Brucella Endocarditis

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1. Introduction

Brucellosis is a common public-health problem. Human beings are incidental hosts and acquire the disease by direct contact with infected animals or consumption of their products, particularly unpasteurized dairy products. Brucella is a fastidious, intracellular gram-negative coccobacillus. Brucellosis is an endemic disease in Mediterranean area, Persian Gulf borders, India, and South or Central America countries. Infants and children are affected by ingestion of unpasteurized raw milk. Brucellosis is a systemic disease, and diagnosis may be difficult in the absence of contact-history with infected animal or contaminated food. The common presentation is fever of unknown origin, and symptoms usually begin 2-4 weeks after the inoculation. Isolation of organism from blood culture may require 4 weeks of incubation. It is important to inform the microbiology laboratory that infection with Brucella is suspected (1).

Infected endocarditis is a microbial infection of heart endocardium. Native and mechanical cardiac valves are the most common sites of involvement. In all age groups those with structural heart disease are usually affected. Endocarditis can involve septal defects, intracardiac surgical patches, surgical and nonsurgical intracardiac shunts. Neonatal endocarditis most often occurs in the normal heart. Other reasons include: surgical or nonsurgical cardiovascular interventions, increased use of intracardiac prosthetic devices, and prolonged insertion of central venous catheter.

A limited number of pathogens are responsible for most cases with endocarditis. Gram positive cocci account for over 90% of bacteria, of which Streptococcus viridans and Staphylococcus aureus are the most common. Studies indicate that these two microorganisms have a special propensity for adherence to the heart valves of humans and canine animals. In contrast, gram negative bacteria have poor adherence to this system and are isolated in less than 10% of patients with endocarditis: these include: Enterococci, Pseudomonas, Neisseria, and Haemophilus species (2).

Brucella endocarditis is a rare complication of Brucella systemic disease. The aim of this article is to discuss the various aspects of this combined disease.

2. Discussion

Endocarditis is a rare complication of brucellosis; it develops in 1-2% of patients. This complication is responsible for 80% of mortality rate in brucellosis (3, 4). In a research by Keshtkar et al. all the English, and French articles about “Brucella”, “endocarditis”, and “Brucella endocarditis” in PubMed, Google, and SCOPUS search engines were reviewed from January 1966 to July 2011. They found 121 articles with 308 cases of brucella endocarditis. Turkey and Iran had reported most of the cases (41.9%, 10.1% respectively), and 95% of cases were from the Middle East or Mediterranean countries. Diagnosis was confirmed with culture or serology tests and in one patient with PCR (polymerase chain reaction), 82.5% of patients were infected with Brucella melitensis, and 14% with Brucella abortus. The age of patients ranged from 5 to 77 years with a mean of 41 years, and 75.3% were male. Predisposing cardiac condition was evaluated in 233 patients. No underly-
Severe injury of native valves due to rheumatic heart disease usually results in valve replacement with pros-
50% of patients with Brucella endocarditis have underlying valvular diseases (3). Both biologic and mechanical valves have been affected frequently. In endemic area such as Saudi Arabia 10% of prosthetic valves endocarditis are due to Brucella, and vegetations usually appear like a bulky mass. All reports recommended a combination of antimicrobial agents and replacement of the prosthetic valve (13, 14). Valve replacement in acute phase of infection may lead to paravalvular leakage. Brucella may be detected in culture of the infected valve even after 8 weeks of adequate treatment (15). Presence of bacteremia after adequate antimicrobial treatment in patients with prosthetic valves infected with Brucella, should awaken suspicions of endocarditis (16). Growing up in children with implanted prosthetic valve results in malfunction and stenosis of valve, which may need reoperation for valve replacement. Another problem is the paucity of appropriate-size mechanical valve for this age group of patients. For this reason biologic valves are preferred for children. Kazuzu et al. from Turkey (2005) reported a 10-year-old girl with normal heart who was affected with brucella endocarditis. Echocardiography revealed mitral regurgitation with 3 mobile vegetations on the valve surface. On the 4th day of treatment the patient experienced loss of consciousness. Brain magnetic resonance angiography showed acute ischemic infarct in the right parietal region. The patient underwent surgery. Resection of vegetations combined with annuloplasty with a biologic ring and preservation of the rest of native valve was performed. Medical therapy continued for 10 weeks after the operation until normalization of Wright agglutination titer (17). Another report from Turkey presented a child who required aortic valve replacement after brucella endocarditis (18).

