



Kasuistika | Case report

Brucella infective endocarditis

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SOUHRN

Brucelóza je zoonotické infekční onemocnění, vyskytující se celosvětově, hlavně v rozvojových zemích. K jejímu přenosu na lidi dochází často po konzumaci výrobků z nepasterizovaného mléka a přímým kontaktem s tkáněmi infikovaných zvířat. I když může mít onemocnění za následek řadu komplikací, postižení kardiovaskulárního systému, zjišťované v méně než 2 % případů, se v klinické praxi manifestuje jako endokarditida. Diagnóza endokarditidy se stanovuje až v pozdější fázi onemocnění, kdy již postihlo hlavně aortální chlopně; výsledkem je vysoká morbidita a mortalita. Přinášíme kasuistiku a přehled literatury o endokarditidě s brucellou jako patologickým agens; jde sice o vzácné, avšak závažné onemocnění.

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ABSTRACT

Brucellosis is worldwide a zoonotic infective disease especially seen in developing countries. Frequently it is transmitted to humans through the consumption of products derived from unpasteurized milk and through direct contact with infected animal tissue. Although the disease leads to many complications, cardiovascular involvement that is seen in less than 2% of cases usually manifests itself in clinical practice as endocarditis. Endocarditis is diagnosed lately in the course of the disease with mostly aorta valve involvement and leads to serious morbidity and mortality. Here we present a case report and literature review on brucella endocarditis which is a rare but serious clinical condition.

Introduction

Although brucellosis is a worldwide frequent infection, it is much less diagnosed and reported. The most important reason for this discrepancy is that brucellosis can easily be overlooked by a physician in daily practice. Human brucellosis is caused by generally one of three *Brucella* species: *Brucella melitensis*, *Brucella abortus* and *Brucella suis* [1]. Brucellosis is a zoonotic disease transmitted to humans through the consumption of products derived from unpasteurized milk and through direct contact with infected animal remains. Individuals who have regular contact with livestock and their products, slaughterhouse workers, veterinary staff and shepherds, as well as people working in microbiology laboratories, who become infected through inhalation of aerosolized particles, are under risk [2]. The disease is endemic at Mediterranean region, Middle East, South Asia and Mid-South America [3]. *Brucella* endocarditis is rare in western countries where the infective agent is *B. abortus* which leads to moderate disease and uncommon suppurative and disabling complications. However in countries where *B. melitensis*, which leads to more severe disease and disabling symptoms, and rheumatoid cardiac disease prevalence is higher, brucella endemic infective endocarditis is seen as an endemic disease [4].

In a literature review which investigated cases of brucellosis in Turkey between the years of 1990 and 2009, and brucella endocarditis was observed in 51 of 4 204 patients [5]. It is more frequent in men than women [6]. It has a much higher mortality rate than endocarditis caused by other pathogens due to its rapid and wide tissue destruction. The high mortality rate might be due to late diagnosis of the infection, because due to the clinical presentation various diseases such as some malignancies might be considered primarily instead of brucellosis.

Case report

A 32-year-old man was admitted to hospital due to fever and 8 kg weight loss for six months. He was working in a farm which includes cowshed. He did not have a history of cardiac disease. His body temperature was 38.3 °C and diastolic murmur of grade 3/6 at aortic area were found on physical examination. In transthoracic echocardiography examination, active vegetation was present on aortic valve (Fig. 1). *Brucella* agglutination tests (Rose-Bengal and Wright) were studied in serum sample. Both Rose-Bengal and Wright tests (the latter in a titer of 1/640) were positive. A heart valve operation was planned following a 6-week antibiotic therapy with rifampicin and doxycycline with a combination of streptomycin for 3 weeks. *Brucella melitensis* was isolated from blood culture drawn on admission. The patient underwent a successful aortic valve replacement surgery and doxycycline and rifampicin therapy was continued 6 months after surgery.

Symptoms and finding

In humans, brucellosis is a multi-systemic disease that is manifested in a wide variety of ways, the most common

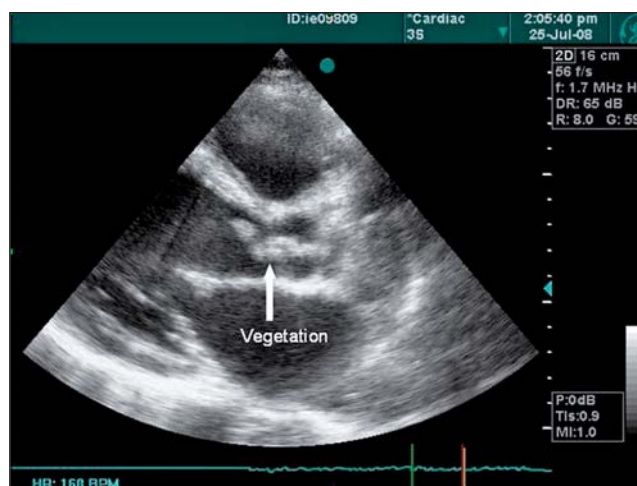


Fig. 1 – On transthoracic echocardiography, parasternal long axis view showing a large vegetation on aortic valve in a case of brucella infective endocarditis.

form of presentation being fever of unknown origin, together with constitutional symptoms such as asthenia, sweating and joint pain. Approximately 25–35% of brucellosis cases present with focal complications, affecting at most the osteo-articular apparatus [2]. A significant portion of the patients with infective endocarditis may present in addition to non-specific symptoms such as fever, fatigue, dyspnea, night sweating, loss of appetite and weight, classical heart failure symptoms such as dyspnea, palpitation and early tiredness. Despite usual causes of infective endocarditis, patients with brucellosis usually suffer from symptoms for 6–2 months. Fever is the most common finding. Additionally, new onset or increased cardiac murmur is considerably significant for endocarditis. Although not specific to brucella endocarditis, arthritis, splenomegaly, petechia, roth spots, Osler nodules, Janeway lesions, splinter hemorrhage, finger clubbing may be present.

