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Case report

Pancytopenia revealing acute brucellosis

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ABSTRACT

Brucellosis is the most prevalent bacterial zoonosis worldwide. The WHO estimates that the infection is responsible for more than 500 000 cases per year across the world [1].

Hematological complications like mild anemia and leukopenia have been frequently associated with acute brucellosis, but pancytopenia and thrombocytopenia are less frequently encountered [2]. We are reporting the case of a 73 year old male patient, with pancytopenia that revealed acute brucellosis. Following 6 weeks of antibiotic therapy, our patient showed favorable clinical outcome, and the complete blood count returned to normal. Acute brucellosis should be highly suspected in patients with pancytopenia.

Background

Brucellosis is a zoonosis that rages all around the Mediterranean. It remains endemic in Morocco, particularly in some rural areas. Brucellosis is caused by small, fastidious gram negative bacteria of the genus *Brucella*. *Brucella melitensis* is the most common of the species responsible for the most invasive, and severe diseases worldwide followed by *brucella abortus, brucella suis* and *brucella canis* [1].

Clinically, Brucellosis can mimic various multisystemic diseases, showing wide clinical polymorphism. It produces a variety of non specific hematological abnormalities. Bone marrow and the spleen are commonly affected, and such affection may result in a hypoplastic pattern on the peripheral blood smear. During this disease, Hematological disturbances are marked by leukopenia and anemia, but thrombocytopenia or Pancytopenia remain very rare.

Case report

This is a 73 year old man living in the city of Laayoune in southern Morocco, with a medical history of diabetes, under insulin treatment and oral antidiabetic drugs, the patient also had a coronary dilation at the age of 59, he was hospitalized for fever and chills evolving for 2 weeks, with a deterioration of his general condition. The clinical examination showed a soft and depressable abdomen, there was a splenomegaly, but no hepatomegaly. Cardiac and pulmonary auscultation was normal with a BP 120/70 mmHg.

Blood count revealed a pancytopenia with hemoglobin of 11 g/dl and platelets at 63 000 G/L and white blood cells (WBC) of 3475/mm3 (neutrophils 60 %, lymphocytes 37 %). Biochemical investigation showed a lactate dehydrogenase (LDH) at 599U/L; C reactive protein (CRP) 79 mg/l; Procalcitonine at 4.82 mg/l, glycemia at 1.18 g/l HBA1c 7.40 %. Microalbuminuria was negative, and the total cholesterol was 1.37 g/l triglycerides 2.62 g/l.

The cytobacteriological examination of the urine was sterile and the search for a source of infection was negative. Viral Serologies B, C, HIV, and the search for antinuclear antibodies were all negative. Electrophoresis of serum proteins concluded a restriction of heterogeneity of the gamma zone. The level of Vitamin B12 was normal.

In order to explore pancytopenia a myelogram was done. It allowed to highlight many megakaryocytes with erythroblastic hyperplasia but without signs of dysplasia. In addition, there were many activated macrophages with a 5 % eosinophil level, but there were no parasites or metastatic cells. The marrow was in favor of a reactionary marrow.

Due to the persistence of the clinical symptoms marked mainly by undulant fever and after re-interviewing the patient, he stated that he had consumed unpasteurized milk. A test for brucellosis

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was requested. The Rose Bengal test (Brucellosis slide BioMerieux® France) was positive, Wright's serodiagnosis was 1/20 positive. Antibiotic therapy with rifampicin (900 mg/day) and doxycycline (200 mg/day) was initiated for 6 weeks, and the clinical and laboratory outcome was favorable, also the complete blood count returned to normal (Hb: 13 g/dl, platelets: 180 × G/L, WBC: 4500/mm3.

Discussion

Brucellosis is a well-tolerated anthropozoonosis in animals. It is responsible in females of repeated abortions of a lowering fertility in females. Infected animals excrete the bacteria in the environment through their feces, and in milk or abortion products in infected females [3].

Man is infected directly by infected animals, dermally, conjunctively or aerially. Contamination can also occur indirectly, via food, after ingestion of contaminated products [3]. This is the case of our infected patient following the ingestion of contaminated dairy products.

Brucellosis can be accidentally contracted by laboratory personnel when handling Brucella cultures [4], or when handling animal vaccines among professionals at risk [5]. Finally, the human-to-human transmission is exceptional, usually takes place through sexual intercourse. [3].

After mucocutaneous or digestive contamination, the bacilli multiply in the lymph nodes, disseminate by septicemia and colonize the cells of the reticuloendothelial system, It is the acute phase of the disease. The disease then progresses in some individuals to a subacute phase, with the possibility of secondary locations. They can be osteoarticular, gastrointestinal, cardiovascular, genitourinary, hematological and cutaneous [3,6]. This disease with durations of more than one year is called chronic brucellosis, with or without discovery of an infectious focus [6].

The clinical expression of the acute phase is marked by a sensation of discomfort with chills, aches, arthromyalgia and often abundant sweats, all achieving the typical picture of the disease of an undulant fever, whose general repercussion is sometimes modest [7]. Hematological disturbances are marked by anemia and leukopenia [2] the percentage of pancytopenia is relatively rare. A literature review reported a frequency between 3 and 21 % depending on the series [8–10]. Several authors report only isolated observations.

The pathogenesis of pancytopenia in brucellosis has not been clearly understood, several mechanisms that can explain these hematological abnormalities are mainly hypersplenism, haemophagocytosis, the existence of a medullary granulomatosis or medullary hypoplasia. Immune destruction is exceptional [2]. Sometimes these different mechanisms can be intricate. In about 7 % of cases, the mechanism of pancytopenia is unclear [11]. In our observation hypersplenism is the most probable cause given the result of the myelogram which objectified erythroblastic hyperplasia. Moreover, in our observation, there was a splenomegaly but no hepatomegaly. According to the data of the literature, splenomegaly is present in 35–60 % of patients with brucellosis and in 86–88 % of those patients with pancytopenia and *Brucella melitensis* [12]. Pancytopenia during brucellosis could be explained by the existence of a direct inhibitory effect on proliferating marrow cells or indirectly by inducing parasitised macrophages or activated lymphocytes to release mediators which inhibit haematopoiesis [12].

The definitive diagnosis of brucellosis is based on the isolation of the bacterium in culture [3]. For our patient the blood culture was not requested, it is the serology that contributed to the diagnosis. In fact, the technique of tube agglutination or seroagglutination Wright (SAW) is the first serological technique described, and remains the reference recommended by the WHO because of its standardization [3].

The preferential treatment for brucellosis is Rifampicin-tetracycline or streptomycin for 6 weeks; relapses are rare and usually occur in the first year of treatment and are due to poor adherence to treatment. The achievement of the antibiogram is not essential. Most strains are sensitive to the antibiotics indicated during brucellosis [3]. Our patient was treated by rifampicine 900 mg per day, doxycycline 200 mg per day for 6 weeks with favorable clinical outcome.

Hematological disturbances during brucellosis are reversible and transitory. The proof of this is that during the clinical observation of our patient, after the treatment we found the normal values of blood count.

Conclusion

In the presence of clinical observations characterized by undulant fever and hematological disorders marked mainly by pancytopenia, especially in our country where the disease is still endemic, the diagnosis of brucellosis should be mentioned.

Author contributions

Ben Lahlou Yassine; Author.

Elmostapha Benaissa, Adil Maleb, Mariama Chadli: have been involved in drafting in the manuscript.

Mostafa Elouennass: have given final approval of the version to be published.

Declaration of Competing Interest

The authors report no declarations of interest.

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