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A Clinical Case of Aortic Root Abscess Caused by Brucellosis: Molecular Diagnosis, Surgical Treatment and Successful Management

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Abstract: Endocarditis is a rare complication of brucellosis, often fatal and the treatment is controversial. In the present report, an unusual case of repeated bacteraemia caused by *Brucella melitensis* in a 17 years old Sudanese patient is described. The patient was strongly positive for brucellosis by serological reaction but conventional microbiological cultures form blood and valve tissue were largely unsuccessful. However, PCR detected nucleic acid sequence specific for *Brucella melitensis*. The patient was successfully treated by a combination of surgical resection and antibiotics. It is suggested that simultaneous application of bacterial culture and PCR could be more useful than either test alone for the diagnosis of brucellosis in suspected patients.

Key words: PCR, bacterial nucllein, infectious bacteria, *B. Melitensis*, *B. Abortus*, Sudan

INTRODUCTION

In the present report, a 17 years old male patient was admitted to Ahmed Gasim Cardiac Center, Khartoum North, Sudan, with high fever and fatigue. Severe regurgitation of the aortic valve was the main finding of the echocardiograhic study. While blood cultures for brucella were negative, strong suspicion of brucellosis was verified with serological reaction that was positive at a dilution of 1:320. We decided to proceed to surgical treatment and the patient underwent aortic valve replacement.

RESULT AND DISCUSSION

The patient suffered aortic valve vegetations with accompanying ulcerations which lead to complications that subsequently developed into annulus abscesses at the root of the aorta. Replacement with mechanical valves was performed after 2 weeks of prompt antibiotic regimen. Valve culture and post-operative blood samples were also found sterile. Application of Polymerase Chain Reaction (PCR) to DNA extracted from aortic valve tissue resulted in amplification of a 600-bp PCR product specific for Brucella organism (Fig. 1). Species-specific PCR amplification produced a 710-bp PCR product specific for *B. meletensis* (Fig. 2). The post-operative recovary was good and high empirical doses of antibiotic treatment were recommended. Brucellosis is one of the most important diseases in rural areas of developing countries including the Sudan. The villagers usually keep goats as a poor man's cow for milk production and meat consumption. Goats infected with brucellosis shed the organism in the milk as well as other body fluids. Humans are likely to become infected through consumption of row or non pasteurised milk. In Sudan, it has been reported that the social habit of eating raw meat, e.g., raw liver or other offal with spices (Marrara or umfitfit) was considered as an important epidemiological factor in contracting the disease (Mohamed, 1989). Brucellosis infected patients usually received high empirical doses of

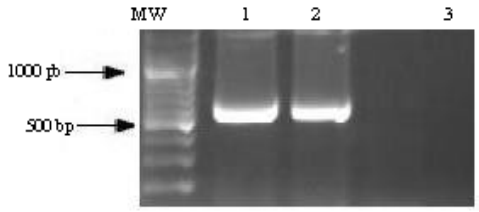

Fig. 1: Detection of Brucella 600-bp PCR Product from DNA extracted from the patient's valve tissues. Lane MW: 100 bp Molecular weight marker; Lane 1: Brucella DNA (Positive control); 2: DNA extracted from valve tissue of the patient; Lane 3: nucleic acid free sample (negative control)

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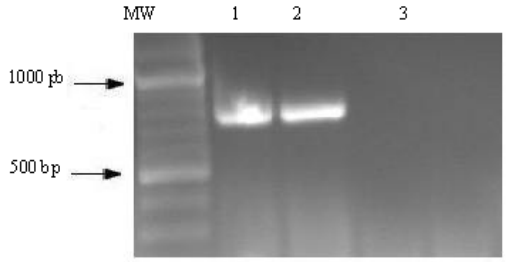

Fig. 2: Specific identification of *Brucella melitensis* 721-bp PCR Product from DNA extracted from the patient's valve tissues. Lane MW: 100 bp Molecular weight marker; Lane 1: *Brucella melitensis* DNA (Positive control); 2: DNA extracted from the valve tissue of the patient; Lane 3: Nucleic acid free sample (negative control)

antibiotics and hence positive blood cultures are not always present, despite the high level of circulating antibodies. Therefore, diagnostic suspicion and therapeutic vigilance are mandatory for the successful management. Brucella endocarditis constitutes a rare but severe complication of brucellosis. In the majority of cases, immediate heart surgery is recommended due to inability to control the infection and the progression shift to congestive heart failure. When valve replacement is undertaken, valvular tissue (including vegetation) should be examined histologically and cultured for the presence of microorganisms, which may allow postoperative antibiotics to be tailored accordingly.

