Gonococcal Endocarditis in a 47-year-old Japanese Man

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Abstract

A 47-year-old sexually active Japanese man was admitted with a persistent fever and weight loss. A physical examination revealed a cardiac murmur. A transthoracic echocardiogram was nondiagnostic, although blood cultures grew *Neisseria gonorrhoeae*. Gonococcal endocarditis was diagnosed based on the modified Duke criteria. The administration of antimicrobial therapy resulted in an adequate initial resolution; however, two months after completing the therapy, the patient developed cardiac failure. Severe aortic regurgitation was identified, and the patient underwent emergent aortic valve replacement. Despite the rarity of gonococcal endocarditis, this disease should nevertheless be considered in patients presenting with a fever, cardiac murmur and a consistent sexual history.

Key words: *Neisseria gonorrhoeae*, endocarditis, disseminated gonococcal infection

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Introduction

Gonorrhea is a common sexually transmitted bacterial infection. According to the Centers for Disease Control (CDC), more than 700,000 people in the United States acquire new gonococcal infections annually, although the incidence reported by the CDC was 309,341 people in 2010 (1), suggesting that the infection may go undetected for some time.

The usual manifestations of gonorrhea are urethritis in men and cervicitis in women. Disseminated gonococcal infection is an uncommon complication, and the reported incidence is negligible in Japan (2). The usual features of disseminated gonococcal infection include migratory polyarthritis, tenosynovitis, dermatitis and septic arthritis (3). Gonococcal endocarditis is rare, occurring in 1-2% of disseminated gonococcal infections. We herein report a case of gonococcal endocarditis and review the disease.

Case Report

A 47-year-old Japanese man was admitted to our hospital with a persistent fever and weight loss.

The patient had repeatedly traveled to China in the recent past and admitted to frequent sexual encounters with sex workers. One month before the onset of symptoms, the patient had unprotected sexual intercourse with a Chinese female sex worker. Two weeks prior to admission, a persistent fever of over 39°C developed with associated weight loss of 5 kilograms. There were no other associated symptoms. The patient had no previous history of cardiac or valvular disease.

On a physical examination, the patient appeared well, alert and oriented, with a normal Glasgow Coma Scale score. His temperature was 39°C, his blood pressure was 110/70 mmHg, his heart rate was 100 beats per minute, his respiratory rate was 16 breaths per minute and pulse oximetry was 98% on ambient room air. Pharynx and cervical lymph node examinations were normal. A grade III/VI sys-
tolic murmur and grade II/IV diastolic murmur were auscultated at the second intercostal space on the right parasternal border. The findings of an examination of the respiratory system were normal. There was no extremity edema, joint swelling or peripheral stigmata of infectious endocarditis.

The laboratory findings obtained on admission (Table) demonstrated leukocytosis and an elevated C-reactive protein level. A chest radiograph and transthoracic echocardiography were both within the normal limits. On the second day of hospitalization, the admission blood cultures were reported to be positive without a specific identification of the causative pathogen. As a result, treatment with intravenous ceftriaxone was commenced, which resulted in the rapid defervescence of the patient’s fever and resolution of his other symptoms. Three sets of blood cultures obtained prior to the administration of antimicrobial therapy and more than 12 hours apart were all positive, whereas cultures obtained on the third and fifth days during antibiotic therapy were all negative. On the sixth day of admission, detailed microbiological studies revealed the causative organism to be *Neisseria gonorrhoeae*, as identified on the HN-20 rapid test (Nisui Pharmaceutical Co., Ltd., Tokyo, Japan) and Gonocheck II test (EY Laboratories, Inc., San Mateo, USA). The organism was fully sensitive to standard antibiotics, including benzylpenicillin, cefotaxime, tetracycline and ofloxacin. However, the sensitivity testing was performed using the disk method; therefore, the minimum inhibitory concentration (MIC) was not available. Consequently, intravenous benzylpenicillin was substituted as narrow spectrum therapy. Transesophageal echocardiography was performed, however, no valvular vegetation could be identified. The titers of antinuclear antibodies and rheumatoid factor were unremarkable, as were the serum C3, C4 and CH50 levels. Hepatitis B virus, hepatitis C virus and human immunodeficiency virus tests were all negative. Serum Chlamydia trachomatis- IgG and -IgA tests, in addition to a urinary Chlamydia polymerase chain reaction test, were all positive, whereas a urine culture was negative.