Diagnosis

The diagnosis of brucella infective endocarditis requires isolation of bacteria in blood or tissue culture with modified Duke criteria or identifying *Brucella* with serological tests. Etiological diagnosis is not easy; it requires a high level of suspicion and is based on the association of epidemiological data with serological test results and isolation of *Brucella* in previously collected blood or tissue samples. The sensitivity of blood cultures is extremely variable (15–70%) [2,7,8]. The reason for this variability is the time elapsed between symptoms onset and diagnosis, previous recent antibiotic therapy and culture conditions such as culture medium and incubation time. While positivity of blood culture in *Brucella* infection is between 15% and 70%, in *Brucella* infective endocarditis this rate is above 80% [9,10]. *Brucella* is an organism with slow growth rate, which requires a special environment for growth. It is important to obtain the blood culture sample before the start of antibiotic therapy, however even during current antibiotic therapy blood culture sample should be

collected [7,8]. Even in patients under antibiotic therapy in vegetative cultures bacterial growth can be detected [9]. Serological methods are more sensitive but have lower specificity. Wright agglutination titer 1/160 and over is very sensitive and specific for diagnosis of brucellosis [8]. Especially the difficulty of interpreting results in endemic regions and late or absent seroconversion in some patients limits its usage [3,7].

Transthoracic echocardiography plays a crucial role in diagnosing cardiac complications. A trans-esophageal approach may be required in some cases. The aortic valve is most frequently affected, however mitral valve involvement is more common in cases with previous structural changes such as rheumatic valve disease. The most common echocardiographic findings are large vegetation, ulcerations and abscesses, but any structural element of the affected valve may be involved. In prosthesis valve involvement complication such as bulky vegetation, para-valvular leakage, aneurysm, abscess and valve malfunction can be present [11]. The most frequent complication is congestive heart failure, with an incidence of 75–90%. It has a similar rate of embolic events that seen in endocarditis caused by other microbiological agents [4,12].

Treatment

There is considerable uncertainty and controversy regarding appropriate treatment for this clinical entity which leads to significant morbidity and mortality. There is no available clear data with regard to the most effective antibiotic regimen and their durations, and the role and timing of surgical treatment. Given the intracellular nature of *Brucella* which makes most commonly used antibiotics ineffective and the degree of tissue destruction, some authors recommend early surgical valve replacement combined with pre- and postoperative antibiotic therapy [7]. However more recently, some authors have rejected the suggestion that valve replacement is always required. They proposed for some patients a more conservative approach based on long-term combined antibiotics therapy. Cohen et al. described several series of patients with brucella endocarditis treated conservatively, with similar outcomes to those obtained with early surgical intervention as long as there was no heart failure, valve damage or valve prosthesis [13]. Another literature review compared clinical features of medically and surgically treated patients and showed that cardiac failure, abscess and massive valve damage are predictive factors for invasive approach [12]. As for the prosthesis valve infections, treatments of cardiac device infections due to brucella are surgical [14]. Antibiotic therapy is advisable to continue 6 months after surgery [15]. A short time interval between disease onset and initiation of appropriate antibiotic therapy appears to be associated with a favorable clinical course [7]. The most effective regime and duration of antibiotic therapy have not been fully determined, although it is clear that a combination of antibiotic agents for prolonged periods is necessary. Prevailing opinion is a combination therapy with doxycycline and rifampicin for 8–12 weeks, together with an aminoglycoside for the first four weeks of the treatment. In a meta-analysis it was demonstrated that

drugs such as trimethoprim-sulfamethoxazole, quinolones or streptomycin combined with doxycycline, have lower recurrence rates compared to rifampicin [16]. In a recent study published in this issue in Turkey, IV ceftriaxone or aminoglycoside therapy is emphasized as a good option at the beginning of treatment [17].

Conclusion

Brucellosis is a disease which is usually under- and lately diagnosed disease. A serious suspicion and clinical story is needed to not overlook the rare complication of infective endocarditis. Blood culture and serology are important for diagnosis. Echocardiogram is important for the diagnosis and follow-up of complications such as vegetation, abscess, ulceration, prosthesis valve malfunction and cardiac failure associated with infective endocarditis. While the treatment of conditions such as prosthesis valve and other intracardiac device infections, serious valve damage and cardiac failure are definitely surgical, in less severe cases where these complication do not exist and in patients for whom surgical treatment is considered, pre- and post-operative combined antibiotics therapy is essential for the treatment.

Conflict of interest

No conflict of interest.

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Ethical statement

The research was done according to ethical standards.

Informed consent

The presented patient agreed with publication of her disease history.

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