Endocarditis Caused by Stenotrophomonas maltophilia: Case Report and Review

Félix Gutiérrez Rodero, María del Mar Masiá, Javier Cortés, Victoria Ortiz de la Tabla, Vicente Mainar, and Antonio Vilar

Stenotrophomonas (Xanthomonas) maltophilia is a rare cause of endocarditis. The extensive resistance of this organism to several antibiotics leaves few options for antimicrobial therapy. In vitro synergism of the combination of trimethoprim-sulfamethoxazole (TMP-SMZ) and ticarcillin/clavulanic acid (TIC/CA) has been demonstrated. To our knowledge, we report the first case of ventriculocerebral fluid shunt–associated endocarditis due to S. maltophilia. The patient was cured with combination therapy with TMP-SMZ and TIC/CA along with catheter removal. This is also the first report of S. maltophilia endocarditis successfully treated with this antibiotic combination. In a review of the medical literature, only 16 cases of S. maltophilia endocarditis were found. Most patients were intravenous drug users (43.8%) or had either prosthetic heart valves (50%) or an indwelling vascular catheter (18.8%). Although S. maltophilia is usually considered a nosocomial pathogen, about one-half of the cases were community-acquired. Twelve of sixteen patients had left-sided endocarditis. Therapy with a combination of two or more antibiotics was employed in most cases. Seven patients had been given TMP-SMZ therapy, but none had been treated with TIC/CA before. One-half of the patients required cardiac surgery. The overall mortality rate was 33%. Although the optimal antibiotic treatment for S. maltophilia endocarditis remains unknown, the case reported herein reinforces in vitro findings that the combination of TMP-SMZ and TIC/CA may be effective therapy.

Case Report

A 60-year-old woman was hospitalized because of fever, chills of several months’ duration, cough, and right pleuritic pain that had developed 3 weeks before admission. Her medical history was significant for subarachnoid hemorrhage with hydrocephalus 18 years earlier for which a ventriculocerebral CSF shunt was created. Fourteen years later, in 1990, the intracranial shunt reservoir was removed because of malfunction, and the extracranial catheter was left in place. A CT obtained after the procedure did not show hydrocephalus.

Three years later, in 1993, she had fever and signs of local tissue inflammation with purulent discharge located on the cervical trajectory of the shunt. A surgical procedure, including drainage with debridement of infected and devitalized tissues, was carried out in another hospital. An attempt was also made to remove the catheter by pulling it out, but a piece of it stuck to the wall of the jugular vein and could not be removed. The patient remained febrile, and 4 months later, she underwent another operation during which the portion of the catheter stuck to the jugular vein was finally removed. Nevertheless, her fever continued, and she was referred to our hospital.

At the time of admission to our hospital, her temperature was 39°C. There was a grade 3/6 systolic ejection murmur along the left sternal border, and petechiae were noted on both lower limbs. The remainder of the physical examination, including a funduscopic evaluation, was unremarkable. Laboratory findings included a hemoglobin level of 10.1 g/dL, a WBC count of 8,200/mm³ (normal differential blood cell count), and an erythrocyte sedimentation rate of 46 mm/h. Biochemical analysis of serum disclosed unremarkable results, except for an alkaline phosphatase level of 329 U/L (normal, 98–279 U/L) and a γ-glutamyltransferase
level of 132 U/L (normal, 11–50 U/L). Urinalysis revealed blood, and microscopic examination of urine showed 25 RBCs per high-power field.

Coagulation studies and an electrocardiogram were unremarkable. A chest roentgenogram showed a right-upper-lobe infiltrate with central cavitation. An abdominal ultrasonogram was normal. A two-dimensional echocardiogram revealed a vegetation on the septal leaflet of the tricuspid valve along with moderate regurgitation.

Three of three cultures of blood obtained at admission were positive for *S. maltophilia*. MICs were determined by the broth microdilution method (Neg Combo 61, Dade MicroScan, Baxter Laboratories, West Sacramento, CA). Breakpoints were based on the standards of the National Committee for Clinical Laboratory Standards [18]. Following determination of the MIC, the MBC was measured by subculturing the wells of a Neg Combo 61 panel containing concentrations of antimicrobial agent equal to and greater than the MIC to know whether the initial inoculum was inhibited or killed [19].

The subcultures were prepared and incubated as follows. The contents of each well were mixed with a mechanical microdilution tray shaker-mixer to achieve a uniform suspension of organisms. Thereafter, the entire contents of each well were removed with use of a 100-μL micropipette. Each sample was inoculated onto a separate plate with blood agar, spreading the sample over the entire surface. Plates were incubated at 37°C for 24 hours. The MBC endpoint was defined as the lowest concentration of antimicrobial agent that killed ≥99.9% of the test inoculum.

