Rupture of Renal Mycotic Aneurysm that Developed during the Treatment of Streptococcal Infective Endocarditis and Vertebral Osteomyelitis

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Abstract

A 50-year-old woman received two weeks of cefazopran and two weeks of imipenem for streptococcal endocarditis and vertebral osteomyelitis. Subsequently she received four weeks of oral levofloxacin and eight weeks of oral clarithromycin due to persistent elevation of C-reactive protein. Finally, she was admitted to our hospital due to massive hematuria. Abdominal CT showed rupture of an aneurysm in the right kidney and emergent coil embolization was performed. Multiple sets of blood culture grew *Streptococcus oralis*, and transthoracic echocardiography revealed vegetation at the aortic valve. Retrospective review of the abdominal images revealed the emergence of the aneurysm during the treatment.

Key words: infective endocarditis, vertebral osteomyelitis, mycotic aneurysm, appropriate antibiotic therapy

(Intern Med 51: 1255-1258, 2012)

(DOI: 10.2169/internalmedicine.51.6418)

Introduction

A mycotic aneurysm is defined as a localized, irreversible dilatation of an artery to at least one and a half times its normal diameter due to destruction of the vessel wall caused by infection. Among the several proposed pathogeneses of mycotic aneurysms, septic emboli to the vasa vasorum secondary to infective endocarditis has been the most common (1). Mycotic aneurysms secondary to infective endocarditis generally occur at points of bifurcation of the affected artery and half of them are intracranial. Extracranial mycotic aneurysms, such as aneurysms in the aorta and limb arteries, have been reported, however, those occurring in renal arteries are rare (2-6).

The natural history of mycotic aneurysms has been unclear, since most of the mycotic aneurysms are not detected until they rupture. The time between the diagnosis of infective endocarditis and the rupture of intracranial mycotic aneurysms has been reported to be 0 to 35 days, however, mycotic aneurysms may rupture even after completion of antibiotic therapy (7, 8). It is also unclear when these my-

cotic aneurysms appear and develop during the course of infective endocarditis. We herein report a case of ruptured renal mycotic aneurysm that emerged during the antibiotic therapy for streptococcal endocarditis and vertebral osteomyelitis.

Case Report

A 50-year-old woman visited our hospital because of persistent lumbar pain. The pain started 3 months earlier and had gradually worsened. The patient had been diagnosed as patent ductus arteriosus by routine medical examination in childhood and received odontectomy without antibiotic prophylaxis 5 months earlier. The vital signs and physical examinations were normal except for continuous heart murmurs (Levine III/VI). Her respiratory sound was clear and no erythema or tenderness was seen in her extremities. She received regular dental scaling and had no apparent dental problems. Blood examination revealed that white blood cell counts were 10,100 cells/ μ L, alkaline phosphatase 1,064 IU/L, C-reactive protein 5.7 mg/dL, and erythrocyte sedimentation rate 81 mm/hour. Her chest CT showed multiple nod-

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Received for publication August 19, 2011; Accepted for publication January 29, 2012

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Figure 1. Chest CT showing nodules suggestive of septic emboli (arrow).

Figure 2. T2-weighted lumbar MRI showing lesions suggestive of vertebral osteomyelitis and discitis.

ules suggestive of septic emboli (Fig. 1). The lumbar MRI showed an abnormal signal in the anterior area of L4/L5. The lesion was a low signal on T1-enhanced image and a high signal on T2-enhanced image, which was compatible with vertebral osteomyelitis (Fig. 2). Culture of the transcutaneous biopsy of the vertebral bone also grew *streptococcus* species. Transthoracic echocardiography revealed no vegeta-

tion and the patient was admitted to a nearby hospital with a diagnosis of streptococcal vertebral osteomyelitis. On admission to the prior hospital, multiple blood cultures were taken and all of the sets grew *streptococcus* species. She had a fever of 38.2°C and based on the modified Duke's criteria, she was diagnosed as both infective endocarditis and vertebral osteomyelitis and received a 2-week course of cefazopran (1 g twice a day) and another two-week course of imipenem (0.5 g twice a day). She was discharged and received a one-month course of levofloxacin (100 mg three times a day) and a two-month course of clarithromycin (200 mg twice a day) due to a sustained low level elevation of C-reactive protein.

Three months after having been discharged from the hospital, she felt sudden right abdominal pain and had massive hematuria. She was transferred to our hospital in a state of shock; contrast-enhanced CT scan and abdominal angiography showed ruptured renal artery aneurysm (Fig. 3a, b). Coil embolization was performed and the bleeding subsided. Two sets of blood culture at this time revealed *Streptococcus oralis*. Transthoracic echocardiography revealed a pedunculated vegetation (17 mm×4 mm) at the aortic valve and she was diagnosed as infective endocarditis.

The susceptibility test showed that this *S. oralis* was susceptible to penicillin G (MIC ≤ 0.06 mcg/mL), therefore we started penicillin G (16 million units/day) and continued treatment for six weeks because complication with vertebral osteomyelitis was suspected. The size of the vegetation was large, however, the patient had no heart failure and the pathogen was susceptible to penicillin, therefore surgical intervention was not performed. All of the blood cultures were successively negative and C-reactive protein and erythrocyte sedimentation rates returned to normal at the end of the therapy. She was discharged from hospital and did not have any recurrence.

