Mitral valve endocarditis during brucellosis relapse

Endokarditis mitralnog zaliska u toku recidiva bruceloze

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Abstract

Introduction. Endocarditis is the most common cardiovascular manifestation of brucellosis with high mortality rate. Brucella is less accessible to antibiotic (but not for all) and relapse can occur after a various period of clinical latency. Case report. A 55-year-old farmer was diagnosed with acute systemic Brucella infection in May 2008 and treated with antibiotic therapy in regional hospital for two months and for three months after discharge. He began to feel myalgia, arthralgia, malaise, shortness of breath, abdominal pain, vomiting, diarrhoea and lost weight eight months after initial symptoms occurred. Because symptoms progressed he was admitted to our hospital in February 2009. Based on a combination of epidemiological, clinical data (on admission he was cachetic, adynamic, dyspneic, hypotensive 80/50 mmHg, fever up to 39.5°C), positive serological Wright test for brucellosis (1:5120), and echocardiographic examination findings, the diagnosis of very severe relapse of brucellosis was confirmed intraoperatively. The patients' condition was improved and he was operated. The diagnosis of infective endocarditis was confirmed postoperatively. Mitral valve replacement was performed, and combined triple antibiotic treatment (amikacin + ciprofloxacin + cefazolin, for 2 weeks and cephazolin + doxycycline + rifampicin, for 2 weeks) was continued, followed with two antibiotics (doxycycline + rifampicin) for 5 months. The patient completely recovered without any signs of infection 30 months postoperatively. Conclusion. A combined antibiotic therapy and surgery reduce complications and mortality associated with Brucella endocarditis and improve quality of patients' life.

Key words: brucellosis; endocarditis; mitral valve prolapse; recurrence; anti-bacterial agents; surgical procedures, operative; treatment outcome.

Apstrakt

Uvod. Endokarditis je najčešća kardiovaskularna manifestacija bruceloze i ima visoku stopu mortaliteta. Brucella je intracelularni patogen, što je čini slabije dostupnom za antibiotike (mada ne za sve), pa se relaps može javiti posle različito dugog kliničkog latentnog perioda. Prikaz bolesnika. Poljoprovredniku, starom 55 godina, postavljena je dijagnoza bruceloze u maju 2008. i lečen je kombinacijom doksiciklin, gentamicin i imipenem, replacing gentamicin by rifampicin) for 4 weeks and for the next 2 weeks was receiving trimetoprim/sulfamethoxazole and rifampicin. The patients' condition was improved and he was operated. The diagnosis of infective endocarditis was confirmed intraoperatively. Mitral valve replacement was performed, and combined triple antibiotic treatment (amikacin + ciprofloxacin + cefazolin, for 2 weeks and cephazolin + doxycycline + rifampicin, for 2 weeks) was continued, followed with two antibiotics (doxycycline + rifampicin) for 5 months. The patient completely recovered without any signs of infection 30 months postoperatively. Conclusion. A combined antibiotic therapy and surgery reduce complications and mortality associated with Brucella endocarditis and improve quality of patients' life.

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ljenjo je se kombinovanom trojnom antibiotskom terapijom (amikacin + ciprofloksacin + cefazolin, dve nedelje i cefa-
zolin + doksiciklin + rifampicin, 2 nedelje), uz kasniju pri-
menu dvojne antibiotске terapije (doksicikline + rifampicin)
tokom 5 meseci. Bolesnik se oporavio 30 meseci posle ope-
racije, bez ikakvih znakova infekcije. Zaključak. Kombina-
cija antibiotskog i hirurškog lečenja može smanjiti kompli-
kcije i mortalitet koji prati brucelozni endokarditis i, tako-
de, može poboljšati kvalitet života bolesnika.

**Ključne reči:**
bruceloza; endokarditis; zalistak, mitralni prolaps; recidiv; antibiotici; hirurgija, operativne procedure; lečenje, ishod.

**Introduction**

Brucellosis affects more than 500,000 people worldwide each year, and this makes it the most frequent zoonosis. Brucellosis may appear in four different forms, namely, acute, subacute, chronic, and relapse. Even with the appropriate treatment, the incidence of brucellosis relapse remains high, ranging from 5% to 40% of patients in the largest series reported to date.

*Brucella* infection may involve any organ or tissue in the body. Organ involvement can be assigned as focal or complication. Endocarditis is the most common presentation of cardiovascular involvement, which is reported in less than 2% of patients with brucellosis.

We presented a patient with *Brucella* endocarditis, as a complication of *Brucella* relapse infection, who was successfully treated by medical and surgical therapy.

