

MYCOBACTERIUM ABSCESSUS ENDOCARDITIS: A CASE REPORT AND LITERATURE REVIEW

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Infective endocarditis owing to *Mycobacterium abscessus* infection is rarely reported. Most cases of infective endocarditis caused by *Mycobacterium abscessus* are seen in patients after valve replacement. Although early surgical intervention is recommended and medical treatment with antibiotics according to the susceptibility to the pathogen, such as amikacin, imipenem, cefoxitin, quinolones and macrolides, are applied, the course of such endocarditis is usually subacute and often has fatal outcomes. The present case was a 29-year-old male patient who was an intravenous drug user who had recurrent endocarditis caused by *Mycobacterium abscessus*. Unusually, our reported case was infected on his native valve. However, we experienced recurrence despite antimicrobial therapy. For culture-negative endocarditis, physicians should consider the possibility of *Mycobacterium abscessus* infection and related treatment difficulties.

Key Words: endocarditis, *Mycobacterium abscessus*
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Infective endocarditis (IE) is the proliferation of microorganisms on the endocardium of the heart. Endocarditis caused by *Mycobacterium abscessus* (*M. abscessus*) is rare and only five cases have been published since 1975. Four of the five patients with *M. abscessus* endocarditis were associated with prosthetic valve infection. Only one patient with native valve endocarditis caused by *M. abscessus* has been published [1]. *M. abscessus* endocarditis has been found to be associated with history of surgery (cardiac, valvular), foreign bodies, trauma, intravenous (IV) injections, hemodialysis or immunocompromised status. Here, we present a case of native valve endocarditis with *M. abscessus* infection.

CASE PRESENTATION

A 29-year-old male patient who was an IV heroin abuser had an episode of methicillin susceptible *Staphylococcus aureus* (MSSA)-associated tricuspid valve infective endocarditis that was previously treated once in January 2006. Mild tricuspid regurgitation (TR) and vegetation (0.6×0.9 cm) were involved in the septal leaflet of the tricuspid valve as determined by echocardiography. In June 2006, he was readmitted with a fever extending for 1 month. Vegetation (0.75×1.66 cm) with high echogenicity involving the septal leaflet of the tricuspid valve and moderate TR was found by echocardiography. A smear from culture medium of blood culture (BACTEC system, SA bottle) showed acid-fast stain (AFS)-positive bacilli. He was treated for miliary tuberculosis (TB) initially with rifampin 600 mg/day and isoniazid 300 mg/day, ethambutol 800 mg/day, pyrazinamide 1,500 mg/day plus streptomycin 1 g/day, and he was discharged in July 2006 with afebrile status. He continued with oral



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rifampin 600 mg/day and isoniazid 300 mg/day, ethambutol 800 mg/day and pyrazinamide 1,500 mg/day after discharge.

In August 2006, he was admitted again with relapse of the fever. The blood culture obtained at the patient's hospitalization in June 2006 was identified to be *M. abscessus* according to a polymerase chain reaction (PCR)-restriction fragment length polymorphism (RFLP) analysis of the 65-kDa heat shock protein (Figure 1) [2]. Echocardiography revealed a 2.3 × 1.9 cm vegetation over the septal leaflet of the tricuspid valve and severe TR. The vegetation was bigger than that recorded during the previous echocardiogram in June 2006. In response to the presence of *M. abscessus* in the blood culture, he started treatment with clarithromycin 500 mg/day and imipenem 250 mg twice daily for 4 weeks. He was discharged with afebrile status and was free from heart failure. Echocardiography before discharge revealed that the vegetation size had decreased to 1.73 × 1.69 cm. He continued with oral clarithromycin 500 mg/day plus moxifloxacin 400 mg/day treatment until November 2006.

In November 2006, he was readmitted for recurrent infective endocarditis. Echocardiography revealed severe TR with two vegetations (0.72 × 1.06 cm; 2.41 × 1.04 cm) over the septal and anterior leaflets of the tricuspid valve (Figures 2A and 2B). Chest X-ray revealed pneumonia over the right middle lung field. Initial laboratory data revealed: white blood cell count (WBC) 7,730/μL; hemoglobin 10.1 g/dL; platelets 120,000/μL; blood urea nitrogen 35.6 mg/dL; creatinine 2.04 mg/d; and C-reactive protein (CRP) 104 mg/L.

