CASE REPORT

MRSA tricuspid valve infective endocarditis with multiple embolic lung abscesses treated by combination therapy of vancomycin, rifampicin, and sulfamethoxazole/trimethoprim

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SUMMARY
A 26-year-old pregnant woman who was an intravenous drug user (IDU) was admitted to our hospital for the treatment of tricuspid valve infective endocarditis (IE) and lung abscesses due to methicillin-resistant Staphylococcus aureus (MRSA). We started to treat her with vancomycin (VCM) alone and then in combination with rifampicin (RFP), but her condition did not improve. Then we added sulfamethoxazole/trimethoprim (SMZ/TMP) to VCM and RFP. After that, she improved rapidly. In Japan, there are very few reports about tricuspid valve IE caused by MRSA in IDUs. This case suggests that the combination of VCM, RFP, and SMZ/TMP may be effective for the treatment of severe MRSA infections.

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Introduction

Vancomycin (VCM) is a drug of first choice in the treatment of methicillin-resistant Staphylococcus aureus (MRSA) infections, but it has a high rate of treatment failure. Combination therapy may be considered in selected invasive MRSA infections refractory to standard VCM monotherapy. We present a case of MRSA tricuspid valve (TV) infective endocarditis (IE) with multiple embolic lung abscesses, in which the addition of sulfamethoxazole/trimethoprim (SMZ/TMP) to the combination of VCM and rifampicin (RFP) was effective.

Case history

A 26-year-old woman who was an intravenous drug user (IDU) was admitted to another hospital for the
treatment of TV IE caused by *methicillin-sensitive Staphylococcus aureus*. She was discharged after 4 weeks of treatment with penicillin G (2 million units/day), but she did not stop being an IDU after that. Four months later, she became pregnant. Ten months later, 3 days before admission to our hospital, she suffered from fever (>38°C) and cough. General fatigue and back pain also developed and she was admitted to the obstetrical department of our hospital.

Her blood pressure was 100/60 mmHg, heart rate was 105 min⁻¹ and SpO₂ under room-air condition was 98%. Many marks of intravenous drug injection existed on her hands. She had no peripheral manifestations of IE, such as petechiae, Roth spot, and Osler node. Levine 2/6 systolic regurgitant murmur was audible at 4th left intercostal space. She had coarse crackles in both sides of the chest.

Abnormal laboratory findings were white blood cell count 12,200 µl (neutrophils 92%), hemoglobin 9.8 mg/dl, C-reactive protein 12.7 mg/dl, and positive hepatitis C virus antibody. Echocardiography revealed vegetation (3 mm × 7 mm) on the anterior TV and anterior TV prolapse with loss of coaptation and with moderate TV regurgitation (peak velocity: 300.3 cm/s), and enlarged right atrium and ventricle (4 chamber view, RV: 55 mm, Fig. 1). Chest X-ray and chest computed tomography (CT) showed multiple lung abscesses and pleural effusion (Fig. 2). Cardiac shadow was enlarged. Blood and sputum culture revealed MRSA, which were sensitive to VCM, RFP, and SMZ/TMP. She was referred to the

![Figure 1](image-url)  
**Figure 1** Two-dimensional echocardiogram (Day 5) revealing vegetation (white arrow: 3 mm × 7 mm) on the tricuspid valve and moderate tricuspid valve regurgitation.
department of cardiology for the treatment of IE and multiple embolic lung abscesses after emergent Caesarean section.