The isolate was susceptible to TMP-SMZ (MIC, <2/38 μg/mL; MBC, >2/38 μg/mL) and TIC/CA (MIC, 32 μg/mL; MBC, 64 μg/mL), moderately susceptible to gentamicin (MIC, 8 μg/mL; MBC, >8 μg/mL), and resistant to ticarcillin (MIC, >64 μg/mL), imipenem (MIC, >8 μg/mL), cefotaxime (MIC, >32 μg/mL), ceftazidime (MIC, >16 μg/mL), aztreonam (MIC, >16 μg/mL), amikacin (MIC, >64 μg/mL), ciprofloxacin (MIC, >2 μg/mL), and piperacillin (MIC, >64 μg/mL). The strain was resistant to piperacillin/tazobactam by the Kirby-Bauer disk diffusion method with a 100/10 μg disk (Difco Laboratories, Detroit) (diameter of inhibition zone, <17 mm) [20].

The patient was treated intravenously with TMP-SMZ (240 mg every 6 hours) and TIC/CA (4 g every 4 hours). Her condition improved clinically, and her fever abated on day 7 of combined antibiotic treatment. Resolution of all symptoms and signs of infection was achieved within 2 weeks, and serial chest radiographs showed that the infiltrate and cavitation had cleared. Follow-up cultures of specimens taken on day 7 and day 21 of antibiotic treatment were negative. A follow-up echocardiogram obtained on day 30 of therapy still showed the cardiac vegetation on the tricuspid valve. In addition, it revealed irregular echoes in the right ventricular cavity with a distribution consistent with a ventricular catheter.

Cardiac catheterization via a cannula in the right femoral vein was carried out. By using an intravascular retriever set with a helical loop basket (Cook, Bloomington, IN), a short fragment of catheter was picked up and removed from the ventricular cavity. Culture of the extracted catheter subsequently yielded *S. maltophilia*.

The patient continued receiving treatment with TMP-SMZ and TIC/CA for 3 weeks after catheter removal. Overall, she completed a 7-week therapeutic course of the antibiotic combination. Before she was discharged from the hospital, a third echocardiogram showed only some irregular echoes on the tricuspid valve, which were thought to be consistent with a residual vegetation. She remained well at follow-up examinations over a 15-month period.

**Literature Review**

A MEDLINE (National Library of Medicine) search of the literature for contemporary case reports of *S. maltophilia* endocarditis was performed by using the key words *Xanthomonas maltophilia, Pseudomonas maltophilia*, and *Stenotrophomonas*, which were cross-referenced with endocarditis and cardiac infection. The references of the case reports were examined for additional cases, especially those cited in older articles not entered in the bibliographic database. The review of the literature to November 1995 revealed 16 previously reported cases of endocarditis caused by *S. maltophilia* [2, 8–17]. Fifteen of these cases and our case are summarized in table 1.

**Discussion**

*S. maltophilia* is primarily considered a nosocomial pathogen. Infections due to *S. maltophilia* have become increasingly important in the hospital setting [6, 21]. Patients compromised by debilitating illnesses, surgical procedures, or indwelling vascular catheters are most prone to *S. maltophilia*. Prior antimicrobial therapy with aminoglycosides, imipenem, expanded-spectrum cephalosporins, and fluoroquinolones has become increasingly resistant to piperacillin/tazobactam by the KITby-Bauer disk diffusion method with a 100/10 μg/mL, *S. maltophilia* is primarily considered a nosocomial pathogen. Infections due to *S. maltophilia* have become increasingly important in the hospital setting [6, 21]. Patients compromised by debilitating illnesses, surgical procedures, or indwelling vascular catheters are most prone to *S. maltophilia*. Prior antimicrobial therapy with aminoglycosides, imipenem, expanded-spectrum cephalosporins, and fluoroquinolones has become increasingly resistant to piperacillin/tazobactam by the KITby-Bauer disk diffusion method with a 100/10 μg/mL. The isolate was susceptible to TMP-SMZ (MIC, <2/38 μg/mL; MBC, >2/38 μg/mL) and TIC/CA (MIC, 32 μg/mL; MBC, 64 μg/mL), moderately susceptible to gentamicin (MIC, 8 μg/mL; MBC, >8 μg/mL), and resistant to ticarcillin (MIC, >64 μg/mL), imipenem (MIC, >8 μg/mL), and cephalosporins (MIC, >32 μg/mL), cefotaxime (MIC, >16 μg/mL), aztreonam (MIC, >16 μg/mL), amikacin (MIC, >64 μg/mL), ciprofloxacin (MIC, >2 μg/mL), and piperacillin (MIC, >64 μg/mL). The strain was resistant to piperacillin/tazobactam by the Kirby-Bauer disk diffusion method with a 100/10 μg disk (Difco Laboratories, Detroit) (diameter of inhibition zone, <17 mm) [20].