Blood culture still showed AFS-positive bacilli but negative findings for common aerobic pathogens. Because of suspected TB-associated IE, he was treated with rifampin 600 mg/day and isoniazid 300 mg/day, ethambutol 800 mg/day plus clarithromycin 500 mg twice daily. Surgical intervention was strongly suggested, but the patient hesitated and finally received continued medical therapy. Chest computed tomography

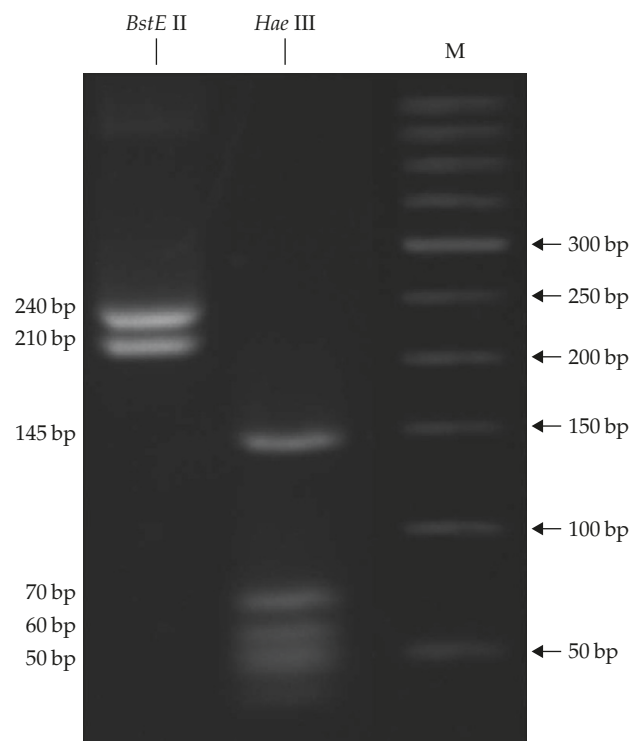


Figure 1. PCR-RFLP for isolates of *M. abscessus*. The restriction enzyme used to generate the PCR-RFLP pattern for each lane is indicated. Lane M = molecular size marker (50-bp ladder).

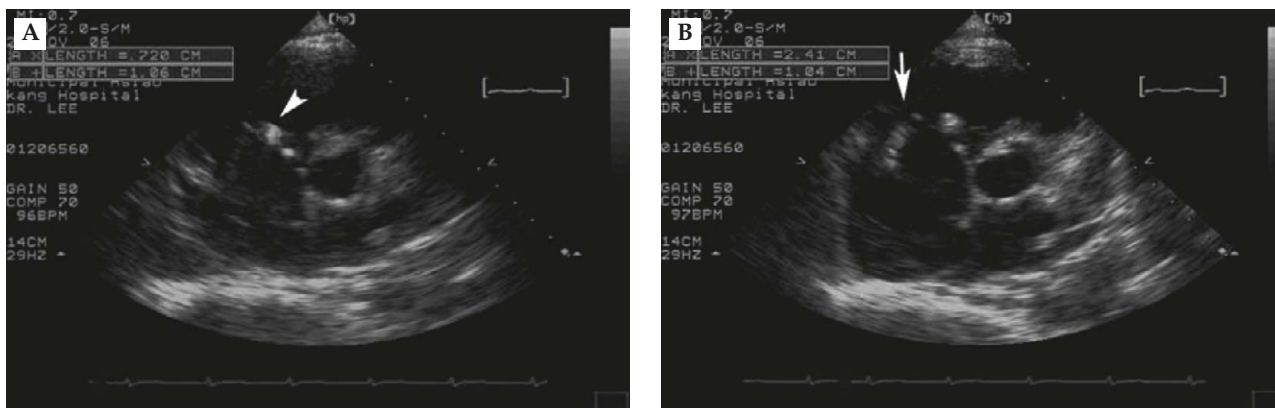


Figure 2. Echocardiography: parasternal short axis view. Two vegetations are shown. (A) Vegetation A (0.72 × 1.06 cm) was observed at the septal leaflet of the tricuspid valve (arrowhead). (B) Vegetation B (2.41 × 1.04 cm) was observed at the anterior leaflets of the tricuspid valve (arrow). The echogenicity of the vegetation is high compared with the adjacent heart tissue.

demonstrated TB pneumonia-like lesions in the right lower and middle lung with right pleural effusion and pericardial effusion. Blood cultures still produced *M. abscessus*. A sputum smear revealed AFS-positive bacilli and sputum culture grew *M. abscessus*. Since the *M. abscessus* endocarditis relapsed after imipenem, clarithromycin and moxifloxacin treatment, clarithromycin plus amikacin were chosen as the treatment regimen. After treatment with clarithromycin 500 mg twice daily plus amikacin 750 mg/day for 2 weeks, he became afebrile and vital signs stabilized. There were no signs of heart failure. The pneumonia-like lesions improved after antibiotic treatment, and laboratory data before discharge were: CRP 73 mg/L (normal range, <5 mg/L); and WBC 6,670/ μ L. He was discharged with continuing oral clarithromycin 500 mg twice daily plus ciprofloxacin 400 mg twice daily for 8 weeks at our clinic, and was then lost to follow-up.