We started VCM 1.5 g/day (30 mg/kg) in two equally divided doses (Fig. 3). Her symptoms and laboratory data did not improve 5 days after treatment. We increased VCM dose (3 g/day in two equally divided doses) because of low VCM trough and peak concentrations (4 μg/ml and 19 μg/ml) and added RFP (600 mg/day). We considered to maintain VCM trough concentrations ranging 15–20 μg/ml and peak concentrations ranging 30–45 μg/ml in order to keep efficacy and prevent toxicity. Nine days after this conventional combination treatment for MRSA IE, her clinical findings did not improve and her VCM trough concentrations were still low (9.0 μg/ml). Therefore, we increased dosages of VCM (4.0 g/day in two equally divided doses) and RFP (900 mg/day). Twelve days after treatment, although her blood culture was negative for the first time, VCM trough concentrations increased to 59 μg/ml. Her renal function worsened and red man syndrome appeared. We stopped VCM transiently for 3 days and added SMZ/TMP (4 g/day) to RFP. Her symptoms, blood tests, and imaging tests improved rapidly. Sixteen days after treatment we started VCM (1.5 g/day in two equally divided doses) again. Vegetation of TV disappeared 49 days after treatment and the size of right atrium and ventricle decreased (apical 4 chamber view, RV: 39 mm), probably because of decreased circulating volume after delivery and improved heart failure. Echocardiography also revealed the anterior TV prolapse with partial loss of coaptation and mild TV regurgitant flow (peak velocity: 230 cm/s). Multiple lung abscesses disappeared 54 days after treatment by chest CT. She was discharged without complications.

![Figure 2](image)

*Figure 2* Chest X-ray (Day 7) and chest CT (Day 8) revealing multiple lung abscesses and pleural effusion.

![Figure 3](image)

*Figure 3* Clinical course after initiation of treatment. AD, admission; BT, body temperature; Cre, serum creatinine.
Discussion

In the USA, the vast majority of right-sided IE occur in IDUs and a majority of IDUs with IE have rightsided infections, in which TV is infected in more than 50% [1]. In IDUs the valves were normal before infection in 75–93% of patients [2]. Injection of illicit drugs may produce transient or permanent endothelial damage of the TV, and non-bacterial thrombus may occur on the damaged valve and be infected by the pathogens which are usually originated from the skin, explaining the predominance of Staphylococcus aureus [2]. Still more, the low pressure gradient between the right ventricle and right atrium may be responsible for the absence of a murmur with TV IE [3]. Septic pulmonary emboli are present in 87% of TV infections particularly caused by S. aureus [4]. In Japan, right-sided IE usually occurs on the predisposing structural TV lesions accompanied by congenital heart disease, and cases of TV IE in IDUs are rare. Only 7 IDU cases were reported from 1985 to 2000 [5] and one case was caused by MRSA, but it is increasing owing to the increase in IDUs. Even in Japan we should pay attention to the possibility of TV IE without predisposing structural valve disease. Our patient was an IDU pregnant woman and had TV IE with multiple embolic lung abscesses caused by MRSA. Hyperkinetic circulation and dilation of TV annulus during pregnancy might be associated with an increase in TV regurgitation and a detectable murmur due to anterior TV prolapse [6].

Although VCM is a drug of first choice in the treatment of MRSA infection [4], VCM has slow clinical response and unacceptably high rate of treatment failure. Regarding right-sided IE caused by either MSSA or MRSA, VCM was reported to be less effective because of limited bactericidal activity, poor penetration into vegetations, and increased drug clearance among IDUs [4]. The MRSA strain of our patient was sensitive to old agents such as RFP and SMZ/TMP. Most staphylococci have high susceptibility to RFP, but RFP has been suggested as adjunctive therapy in patients who do not respond adequately to conventional antimicrobial therapy [4,7], because resistance develops rapidly when this agent is used alone. SMZ/TMP was reported to be a useful alternative to VCM for treatment of MRSA infections in IDUs, but clinical experience with this agent for MRSA IE is limited [4]. Some reports suggest that the combination of VCM, RFP, and SMZ/TMP is effective for severe MRSA infections, which were refractory to VCM monotherapy [8]. These include infections such as IE, meningitis, and prosthetic device infections [9]. Our patient had recurrent MRSA IE and multiple lung abscesses to which VCM had poor penetration. Therefore, recommended values of both VCM trough and peak concentrations were higher than usual. We administered only VCM as an initial therapy and then added RFP together with the increase in VCM dose, but the condition of the patient did not improve. We decided the addition of SMZ/TMP to the combination of VCM and RFP, which was highly effective to control the infection.

We conclude that for refractory MRSA IE the combination of VCM, RFP, and SMZ/TMP should be considered and that right-sided IE of IDUs should be remembered even in Japan.

References