**Case report**

A 55-year old farmer from the Republic of Srpska, entity of Bosnia and Herzegovina was admitted in the regional hospital in May 2008 with the symptoms of acute systemic *Brucella* infection. Epidemiological history revealed that the patient came from the village where *Brucella* infection was present from time to time. In addition, he was a cattleman by vocation and consumed unpasteurized milk products of his private production. During June and July 2008, the patient was treated in the regional hospital with ceftriaxone 4 g/day and metronidazole 1,500 mg/day until the diagnosis of brucellosis was made and then with doxycycline 200 mg/day and gentamicin 160 mg/day. When the patient went home, he was receiving doxycycline 100 mg/day for 3 months. All that time, the patient underwent regular controls and felt well. During that period the patient did not return to his job, ie he did not have contact with animals, and there was no other case of *Brucella* infection in his village. But, again in December 2008, he began to feel myalgia, arthralgia, malaise, shortness of breath, abdominal pain, vomiting, and diarrhea, began to lose weight and was treating with symptomatic therapy. As symptoms prograded he was admitted to the regional hospital in January 2009. Ten days afterwards, on February 10, 2009 he was transferred to our division with symptoms of fever up to 39.5°C, chills, sweating, fatigue, shortness of breath, loss of appetite, vomiting, diarrhea, weight loss, intermittent myalgia and headache.

On admission the patient was cachectic, pale, adynamic, dyspneic, hypotensive (80/50 mmHg) and febrile. Heart auscultation revealed regular rhythm, S3 heart sound and 4/6 holosystolic murmur on the apex. Abdomen palpation revealed painful epigastric region.

Laboratory blood tests showed erythrocyte sedimentation rate 64 mm/h (normal <= 20 mm/h), C-reactive protein 61 mg/mL (normal range <4 mg/L), hemoglobin 99 g/L (normal range 130–180 g/L), red blood cells 3.4 × 10¹²/L (normal range 4.15–4.90 × 10¹²/L), serum iron levels 3.4 μmol/L (11–29 μmol/L), platelets 77 × 10⁹/L (normal range 130–400 × 10⁹/L), aspartate aminotransferase 55 IU/L (normal range 0–35 U/L) and serum creatinine 134 μmol/L (normal value < 133 μmol/L). Blood cultures were negative despite prolonged (3 weeks) incubation. The suspicion of brucellosis was verified with positive Wright sero-reaction, 1 : 5,120 (positive 1 : 320).

Electrocardiography showed sinus rhythm, left atrial enlargement, incomplete right bundle branch block, while chest X-ray revealed cardiomegaly and enhanced opacity of the pulmonary vasculature. Transthoracic echocardiography showed mitral valve prolapse with the rupture of *chordae tendineae* of the anterior mitral leaflet, oscillating vegetation (21 × 13 mm) on that leaflet, calcification on the posterior leaflet 13 mm) on that leaflet, calcification on the posterior leaflet, mitral annulus and severe mitral regurgitation, enlargement of the left atrium (49 mm) and left ventricle end diastolic dimension (60 mm) with normal systolic left ventricular function (ejection fraction 62%; normal range 60%–70%), and moderate tricuspid regurgitation. Pulmonary artery systolic pressure was 70 mmHg normal pulmonary artery systolic pressure at rest is 18 to 25 mmHg (Figure 1).

**Fig. 1 – M and 2-D echocardiogram, parasternal long axis view presenting the huge vegetation (arrow) attached to anterior mitral leaflet (during medical therapy)**

At the beginning of hospitalization the patient was treated with vancomycin 1,000 mg/day, ciprofloxacin 200 mg/day and gentamicin 80 mg/day. When the suspicion to Brucella infection was verified, the patient was immediately switched to triple antibiotic regimen including doxycycline 200 mg/day, gentamicin 80 mg/day and imipenem 1,500 mg/day and after 2 weeks gentamicin was replaced by rifampicin 600 mg/day. This therapy was administered for 4 weeks and then for the next 2 weeks, the patient was receiving trimetoprim/sulfamethoxazole 960 mg/day and rifampicin 600 mg/day.

After 4 weeks of antibiotic and symptomatic therapy, the patient’s condition was significantly improved, he was not febrile any more, the laboratory tests were much better, but echocardiography still showed huge, mobile mitral valve vegetation (Figures 2a and 2b) and perforation of the anterior mitral leaflet. Heart catheterization confirmed pulmonary hypertension. Selective coronaryography which is routinely performed in patients older than 40 years of age undergoing, besides coronary revascularization, any other form of heart surgery, failed to show significant coronary artery stenosis. Computed tomography which is also routinely performed in patients with infective endocarditis in preoperative evaluation before the heart operation showed small old multiple cerebral infarctions. On the 29th of March 2009, when general condition was tolerable, the patient was operated on. The diagnosis of the infective endocarditis was confirmed intraoperatively (Figures 3a and 3b). Mitral valve replacement was performed, using the No. 27 mm St. Jude bileaflet prosthetic valve. Histopathologic examination revealed the signs of infective endocarditis, and cultures from the valve were negative. Antibiotic treatment was continued four weeks after the operation with three antibiotics: amikacin 1000 mg/day, ciprofloxacin 400 mg/day and cefazolin 2 g/day for 2 weeks parenterally, followed by cefazolin 2 g/day, doxycycline 200 mg/day and rifampicin 600 mg/day for another 2 weeks. Postoperative period was complication-free. During the following 5 months, the patient was treated orally with doxycycline 200 mg/day and rifampicin 600 mg/day. Clinical follow-up was done on regular basis. In September 2011, 30 months after the operation, the patient felt well, completely recovered and without any signs of infection.
Discussion