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Table 1. Summary of data on 16 cases of endocarditis due to *Stenotrophomonas maltophilia*.

<table>
<thead>
<tr>
<th>Case no. [reference], age (y)/sex</th>
<th>Predisposing factor(s)</th>
<th>Valve(s) involved</th>
<th>Cardiac underlying disease(s)</th>
<th>Treatment</th>
<th>Cardiac surgery needed</th>
<th>Outcome</th>
<th>Adverse event(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 [9], 32/M</td>
<td>IVDU, surgically implanted subcutaneous reservoir</td>
<td>Tricuspid native</td>
<td>None</td>
<td>TMP-SMZ</td>
<td>No</td>
<td>Died</td>
<td>CHF</td>
</tr>
<tr>
<td>2 [10], 33/M</td>
<td>IVDU</td>
<td>Aortic native, tricuspid native</td>
<td>Aortic stenosis, atrial fistula</td>
<td>Combination: TIC, Mox, and TMP-SMZ</td>
<td>Yes</td>
<td>Died</td>
<td>CHF, heart abscesses</td>
</tr>
<tr>
<td>3 [2], NR</td>
<td>Central venous catheter</td>
<td>Tricuspid native</td>
<td>Repaired atrial septal defect</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>4 [2], NR</td>
<td>NR</td>
<td>Aortic native</td>
<td>None</td>
<td>NR</td>
<td>NR</td>
<td>Died</td>
<td>NR</td>
</tr>
<tr>
<td>5 [2], NR</td>
<td>Central venous catheter</td>
<td>Aortic native</td>
<td>None</td>
<td>NR</td>
<td>NR</td>
<td>Died</td>
<td>NR</td>
</tr>
<tr>
<td>6 [11], 65/F</td>
<td>Cystoscopy</td>
<td>Mitral prosthetic</td>
<td>NR</td>
<td>Carb, Gm, Km, Chl, Pen, PmB</td>
<td>Yes</td>
<td>Cured</td>
<td>Persistent bacteremia</td>
</tr>
<tr>
<td>7 [12], 33/M</td>
<td>IVDU, invasive dental procedure</td>
<td>Aortic prosthetic</td>
<td>NR</td>
<td>Combination: TMP-SMZ, Amp, and Gm</td>
<td>Yes</td>
<td>Cured</td>
<td>Perivalvular abscesses</td>
</tr>
<tr>
<td>8 [13], 38/M</td>
<td>Contaminated collection tubes used for coagulation studies</td>
<td>Mitral prosthetic</td>
<td>Streptococcal endocarditis</td>
<td>Combination: Sm and Pen</td>
<td>No</td>
<td>Died</td>
<td>Brachial artery emboli</td>
</tr>
<tr>
<td>9 [14], 22/M</td>
<td>IVDU</td>
<td>Aortic prosthetic</td>
<td>NR</td>
<td>Combination: GM and Carb; combination: Amik, Carb, and TMP-SMZ</td>
<td>Yes</td>
<td>Cured</td>
<td>Septic tenosynovitis</td>
</tr>
<tr>
<td>10 [14], 57/M</td>
<td>IVDU</td>
<td>Aortic native, mitral native</td>
<td>Rheumatic carditis</td>
<td>Combination: TMP-SMZ and PmB</td>
<td>No</td>
<td>Cured</td>
<td>Septic tenosynovitis</td>
</tr>
<tr>
<td>11 [14], 31/F</td>
<td>IVDU, recent dental extractions</td>
<td>Aortic prosthetic</td>
<td>NR</td>
<td>Combination: Carb, Km, and TMP-SMZ</td>
<td>Yes</td>
<td>Cured</td>
<td>Aortic ring abscesses</td>
</tr>
<tr>
<td>12 [15], 26/M</td>
<td>Recent valve replacement, <em>S. maltophilia</em> found in the pump equipment</td>
<td>Mitral prosthetic, atrial septal patch</td>
<td>NR</td>
<td>Chl, Km, Col</td>
<td>Yes</td>
<td>Died</td>
<td>Septicemia and multiple emboli</td>
</tr>
<tr>
<td>13 [15], 30/M</td>
<td>Recent valve replacement</td>
<td>Mitral prosthetic, atrial septal patch</td>
<td>NR</td>
<td>Chl</td>
<td>No</td>
<td>Cured</td>
<td>None</td>
</tr>
<tr>
<td>14 [8], 35/M</td>
<td>Recent valve replacement</td>
<td>Mitral prosthetic</td>
<td>Rheumatic carditis</td>
<td>Combination: Gm and Carb; TMP-SMZ</td>
<td>No</td>
<td>Cured</td>
<td>None</td>
</tr>
<tr>
<td>15 [16], 28/M</td>
<td>IVDU</td>
<td>Aortic native</td>
<td>None</td>
<td>Combination: Gm and Cpx</td>
<td>Yes</td>
<td>Cured</td>
<td>Myocardial abscesses</td>
</tr>
<tr>
<td>16 [PR], 60/F</td>
<td>Ventriculoatrial catheter</td>
<td>Tricuspid native</td>
<td>None</td>
<td>Combination: TIC/CA and TMP-SMZ</td>
<td>No</td>
<td>Cured</td>
<td>Lung abscesses</td>
</tr>
</tbody>
</table>