Even with appropriate treatment the incidence of relapse is high and ranges from 5% to 40% (19, 20). Obrenovic-Kirenski et al. from Serbia (2012) reported an adult case of mitral valve endocarditis during brucellosis relapse. Mitral valve involvement was complicated by perforation of anterior leaflet of mitral, severe mitral insufficiency, and pulmonary hypertension. The patient improved by mitral valve replacement accompanied with a 6-month postoperative medical therapy. Prior to this report, no cardiovascular involvement during the relapse episode had been described in a study reported the largest series of patients with brucellosis (21). Infection of tricuspid valve in brucella endocarditis is extremely rare. Yazici hu et al. (2012) presented a female patient with fever, fatigue, and severe right heart failure. Echocardiography showed large vegetation on the tricuspid valve. Blood culture had negative results and the titer of anti-brucella antibody was 1/640. The patient recovered on an eight-week medical therapy (22).

Brucella antigen is capable of affecting the endothelial cells of vascular system. This infection produces a potent inflammatory response. The inflammatory response and the reaction of host immune system are suggested as the basis for vascular involvement. Activation of endothelial cells in response to infection accompanied by upregulation of adherent molecules and secretion of proinflammatory chemokines may play an important role in vascular damage. Vascular complications are quite rare and include; arterial aneurysm formation in different vessels, peripheral arteritis, arterial thrombosis, cutaneous vasculitis, deep venous thrombosis, and cerebral vein thrombosis (23). Colomba et al. from Italy (2012) presented a man with brucella endocarditis and manifestations of aortic valve regurgitation as well as subclavian artery thrombosis. Wright agglutination test had positive results, and Brucella melitensis was isolated from blood culture. The aortic valve was replaced with prosthesis by surgery. Medical treatment was administered for 45 days and heparin was given for 10 days (24). McKee et al. from the USA reported a 15-year-old boy infected with Brucella canis after scratch by domestic dog. Echocardiography and cardiac catheterization demonstrated severe aortic regurgitation. Ultra sound examination revealed bilateral aneurysms of the tibioperoneal arteries. Aortic valve was repaired by the Ross procedure and aneurysms were excluded by surgery. Vascular continuity was restored by saphenous vein graft. There was no previous case report of peripheral myotic aneurysms in children (25).

Treatment of choice in brucella endocarditis is combined medical and surgical therapy. Kose et al. from Turkey (2012) reported an adult woman with vegetation on mitral valve treated with medical therapy alone. To their knowledge only 16 cases have been reported in literatures treated with medical therapy alone. Medical treatment alone can be used for mild cardiac involvement and within a short duration of symptoms onset (26). The recommended treatment for bacterial endocarditis in pediatric age group is as follows: doxycycline (2-4 mg/kg/d) maximum 200 mg/d (PO for 4-6 months) plus gentamicin (3-5 mg/kg/d) IM or IV for 2 weeks ± rifampicin (15-20 mg/kg/d; maximum 600-900 mg/d PO) for 4-6 months. Several factors are important for successful treatment including: antimicrobial agent with intracellular killing effect, long-term treatment, and compliance of patient for long-term therapy. Doxycyclines combined with aminoglycosides are the most effective drugs for treatment, and are associated with decline in the recurrence rate (1). There is no specific recommendation for duration of antimicrobial therapy. A combination of clinical, serologic and microbiologic findings helps physicians to decide about the duration of treatment. Normalization of anti-brucella antibody titer is recommended as the end point.
of effective treatment. Periods of treatment reported by different authors vary from 2 to 13 months (26, 27). Indications for surgery are as follows: large vegetation, abscess formation, aneurysm, severe valvular insufficiency, malfunction of prosthetic valve, intractable heart failure, and multiple peripheral emboli (27, 28). Many authors recommended that specific antimicrobial therapy should be continued after the operation until complete clinical recovery occurred, and serum antibody titers and agglutination test reached the normal levels.

Conclusion: Endocarditis due to brucellosis is considered a rare incident involving native, and prosthetic valves. Prompt diagnosis combined with medical and surgical treatment is lifesaving.

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