Despite the resolution of the patient’s high fever, the low-grade pyrexia persisted. Chest radiography revealed bibasal lung consolidation with associated peripheral blood eosinophilia. Bronchoalveolar lavage showed an increased level of eosinophils of 20%. A transbronchial lung biopsy was performed, and the infiltrates were consistent with eosinophilic pneumonia with organization. As a result, the benzylpenicillin was changed to ciprofloxacin, and oral prednisolone was commenced, with a subsequent clinical improvement.

On the 30th day of admission, transthoracic echocardiography was repeated, which revealed a prolapsed aortic valve with aortic valve thickening (Fig. 1). Definitive infectious endocarditis was diagnosed based on the modified Duke criteria, including two major criteria (new valvular regurgitation and persistently positive blood cultures).

The patient’s symptoms and inflammatory markers improved, and the antimicrobial treatment was completed at four weeks. The patient was hemodynamically stable and, as a result, surgical intervention was not deemed necessary. However, two months after completing the therapy, he was readmitted to the hospital due to congestive cardiac failure secondary to severe aortic regurgitation (AR) (Fig. 2). No infectious symptoms were present, and blood cultures were negative. In view of his decompensated status resulting from AR, the patient underwent aortic valve replacement (AVR).

The AVR surgery was uncomplicated. Macroscopically, the right coronary cusp was found to be perforated and prolapsed. An area of vegetation was seen on the left coronary cusp (Fig. 3). A culture of the site of vegetation revealed no bacterial growth. Postoperatively, the patient was well and remains so after two years of follow-up.

### Discussion

Gonococcal endocarditis was relatively common in the pre-antibiotic era, accounting for 11-26% of cases (4). Disseminated gonococcal infection (DGI) complicates 0.5-3% of gonococcal infections (5), with gonococcal endocarditis complicating 1-2% of all DGIs, making the latter a somewhat rare entity in the antibiotic era.

DGI typically develops within two to three weeks of the primary infection (6). The strains that cause DGI exhibit some relatively specific features. Genital symptoms are infrequent because there is a paucity of genital inflammation (7). Our patient similarly lacked such symptoms. Strains causing DGI often contain protein 1A and are resistant to neutrophil-mediated killing. The majority of gonococcal species isolated from DGI patients remain sensitive to penicillin (8), although some cases of penicillin-resistant DGI have been reported (9, 10). Disseminated gonococcal infections have a higher incidence in women than in men. Menstruation is a risk factor for dissemination, and it is thought that the local protective barrier is reduced during this time, allowing gonococci to easily access the systemic circulation (7). In contrast, gonococcal endocarditis is more common in men than in women (4). However, the underlying pathophysiological mechanisms are currently unknown.

The most common symptoms of gonococcal endocarditis are fever (44-64%), arthralgia (30-44%) and rashes (12%). Common physical signs include cardiac murmurs (77-88%); arthritis (18-40%), hematuria [from nephritis] (22%) and rashes (14-21%) (4, 5, 11). A history of pre-existing valvu-

### Table. Laboratory Data on Admission

<table>
<thead>
<tr>
<th>WBC</th>
<th>10,300 /μL</th>
<th>y-GTP</th>
<th>113 IU/L</th>
<th>Urinalysis</th>
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<tr>
<td>Neut</td>
<td>71.4 %</td>
<td>LDH</td>
<td>224 IU/L</td>
<td>Pro (+)</td>
</tr>
<tr>
<td>Lym</td>
<td>18.7 %</td>
<td>CRP</td>
<td>76 IU/L</td>
<td>OB (+)</td>
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<tr>
<td>RBC</td>
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<td>BUN</td>
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<td>WBC (+)</td>
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<tr>
<td>Hb</td>
<td>12.7 g/dL</td>
<td>Cre</td>
<td>0.67 mg/dL</td>
<td>NO (+)</td>
</tr>
<tr>
<td>Ht</td>
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<td>UA</td>
<td>4.4 mg/dL</td>
<td>Bact (+)</td>
</tr>
<tr>
<td>Plt</td>
<td>15.8 × 10⁴ /μL</td>
<td>Na</td>
<td>135 mEq/L</td>
<td></td>
</tr>
<tr>
<td>TP</td>
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<td>K</td>
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<tr>
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<td>Ca</td>
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<tr>
<td>AST</td>
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<td>CRP</td>
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<tr>
<td>ALT</td>
<td>60 IU/L</td>
<td>HbA1c</td>
<td>5.1 %</td>
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</tr>
</tbody>
</table>
Figure 1. Transthoracic echocardiography performed on the 30th day of admission showing an area of vegetation on the aortic valve (arrow) with associated aortic regurgitation (arrowhead). LA: left atrium, LV: left ventricle, Ao: aorta

Figure 2. (a) A chest radiograph obtained during the patient’s first admission showing no remarkable abnormalities. (b) A chest radiograph obtained two months after the completion of antimicrobial therapy showing cardiomegaly and pulmonary congestion.