At his last visit to our clinic in January 2007, we repeated the echocardiography. It revealed that the size of the vegetations had decreased to 0.8 \times 1.5 cm and 2.2 \times 1.1 cm over the septal and anterior leaflets of the tricuspid valve, respectively, and the TR was still severe. The patient had poor medication compliance and "doctor shopping" between hospitals. Even though we planned for him to receive surgical intervention and a full course of antibiotic treatment, he hesitated and was subsequently lost to follow-up and did not receive further management from us. The patient had positive rheumatoid factor, decreased complement level (C3, 28.1 mg/dL; C4, 9.25 mg/dL) and decreased CD4 count (155/mm³), but was negative for human immunodeficiency virus antibody and negative for antinuclear antibodies.

DISCUSSION

Infective endocarditis caused by *M. abscessus* is very rare and unique; accordingly, we have reviewed the literature about the care and prognosis of this disease. *M. abscessus* is grouped with a number of rapid-growth nontuberculous mycobacteria (NTM), which includes *M. fortuitum*, *M. chelonae*, and *M. abscessus*. These rapid-growth NTM have been found in potable and natural water, and in soil. They can also be isolated from contaminated tap water. Infection with *M. abscessus* may lead to localized infections such as subcutaneous abscesses, lymphadenitis, pneumonia,

keratitis, prosthetic valve endocarditis, osteomyelitis, meningitis and disseminated infection [3–5]. The pulmonary lesion and the endocarditis caused by *M. abscessus* in this case were identified based on the PCR-RFLP study of the gene encoding for the 65-kDa heat shock protein [2].

To our knowledge, only one other case has been reported in the literature to have native valve endocarditis caused by *M. abscessus* [1]. In a review of the English-language publications, endocarditis caused by *M. chelonae* (formerly *M. chelonae* subspecies *chelonae*) or *M. abscessus* (formerly *M. chelonae* subspecies *abscessus*) has been documented in only nine cases. Since *M. abscessus* has also been classified as *M. chelonae* before, we reviewed endocarditis with the search terms of *M. chelonae* and *M. abscessus* but not of *M. fortuitum*. Five of the nine cases were infected with *M. abscessus* and the others were infected by *M. chelonae*. Seven of them were associated with prosthetic valve endocarditis, but none of them survived after treatment. The only surviving case was associated with native valve endocarditis [1,3,5–10]. Most of the cases infected with NTM endocarditis were subacute and had fatal outcomes, especially those with prosthetic valve endocarditis (Table). Infective endocarditis owing to NTM infection was considered when associated with the status after valvular and cardiac surgery, immunocompromised hosts, intravenous drug abuse, dialysis, patients who received renal transplant and immunosuppressive therapy, and individuals on corticosteroid therapy [3,5,6,9].

The case we reported is only the second patient to have native valve endocarditis infected by *M. abscessus*. The portal of entry in our case was not clear, but may be attributed to his use of tap water for heroin powder dilution and for injection. Another contributing factor was his immune system compromise with low complement, low CD4 level and positive rheumatoid factor, which may be related to his drug abuse, although the decreased complement level and positive rheumatoid factor may be the result of IE.

Rapid-growth NTM has been reported to be resistant to many antimicrobial agents, including most primary and secondary line antituberculosis agents *in vitro*. However, some strains of *M. abscessus* and *M. chelonae* were found to be sensitive to amikacin, clarithromycin, cefoxitin, erythromycin and quinolone [3,10]. Combination therapy with different classes of antimicrobial agents is usually recommended because

Table. Clinical characteristics of patients with infective endocarditis due to *Mycobacterium abscessus* infection

