Disseminated Gonococcal Infection in An Elderly Japanese Man

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Abstract

We herein present the case of a 69-year-old Japanese man who had unprotected sexual contact with a local commercial sex worker in an East Asian country and was diagnosed as having disseminated gonococcal infection (DGI). The organism was confirmed to be Neisseria gonorrhoeae based on 16S rRNA sequencing and positive results for the cppB gene. This case indicates that a diagnosis of DGI should also be considered in elderly individuals. DGI potentially causes many complications, and the pathogen has recently been reported to be resistant to various antibiotics. Physicians must therefore pay more attention to the possible occurrence of DGI in various clinical settings.

Key words: disseminated gonococcal infection, elderly, imported infectious disease, Neisseria gonorrhoeae, sexually transmitted infection

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Introduction

Disseminated gonococcal infection (DGI) results from the bacteremic spread of the sexually transmitted pathogen Neisseria gonorrhoeae and it is frequently seen in sexually active young adults. Classically, the disease develops within two to three weeks after transmission via sexual intercourse through the mucous membranes of the urethra, cervix, rectum, oropharynx or conjunctivae (1). The organism causes unique symptoms, including tenosynovitis, dermatitis and polyarthralgia (2); however, these clinical symptoms are not specific for DGI. Moreover, most patients with DGI do not simultaneously manifest signs and symptoms involving localized genital infection. Therefore, making a diagnosis of DGI in the early phase of its clinical course is challenging, even in typical cases.

Sexually transmitted infections (STIs) are relatively common among young adults; therefore, a clinical history concerning sexual activity is usually obtained in young adults who may have an STI. However, the possibility of an STI as a differential diagnosis is often excluded in elderly patients. We highlight the importance of considering STIs in elderly patients by presenting a case of DGI occurring in a 69-year-old Japanese man who had recently been to an East Asian country and had unprotected sexual contact with a local commercial sex worker.

Case Report

Case presentation

A 69-year-old Japanese man presenting with a three-day history of general malaise, a sudden onset high fever, pharyngeal pain and arthralgia in the right knee and elbow visited our outpatient department. He had travelled abroad regularly once a month for his business and had been in an East Asian country one week earlier. He had a history of lung lobectomy of the right upper lobe due to lung squamous cell carcinoma (one year earlier) and had received tegafur-gimeracil-oteracil combination therapy for the lung cancer (four months earlier). A precise history concerning

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Figure 1. Macroscopic appearance of the area of erythema on the right forearm. A poorly margined area of erythema measuring approximately 1 cm in diameter was found on the patient’s right forearm. It was not specific to *N. gonorrhoeae* and disappeared three days after the start of treatment.

STIs was not obtained during a medical interview conducted at the outpatient department.

On arrival, the patient’s vital signs were as follows: blood pressure, 149/83 mmHg; heart rate, 98 beats/min, regular; oxygen saturation, 96% on room air; and body temperature, 37.9°C. Although he complained of arthralgia in his right knee and elbow, no abnormalities were found. There was a poorly margined area of erythema measuring approximately 1 cm in diameter on his right forearm (Fig. 1). A laboratory examination showed only a slightly elevated inflammatory state: white blood cells, 8,080/mm^3; and C-reactive protein, 1.07 mg/dL. The results of routine biochemical tests and a urinalysis, including sediment, were normal. After sampling two sets of blood cultures, the patient was prescribed an antipyretic and levofloxacin and returned home on that day. The next day, the blood culture was found to be positive, and Gram-negative diplococci were detected (Bactec9240, Becton-Dickinson). The patient still had a high fever exceeding 39°C that was preceded by chills and rigor, and he was therefore admitted to our hospital.

After admission, the pathogen was identified to be *Neisseria gonorrhoeae*, which was sensitive to ceftriaxone but intermediate to penicillin G (negative for penicillinase) and resistant to levofloxacin (Table). Only after the positive results of the blood culture, Only after the positive results of the blood culture, a history taking and an examination concerning STIs were performed in detail. STIs performed in detail. The patient had engaged in unprotected sexual intercourse, including oral sex, with a local commercial sex worker five days before visiting our outpatient department in an East Asian country and had developed general malaise two days after the episode of sexual intercourse. He was married and heterosexual but had had no sexual contact with his wife for long time. His past medical history included gonococcal urethritis (10 years earlier) and syphilis (five years earlier). A physical examination, including an examination of the pharynx and cervical lymph nodes, revealed no abnormalities.

There were no signs of meningeal, ocular, genitourinary or rectal involvement. Screening tests for STIs were positive for syphilis (negative for rapid plasma reagin but positive for Treponema pallidum latex agglutination), *Chlamydia trachomatis* (anti-IgA=1.92 and anti-IgG=5.57 on an enzyme immunoassay) and hepatitis B virus (positive for both HBs and HBc antibodies and negative for HBs antigens) but negative for hepatitis C virus and human immunodeficiency virus. Bacterial cultures and nucleic acid amplification testing of the urine, throat and skin samples using polymerase chain reaction (PCR) were not performed since the patient intensely rejected any additional sampling.

Under the diagnosis of disseminated gonococcal infection, 1 g per day of intravenous ceftriaxone was administered. By day 3, the patient’s symptoms, including fever, pharyngitis, arthralgia and erythema, had improved, and he was discharged without any sequelae on day 7. The clinical course is shown in Fig. 2.