We retrospectively reviewed the MRI images taken on the first visit for the purpose of assessment of her lumbar pain and confirmed that there was no evident aneurysm in her right kidney (Fig. 4). This indicates that the aneurysm developed during the initial treatment course of streptococcal endocarditis and vertebral osteomyelitis.

Discussion

We herein describe a patient who developed a renal mycotic aneurysm during the treatment of streptococcal infective endocarditis and vertebral osteomyelitis. The causative organism in this patient was *S. oralis* and this oral commensal might have gained entry into the bloodstream upon odontectomy without prophylactic antibiotics.

The term mycotic aneurysm refers to aneurysms of any infectious etiology. In the pre-antibiotic era, mycotic aneurysms were common sequelae of infective endocarditis. However, with the advent of antibiotics, the frequency of mycotic aneurysms has been dramatically dropped and the etiology of mycotic aneurysms has shifted from infective en-

Figure 3. Contrast-enhanced abdominal CT scan showing hemorrhage in the right kidney (a) and abdominal angiography showing rupture of the right renal artery (b).

Figure 4. Abdominal MRI showing the absence of renal aneurysms in both kidneys.

Figure 5. Timeline by hospital day from the time of admission to our hospital until two months after discharge from the hospital.

docarditis to arterial trauma or atherosclerosis. Nevertheless, there still exist some cases of mycotic aneurysms in cases of infective endocarditis and since it often remains clinically silent until it ruptures, it is important for clinicians to always consider the possibility of the occurrence of mycotic aneurysms during and even after the treatment of infective endocarditis.

Surgical intervention is recommended as class IIb (usefulness/efficacy is less well established by evidence/opinion) for infective endocarditis with mobile vegetations in excess of 10 mm. Surgery is also considered in infective endocarditis caused by highly resistant organisms (class I) or persistent vegetations despite appropriate antibiotic therapy (class IIa) (9). The size of the vegetation in the present patient was 17 mm and surgery should have been considered. However, we finally decided to initiate antibiotic therapy first and carefully monitor the patient after having consulted a cardiovascular surgeon.

One of the interesting findings in the present case is that the aneurysm occurred in the renal artery. It has been reported that about half of the mycotic aneurysms in infective endocarditis occur in the brain, however, another half of such aneurysms occur in extracranial arteries and most of them are in the aorta and arteries in the limbs. Mycotic

aneurysms in renal arteries should be included in the differential diagnosis of patients with infective endocarditis complaining flank pain or hematuria, although their incidence is thought to be rare.

Natural history of mycotic aneurysms is also unclear since most cases are clinically silent and hence not detected until they rupture. It is often difficult to clarify when the aneurysm developed because images before the emergence of the aneurysm are usually unavailable.

The present case is interesting in that we successfully showed that the aneurysm did not exist at the beginning and developed during the treatment. The clinical course of our case was prolonged, however whether this was related to the emergence of the aneurysm is unknown since rupture of mycotic aneurysms can happen even after completion of antibiotic treatment of infective endocarditis (7, 8, 10).

There are some issues that should be addressed in the management of this patient. First, the present patient was initially treated with intravenous imipenem/cilastatin and cefazopran. Most guidelines recommend intravenous penicillin G for infective endocarditis caused by penicillin susceptible streptococci, therefore the spectrum of these two antimicrobial agents might have been too broad (11, 12).

In spite of the use of several broad spectrum antibiotics

that cover *S. oralis* for a total of 4 months, the organism was not eradicated and the present patient finally developed rupture of mycotic aneurysm. This could be explained from the viewpoint of antibiotic dosage. The dose of imipenem/cilastatin was 0.5 g every 12 hours and that of cefozopran was 1 g every 12 hours. In serious infections such as infective endocarditis, beta lactam antibiotics with a short half-life should be given frequently since the length of time that antibiotic concentrations are maintained above the pathogen's minimal inhibitory concentration is correlated with clinical success (13). For example, imipenem/cilastatin is recommended at a dose of 0.5 g every 6 hours and cefepime (similar to cefozopran) is recommended at a dose of 2 g every 8 hours in infective endocarditis (12). Considering these recommendations, the initial treatment course might have been inadequate. Oral levofloxacin (100 mg every 8 hours) and oral clarithromycin (200 mg every 12 hours) used in the present case also might have been inadequate, although all of these dosages were based on the package inserts of the antibiotics. Recently, the inappropriateness of package inserts of antibiotics in Japan has been reported, therefore introduction of the standard dosages of antibiotics used in the United States or most of the European countries could be important. Recently, the package insert of levofloxacin has been revised and 500 mg every 24 hours has become the current recommended dosage in Japan (14). Further revision of package inserts based on scientific evidence is expected in the future.

In conclusion, we report a case of rupture of mycotic aneurysm in the renal artery which developed during the treatment of infective endocarditis. Clinicians should keep in mind the possibility of mycotic aneurysms when treating patients with infective endocarditis. Development and rupture of mycotic aneurysms could happen in any stage of treatment of infective endocarditis, especially if the selection of the antibiotics and the doses and durations are inappropriate.

The authors state that they have no Conflict of Interest (COI).

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