboratory should be informed of a potential brucellosis to avoid inadvertently human outbreaks by inhalation (Henning et al., 2012). Indirect diagnosis is performed by the Rose Bengal test (rapid screening method with sensitivity >95%) and Wright's seroagglutination test, as recommended by the WHO (Corbel, 2006). Recently, the implementation of PCR testing might be helpful in the case of previous antibiotic intake or in the presence of tissue specimen, such as joint fluid or liver biopsy (Stahl et al., 2020). Moreover, liver biopsy interpretation can also be prognostic with the presence of fibrosis (Gousseff, 2008). In our case, no liver or esophageal biopsies were performed because blood cultures provided the diagnosis beforehand.

In the case of acute hepatitis after a prolonged stay abroad, physicians should rule out the common causes of hepatitis. Indeed, hepatitis A, which is endemic in Algeria (Lahlali et al., 2018), and hepatitis E is currently recognized as being the first cause of acute viral hepatitis worldwide (Aslan and Balaban, 2020), whereas the seroprevalence of Q fever is estimated to be up to 35% in rural areas in Algeria (Lacheheb and Raoult, 2009). Moreover, syphilis should be incriminated especially in men who are having sex with men.

Considering treatment, the gold-standard antimicrobial therapy in brucellosis, according to the WHO recommendations, is deemed to be "doxycycline 100mg twice daily orally for 6 weeks and streptomycin 15mg/kg daily intramuscularly for 2-3 weeks" (Solera et al., 1997). The treatment with doxycycline 100 mg twice daily orally for 6 weeks and rifampicin 600-900 mg once daily for 6 weeks is also considered as an acceptable first-line alternative, with only 5% of relapse and 7% of failure, according to the literature (Alavi and Alavi, 2013). Indeed, oral rifampicin is more convenient than streptomycin; the all-oral regimen allows a better implementation in clinical practice in areas with less well-developed health infrastructure, which overcomes its slight inferiority of efficacy with up to 8% of failure and 10% of relapses (Ariza et al., 2007). The use of doxycycline and intravenous gentamicin 5 mg/kg daily for 5–7 days is an acceptable alternative regarding the wider availability than streptomycin, with same efficacy in terms of failure rates (Ariza et al., 2007). Moreover, it does allow sparing strep-

tomycin for the treatment of multidrug-resistant tuberculosis. Although our case presented esophageal symptoms, we still decided to initiate a treatment with doxycycline because of its clinical efficacy. Indeed, doxycycline could be responsible for esophageal injuries with esophagitis, ulcer, or stenosis that may occur during the treatment due to doxycycline's pH being below 3 (Al Rawahi and Dutt, 2019).

Conclusion

This case report illustrates the risk of misdiagnosing an authentic brucellosis, presenting as upper gastrointestinal symptoms with impaired general condition. The present case highlights the importance of routine blood cultures, especially in the case of fever in returning travelers after a trip abroad. Our case reports that 6 weeks of oral doxycycline plus a short regimen of intravenous gentamicin might be an appropriate first-line therapy for inpatients.

Availability of data and materials

All material and data described in the manuscript are available upon request to the corresponding author of the present article.

Consent for publication

Written informed consent was obtained from the patient for publication of this case report.

A copy of the written consent is available for review by the Editor of this journal.

Ethics approval and consent to participate

Not applicable.

Author contributions

BD and ADN oversaw conceptualization, data curation, resources and writing: original draft. LD visualized the manuscript. BD supervised, validated, and wrote the definite version of the manuscript. MT was responsible for imaging. LN revised the manuscript and brought supplementary data.

Declaration of Competing Interest

The authors have no competing interests to declare.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.ijid.2022.05.054.

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