The isolation of microorganisms from valvule culture in infectious endocarditis is infrequent. In a series of 232 patients with Infectious Endocarditis (IE), only 15% had positive valvular culture with staphylococci being most commonly identified (Renzulli *et al*., 2000, 2001). In patients not suspected clinically of IE who undergo valve replacement, it is not recommended to culture the excised valve as a significant number of false positive results occur following contamination at surgery (Campbell *et al*., 2000; Chuard *et al*., 1998). The histological examination was reported to be a more reliable indicator for the presence of micro-organisms than culture (Giladi *et al*., 1997; Chuard *et al*., 1998). Fastidious microorganisms have also been demonstrated on heart valves by various stainingtechniques (Bruneval *et al*., 2001). Fastidious bacteria including *Coxiella* sp., *Bartonella* sp., *Chlamydia* sp. and *Brucella* sp. have been isolated from valves in the absence of positive blood culture although prior positive serological tests had already identified the organisms. Should surgical intervention be required in a patient with IE prior to identification of the microbial cause? It is appropriate to examine valvular material by histology and culture. Bacterial DNA probe analysis of explanted tissue and amplification by Polymerase Chain Reaction (PCR) are alternatives to histology and culture. PCR can also be applied to embolic tissue to obtain a bacterial diagnosis (Mueller *et al*., 1999). Heart valve examination by PCR in clinical practice allows identification of the infecting microorganism when blood cultures are negative due to prior antibiotic therapy or the causative organism is fastidious or non-culturable. Further studies are however, needed before PCR becomes a routinely available clinical test. In the present study, the patient underwent aortic valve replacement. The aortic valve vegetations with accompanying ulcerations have lead to complications that subsequently developed into annulus abscesses at the root of the aorta. Replacement with mechanical valves was performed after 2 weeks of prompt antibiotic regimen.

In the present study, the PCR positive result and culture negative result from the same aortic tissue sample is not surprising. This is because PCR positive result could be obtained from dead bacteria, bacterial nucleic acid as well as infectious bacteria. Therefore, the biological significance of a PCR positive result has to be interpreted with caution in light of the presence of bacterial nucleic acid and absence of infectious bacteria. Never the less, the positive PCR result would be helpful to correlate the clinical findings with the diagnostic aspect of the present case. The blood and valve culture negative results are mainly attributed to the fact that the infected patient continued to receive high empirical doses of antibiotics for a very long period of time. Infectious endocarditis caused by brucellosis may lead to cardiac and extra-cardiac complications (Botta *et al*., 2009; Gunes *et al*., 2009; Mohandas *et al*., 2009). These complications include annulus abscesses at the root of the aorta (Keles *et al*., 2001), pericarditis and diffuse intravascular coagulation (Berbarie *et al*., 1997).

Peery and Belter (1960) reported 80% endocarditis and 43% myocardial abscesses in a total of 44 autopsies on individuals who died of brucellosis. The strains that are most often considered culprits for endocarditis are *B. melitensis* and *B. abortus*. The study on this clinical case indicated that a combination of pharmaceutical and surgical management is proven necessary. The intracellular nature of the microbe is responsible for the fact that anti-microbial agents cannot reach it, since they do not penetrate eukaryotic cells. On the other hand, the microbe causes tissue destruction with a tendency for progressive ulceration and significant risk of imbolism. At the same token with the surgical valve

replacement, it is proposed to use a combination of antibiotics such as aminoglycoside, rifabicin and doxycyclin. The required duration of the treatment is unclear, although most clinicians suggest a 3-6 months regime with rifabicin, doxycyclin and an aminoglycoside for the first 2-6 weeks of treatment. Alternatively, an acceptable antibiotic, instead of rifampin is cotrimoxazole (Berbarie *et al*., 1997).

CONCLUSION

Improved diagnostic techniques and therapeutic vigilance are required for the timely and efficient treatment of endocarditis caused by brucellosis. Populations at risk include those who have history of consumption of non-pasteurized dairy products or goat milk. In addition, surgical treatment with replacement of the affected valve in combination with pharmaceutical treatment for a large period of time should be considered for the successful treatment brucella endocarditis.

Moreover, conventional microbiological examination failed to diagnose brucellosis in blood and valve tissue of the infected patient receiving high doses of antibiotics. Furthermore, PCR-based assay provides a rapid method for detection of brucella-specific nucleic acid sequence in valve tissue samples irrespective of their viability.

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