Figure 3. The aortic valve resected via valvular surgery showing a perforated right coronary cusp (arrow) and an area of vegetation on the left coronary cusp (arrowhead).

Valvular disease is uncommon (11, 12). Valvular involvement most commonly affects the aortic valve (50%), followed by the mitral valve (30%), pulmonary valve (5%) and tricuspid valve (2.5%) (12). The mean duration of symptoms before diagnosis is 45 days. The clinical course is intermediate between the acute course of staphylococcal endocarditis and the subacute course of alpha-hemolytic (viridans) streptococcal endocarditis (12). Valvular surgery is necessary in more than half of patients with gonococcal endocarditis (4). The mortality rate is high (19%) despite the administration of appropriate treatment (4).

Decreased susceptibility to antibiotics is a global issue. During the 1990s and 2000s, fluoroquinolone resistance of *N. gonorrhoeae* emerged. Nowadays, there is major concern regarding the emergence of cephalosporin-resistant *N. gonorrhoeae* (13). In our case, the precise strain of *N. gonorrhoeae* was not elucidated; however, the sensitivity to penicillin was optimal. We therefore strongly consider that the strain was a non-resistant type, which resulted in the dis-
antimicrobial agents for the treatment of organism remains a remote possibility.

Our patient also had evidence of coexisting C. trachomatis infection. Moreover, chlamydial infections are known to cause cardiovascular complications, including endocarditis (14). Despite this, endocarditis originating from C. trachomatis infection is exceedingly rare, with only a few cases having been reported to date (15, 16). Considering the patients clinical presentation, positive blood cultures, response to antimicrobial agents and natural history, the likely cause of the endocarditis was N. gonorrhoeae alone. The presence of a valve coinfected with both N. gonorrhoeae and C. trachomatis cannot be entirely ruled out in this case, although there is insufficient literature to support the latter notion, and this finding was also not borne out by the histological analysis of the resected heart valve, which showed no evidence of organisms. However, no specific tests for C. trachomatis were performed because the specimen was fixed in formalin, making polymerase chain reaction testing impossible. Therefore, endocarditis due to coinfection with this organism remains a remote possibility.

Azithromycin and doxycycline are recommended antimicrobial agents for the treatment of C. trachomatis infection. As an alternative regimen, levofloxacin or ofloxacin can be used. Other quinolones, including ciprofloxacin, are either reliably effective against chlamydial infection or have not been evaluated adequately (17). We used ciprofloxacin to treat the patient’s gonococcal infection for a total of 11 days. However, treatment for C. trachomatis endocarditis can require an extended period of therapy compared to other causes of endocarditis, although such recommendations are more clear for non-trachomatis types of chlamydial endocarditis than the trachomatis type (18). Despite this fact, many patients require valvular surgery, even with the administration of adequate antimicrobial therapy (19).

Our patient developed valvular destruction despite the administration of prompt and adequate treatment, which was eventually ameliorated by AVR surgery. In our opinion, it is likely that the patient’s valve was destroyed early in the course of the disease, with a delayed onset of cardiac failure. Recently, Duk-Hyun Kang et al. reported that the use of early surgery in patients with infective endocarditis reduces mortality (20). However, in this case, the patient did not exhibit features requiring early surgical intervention.

Lastly, this case is warning for individuals involved in sex tourism. Our patient mentioned that the sex worker was a virgin and therefore he considered that it would be safe to have unprotected sexual intercourse. However, this case clearly demonstrates that the patient acquired a very serious illness from a sexually transmitted infection (STI). It is therefore important to educate men and women alike regarding the risks of STIs and how to avoid such problems with safer sexual practices, such as condom use and the early utilization of public health facilities to treat STIs promptly. In addition, it is important to reduce the spread of disease by providing effective education and contact tracing measures.

In patients with a consistent sexual history, the presence of a fever and cardiac murmur should alert the clinician to the possibility of gonococcal endocarditis. Occasionally, transesophageal echocardiography can be falsely negative (21); therefore, having clinical suspicion and performing repeated echocardiography is imperative to prevent misdiagnosis.

It is sometimes difficult to inquire about a patient’s sexual history. This case exemplifies the particular importance of using narrative skill in history taking in order to obtain a detailed sexual history of the patient. In addition, owing to the findings of a comprehensive physical examination and echocardiography testing, an accurate diagnosis could thus be made, thus allowing for the successful treatment of gonococcal endocarditis.

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

References


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