Case	Reference	Age (yr)/sex	Involved valve	Prosthetic valve	Pathogen	Culture source	Antibiotics	Disease duration	Outcome
1	Rumisek et al [9]	25/F	Mitral, prosthesis	Hancock porcine bioprosthesis	<i>M. chelonae</i> ssp <i>chelonae</i>	Prosthesis	RIF+ERY	1979.4–1982.10	Died
2	Levy et al [7]	55/M	Aortic, prosthesis	Hancock porcine bioprosthesis	<i>M. chelonae</i>	Prosthesis	Isoniazid + AMK + RIF + clofazimine	1976.12–1977.1	Unknown
3	Liebeskind et al [1]	35/M	Mitral, native	None	<i>M. chelonae</i> ssp <i>abscessus</i>	Blood, CSF, BM	CLR+FOX	7 mo	Died
4	Galil et al [3]	66/M	Tricuspid, native	None	<i>M. chelonae</i> ssp <i>chelonae</i>	Blood, lung, tricuspid valve	CIP + CLR	1994.10–1995	Alive
5	Repath et al [8]	43/M	Mitral, aortic, prosthesis	Starr-Edwards prosthesis	<i>M. chelonae</i>	Blood, BM	ERY + KAN	1971.4–1972.1	Died
6	Altmann et al [6]	45/M	Aortic, prosthesis	Bjork-Shiley artificial	<i>M. chelonae</i> ssp <i>abscessus</i>	Blood, prosthesis	Lincomycin + cloxacillin	1972.6–1973.7	Died
7	Viscidi et al [10]	55/M	Mitral, prosthesis	Kay-Shiley / Bjork-Shiley prosthesis × 2	<i>M. chelonae</i> ssp <i>abscessus</i>	Blood, urine, BM, sputum, wound	AMK + ERY + ethionamide	1979.3–1979.8	Died
8	Wallace et al [5]	53/M	Prosthesis	N/A	<i>M. chelonae</i> ssp <i>abscessus</i>	N/A	N/A	N/A	Died
9	Wallace et al [5]	50/M	Prosthesis	N/A	<i>M. chelonae</i> ssp <i>abscessus</i>	N/A	N/A	N/A	Died
10	This case	29/M	Tricuspid, native	None	<i>M. chelonae</i> ssp <i>abscessus</i>	Blood, sputum	AMK + CIP + CLR	2006.8–2007.5	Alive

M. chelonae = *Mycobacterium chelonae*; ssp = subspecies; RIF = rifampin; ERY = erythromycin; AMK = amikacin; CSF = cerebrospinal fluid; BM = bone marrow; CLR = clarithromycin; FOX = cefoxitin; CIP = ciprofloxacin; KAN = kanamycin; N/A = data not available.

monotherapy was found to cause resistance of NTM [11]. The duration of antimicrobial therapy in patients with NTM-related endocarditis is still controversial. Previous reports have suggested that the antimicrobial treatment should last for at least 6 months or 3 months after aggressive surgical intervention [3]. Owing to frequent failure of medical treatment, early surgical intervention in combination with antimicrobial treatment has been recommended for patients with NTM-related endocarditis [3,4,9,10]. Our case was treated with clarithromycin plus amikacin, and antimicrobial therapy was shifted to the oral form of ciprofloxacin plus clarithromycin for 8 weeks after discharge. It is not clear whether the exacerbation of IE could be restrained by clarithromycin plus ciprofloxacin treatment because the patient in our case study was treated for only 8 weeks and then lost to follow-up.

In summary, infective endocarditis caused by *M. abscessus* and other rapid-growth mycobacterium is not readily diagnosed and treated. For culture-negative endocarditis, awareness of the possibility of NTM infection should be considered, especially when patients have related predisposing factors.

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膿腫分枝桿菌心內膜炎 — 病例報告與文獻探討

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膿腫分枝桿菌 (*Mycobacterium abscessus*) 引起的感染性心內膜炎是非常罕見的。大部分膿腫分枝桿菌引起的感染性心內膜炎是發生在瓣膜置換術後之瓣膜。儘管應用了早期手術介入及根據敏感性測驗使用抗生素如 **amikacin** , **imipenem** , **cefoxitin** , **quinolone** , **macrolides** 的治療, 此種心內膜炎仍然是亞急性且致命的。我們發表一個 29 歲的靜脈毒癮者其感染上由膿腫分枝桿菌引起的復發性心內膜炎。我們報告的病例非常罕見的在其自然瓣膜上受到膿腫分枝桿菌的感染而引起心內膜炎, 儘管在抗生素治療後其仍復發。對於血培養陰性的感染性心內膜炎, 醫師必須要考慮到膿腫分枝桿菌感染的可能性和其治療上的困難性。

關鍵詞：心內膜炎，膿腫分枝桿菌
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