NOTE: Amik = amikacin; Amp = ampicillin; CA = clavulanic acid; Carb = carbenicillin; CHF = congestive heart failure; Chl = chloramphenicol; Col = colistin; Cpx = ciprofloxacin; Gm = gentamicin; IVDU = intravenous drug user; Km = kanamycin; Ml = myocardial infarction; Mox = moxalactam; NR = not reported; Pen = penicillin; PmB = polymyxin B; PR = present report; Sm = streptomycin; TIC = ticarcillin; TMP-SMZ = trimethoprim-sulfamethoxazole.

Eight of sixteen cases occurred in patients with prosthetic heart valves, all of which were mechanical prostheses. Five of the eight patients with native valve endocarditis had no definitive identifiable heart disease. Twelve of 16 patients had left-sided endocarditis (aortic, 6; mitral, 5; both, 1). Two patients, along with the patient described herein, had right-sided endocarditis involving the tricuspid valve. One patient had endocarditis involving both the tricuspid valve and the aortic valve. Definitive data regarding acquisition of infection were available in 13 cases. Six infections were nosocomially acquired and seven were community-acquired. All but two of the community-acquired infections occurred in intravenous drug users.
Most strains of *S. maltophilia* are resistant to β-lactam agents by virtue of their elaboration of at least four different β-lactamases, including L1 and L2. One of these enzymes is an inducible zinc-dependent metalloenzyme that is resistant to β-lactam inhibitors. The other β-lactamases are inhibited by these inhibitors [24]. Kazmierczak and co-workers [25] have postulated that therapeutic combinations containing clavulanic acid are more active against *S. maltophilia* than are those containing tazobactam or sulbactam because the inherent activity of clavulanic acid against these organisms is greater than that of tazobactam or sulbactam.

Although the therapy of choice for severe infections caused by *S. maltophilia* remains unknown, TMP-SMZ, TIC/CA, doxycycline, and an investigational quinolone (clinafloxacin) appear to be the most predictably active antimicrobial agents [26]. Furthermore, by using checkerboard panels and time-kill studies, the synergistic activity of TMP-SMZ and TIC/CA has been demonstrated [7].

Detailed information on the treatment given to 10 patients whose cases were previously reported was provided; nine of these patients received therapy with a combination of two or more antibiotics. In seven cases, treatment included TMP-SMZ; in six of these cases, TMP-SMZ was in combination with other agents. Not a single patient had been given therapy with TIC/CA alone or in combination. Overall, seven (54%) of 13 patients underwent cardiac surgery, and myocardial abscesses were found in four of these patients. The overall mortality was 33% (five of 15 patients for whom this information was available died). Two of the seven patients who underwent surgery died.

To the best of our knowledge, our case is the first report of endocarditis caused by *S. maltophilia* that was successfully treated with the combination of TMP-SMZ and TIC/CA, thus reinforcing in vitro findings and suggesting that this combination may be effective therapy. In contrast to TIC/CA, piperacillin/tazobactam is not an active combination against *S. maltophilia* [26]. Although hospital pharmacies may wish to carry either TIC/CA or piperacillin/tazobactam but not both combinations, it could be important to continue to make TIC/CA available for the treatment of *S. maltophilia* infections.

Removal of the infected device appears to be a necessary step for curing catheter-related infections caused by *S. maltophilia*. In the case reported herein, despite the fact that there was resolution of signs of infection with antibiotic therapy and the fact that follow-up blood cultures became negative, the organism was still isolated from the extracted catheter after 4 weeks of antibiotic treatment. This finding highlights the importance of catheter removal to avoid recurrences and agrees with the results of a previous report of catheter-related infections caused by this organism [2]; in this report, the rate of recurrences was extremely high when the catheter was not removed, independent of the antibiotics administered.

In summary, on the basis of the findings of the present review, endocarditis is an uncommon manifestation of infection caused by *S. maltophilia*: it is usually associated with the use of intravenous drugs, cardiac surgery, and central venous catheters. It commonly involves left valves, and more than one-half of the previously reported cases occurred in patients with mechanical prostheses. Surgery was required in 54% of 13 cases, and the overall mortality was 33%. The combination of TMP-SMZ and TIC/CA may be effective therapy for *S. maltophilia* endocarditis.

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References