**Bacterial analysis**

Although the isolate was identified as *N. gonorrhoeae* by the Vitek2 system (SYSMEX, bioMérieux, Co., Ltd., Tokyo, Japan), the colony obtained from the blood culture exhibited an atypical appearance for *N. gonorrhoeae*. Therefore, a further analysis of the pathogen was performed. Although strand displacement amplification and transcription-mediated amplification methods are common diagnostic tools for assessing *N. gonorrhoeae*, such procedures were not performed since these methods were not introduced at our facility and the commercial based kits are known to present false-positive reactions with other *Neisseria* species (3).

The blood samples were inoculated onto blood and chocolate agar media and cultured at 36°C for 18 hours with 5% carbon dioxide. The InstaGene Matrix (Bio-Rad, Hercules, CA, USA) was used for DNA extraction from the culti-
The incidence of DGI has been reported to be very low (0.5 to 3% of all gonococcal infections) (6, 7). In fact, only 11 cases in Japan (8) and two cases in Korea have thus far been reported (9). The low incidence is primarily attributed to the difficulty in making a diagnosis. Patients with DGI present with only nonspecific symptoms, and a careful physical examination is therefore needed to detect characteristic findings. The sensitivity of bacterial cultures of specimens, including urethral, cervical, rectal, skin and synovial fluid samples, is low (10-14). Therefore, many cases of DGI may remain undiagnosed. However, the pathogen potentially causes endocarditis, meningitis and osteomyelitis as complications and has recently been reported to be resistant to various antibiotics. In general, gonococcal bacteremia intermittently occurs, and only approximately half of patients with DGI demonstrate positive blood cultures (7). Therefore, the sensitivity of blood cultures, a major tool for diagnosis of DGI, is relatively low. With these factors in mind, physicians must pay more attention to DGI in various clinical settings. For the proper diagnosis of DGI, repeated blood cultures should be obtained at intervals in patients under high suspicion for the disease, such as those with predisposing risk factors, including complement deficiencies, pregnancy and systemic lupus erythematosus (6, 7, 15).

Considering the advanced age of our patient, STIs were initially not suspected. Indeed, this is the first case of DGI occurring in a patient over 65 years of age in Japan. The skin manifestations were atypical for DGI, and the joint symptoms were relatively mild. Only the positive results of the blood culture for the 16S rRNA gene (upper column) and cppB gene (lower column) were obtained. The utility of PCR for making a microbiologic diagnosis in cases of culture-negative specimens has been reported (11, 16); however, a positive result cannot be obtained without conducting an examination. The lesson learned here is that in cases of an undetermined diagnosis, a sexual and travel history should be obtained precisely, even when the patient is considered to be too old for STIs. In addition, DGI should be included in the differential diagnosis of polyarthritis in elderly patients.

DGI is generally more common in women than men (1) since subclinical infection with N. gonorrhoeae occurs more often in women and its dissemination is considered to occur in particular during menstruation and the postpartum period. However, Suzaki et al. reviewed 11 cases of DGI in Japan and reported that the patients were primarily young to middle-aged men (a male-female ratio of 9 to 2; age range, 15 to 57 years old; average age, 39.8 years old) (8). The
reason why men outnumber women in the occurrence of DGI in Japan is not conclusive in the literature; however, our patient was also male. Moreover, six of 10 immunocompetent patients had a history of travelling to Southeast Asian countries, and two of the 11 patients were thought to have been infected abroad, as in the present case. Therefore, DGI should be considered as an imported infectious disease, especially in young to middle-aged men in Japan.

The development of DGI is often preceded by asymptomatic mucosal infections, and determining the entry site is therefore usually difficult (2). However, gonococcal pharyngitis has been reported to be a highly relevant focus for DGI (6, 7, 15). Considering the negative results of the urinalysis and the existence of pharyngeal symptoms, we assumed that the pharynx was the primary site of infection in this case.

Historically, the use of cefixime is preferred for N. gonorrhoeae infection as the initial therapy. However, the drug is not currently recommended (17) due to the emergence of resistant strains worldwide (18-20). Instead, levofloxacin is recommended and frequently prescribed. Not surprisingly, in turn, the widespread prevalence of levofloxacin-resistant N. gonorrhoeae strains has been reported: 78.6% in Japan (21), 95.7% in Korea (22), 67 to 83% in Southeast Asia (22), 42 to 52% in Europe (23), 38% in Australia (24) and a high incidence among men who have sex with men in the United States (25). At present, treatment with intravenous ceftriaxone is preferred as definitive therapy for DGI (26, 27). In our patient, the isolate was confirmed to be a relatively rare organism in terms of antimicrobial susceptibility testing; sensitive to ceftriaxone but intermediate to penicillin and resistant to levofloxacin. The antibiotic was changed to ceftriaxone after admission, after which the patient’s condition improved.

Various kinds of infectious and noninfectious diseases mimic the clinical characteristics of DGI. Related to infectious etiologies, viral infections, such as parvovirus B19, measles and rubella, or rare cases of Lyme disease should be considered as causes of acute polyarthritis with systemic rashes. STIs such as acute HIV infection, acute HBV infection or secondary syphilis should be considered in patients with a recent history of unprotected sexual contact. Bacterial arthritis primarily causes monoarthritis; however, meningococcal infection or infective endocarditis can induce polycarticular involvement. From the point of view of polyarthritis, systemic connective diseases, including reactive arthritis, rheumatoid arthritis and psoriatic arthritis, should also be considered.

In summary, we herein presented a case of DGI that occurred in a 69-year-old Japanese man who had been abroad and had unprotected sexual contact with a local commercial sex worker. DGI should be considered in the differential diagnosis, even in elderly patients.

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

This case was presented at the 107th Chugoku Congress of the Japanese Society of Internal Medicine by Nobuhiko Onishi (second author), who received a Junior Resident Award.

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