Brucellosis is a ubiquitous zoonosis, endemic in Mediterranean basin, Arabian Peninsula, South Asia, Central and South America. It is present in the Balkan region as well. The primary transmission route of brucellosis is by the ingestion of unpasteurized dairy products in endemic countries. It is systemic disease which may affect almost every organ or tissue in the body. Organ involvement can be assigned as focal involvement or complication. The most common affected systems are the locomotor, gastrointestinal, genitourinary and hematologic. Cardiovascular complications are rare, occurring in 0.7% to 2.3% of patients in large studies. Despite treatment including several antibiotic regimens, the relapse is estimated to occur in 5%–40%, even up to 50% with a single drug regimen, of patients with acute brucellosis in the following year, depending on antibiotic use, duration of treatment, and drug combination. In the literature, the highest rate of relapses is with osteoarticular manifestation. In the biggest reported series of patients with brucellosis there was no patient with relapse involving the cardiovascular system.

We present our experience in the treatment of rare form of relapse of brucellosis associated with mitral valve endocarditis successfully treated both medically and surgically.

Our patient had the first attack of illness in May 2008. It is well known that most brucellosis infections present in spring and summer months. Although he was treated for few months, the illness recurred in December 2008. Brucella is an intracellular pathogen, which makes it immune to defense mechanisms of the host by phagocytes and polymorphonuclear leucocytes. After surviving intracellular defense mechanisms it stays in reticuloendothelial system. Because of this relapse can occur after a various period of clinical latency. Our patient, despite a prolonged antibiotic therapy, had very severe relapse with mitral valve endocarditis complicated with perforation of anterior mitral leaflet. These complications are rarely described in literature. The diagnosis of brucellosis was based on combination of clinical data, laboratory and positive serologic reactions.

Endocarditis is a rare and very severe complication of brucellosis, with high mortality rate. The left side of the heart is usually affected, predominantly the aortic valve (75%), less common (8.3%) mitral valve. Brucella is slowly destructive organism, with marked tendency to tissue ulceration. Vegetations in Brucella endocarditis are large, carrying the significant risk of embolization, and difficulty in eradicating with medical therapy alone.

The treatment of human brucellosis continues to pose a problem. The best therapeutic approach to Brucella endocarditis involves a combination of medical and surgical treatment. It is reported in literature that only these two treatments together successfully eradicate infection as Brucella can produce very destructive lesions when it is nested in the valvular endocardium. Antibiotic treatment alone is considered ineffective by most authors although there are sporadic cases successfully treated with only medical therapy. This is attributed to the intracellular localization of Brucella, the site that is relatively inaccessible to antibiotics. Even if symptoms improved and subsided with antibiotics, surgery would be still necessary because of the embolic potential of residual vegetation or to relieve valvular obstruction. Literature has reported confronting theories regarding the proper timing of surgical procedure of the affected valve in patients with diagnosed Brucella endocarditis. Although some authors implicate the necessity of surgical treatment as early as possible even during the antimicrobial therapy, others suggest that it is better to postpone the surgical valve replacement after the antimicrobial treatment. The duration of antimicrobial therapy after valve replacement remains a bit disputable. Treatment periods that have been reported by different authors vary from 2–13 months. The decision to discontinue antimicrobial therapy could be determined on patient-to-patient basis, after a thorough clinical observation and evidence of negative IgA antibodies, normal CRP, and reduction of Wright seroreaction titers below 1/64. A patient also must be symptom-free. In our case, the patient was administered 6 month-postoperative antimicrobial treatment in order to eradicate Brucella. Justification for such postulation was confirmed in our case where patient was Brucella-free, symptom-free, and without cardiac complications after 30 months of a follow-up period.

Conclusion

Cardiac involvement in human brucellosis is extremely rare, especially in relapse, but should not be overlooked, since it is a major mortality cause in brucellosis infection. The success of Brucella endocarditis treatment depends on timely and complete medical and epidemiological evaluation, which leads to adequate medicamentous and surgical treatment of a patient. This approach reduces complications and mortality associated with Brucella endocarditis and improves patients’ quality of life.

References


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