Disseminated Gonococcal Infection in Elderly Patients

Petronella H. L. M. Geelhoed-Duyvestijn, MD; Jos W. M. van der Meer, MD, PhD; Alexandra T. Lichtendahl-Bernards, MD; Chris J. Mulder, MD; Katherina A. E. Meyers, MD, PhD; Jan T. Poolman, PhD

- Four elderly patients (71, 53, 57, and 62 years old) had disseminated gonococcal infection. Three patients presented with suppurative arthritis and the fourth with fever, skin lesions, and malaise. Although the signs and symptoms did not differ from those in the younger age group, the diagnosis was not considered clinically. All gonococci were susceptible to penicillin.

(Ann Intern Med 1986;146:1739-1740)

Disseminated gonococcal infection (DGI) occurs in 1% to 3% of the patients infected with Neisseria gonor- rhoeae. As a rule, patients suffering from DGI are younger than 40 years of age; the majority of them are in their 20s. In this age group, patients presenting with arthralgia, monoarthritis or polyarthritis, tenosynovitis, typical skin lesions, and fever will generally be investigated for DGI. In elderly patients the diagnosis of DGI is rarely considered and may be missed unless appropriate cultures are taken.

REPORT OF CASES

The clinical and laboratory data from our four patients are summarized in the Table. Bacteriologic identification of all strains was made by Gram's stain, a positive oxidase reaction, and acid production from glucose but not from lactose, maltose, mannitol, and saccharose; these tests were performed on phenol red agar base supplemented with 10% ascitic fluid. All gonococci were penicillin susceptible (minimal inhibitory concentration, <0.15 mg/L). Only one gonococcus was available for auxotyping (see case 4).

CASE 1.—A 71-year-old widow was admitted to our hospital in 1973 because of migratory arthralgia of the right ankle and left foot, skin lesions, and arthritis of left thumb and right elbow. Two weeks before she had noticed a vaginal discharge. She denied recent sexual contact.

On examination she had a rectal temperature of 38.3°C. The right elbow and left first metacarpophalangeal joint were warm, red, swollen, and painful. Three small hemorrhagic skin lesions were seen on both hands. The erythrocyte sedimentation rate (ESR) was 77 mm/h. The white blood cell count was 7700/mm³ (7.7 x 10⁹/L). Total hemolytic complement was normal. A diagnostic arthrocentesis of the right elbow showed 2 mL of turbid yellow fluid containing 47 200 cells per cubic millimeter (47.2 x 10⁹/L). Gram's stain did not show microorganisms, and culture remained sterile. Blood cultures remained sterile. The diagnosis of DGI was made, and the patient was successfully treated with 10 million units of penicillin G sodium for three days followed by ampicillin sodium, 2 g daily, and probenecid, 500 mg twice daily for seven days.

CASE 2.—A 53-year-old widow was well until six weeks before admission to our hospital in 1977, when she developed arthralgia of both shoulders and fever. Soon afterwards her right wrist and fingers of the left hand became red, swollen, and painful. These symptoms disappeared, and the fever subsided after one week. In the week before admission, her left ankle became red, swollen, and painful. Several months earlier she had had one sexual contact.

On examination her temperature was 37°C. The left wrist was slightly swollen but not red or warm. Extension and flexion were slightly hampered. The left ankle was red, swollen, and extremely painful. There was no vaginal discharge.

The ESR was 58 mm/h; the white blood cell count was 6700/mm³ (6.7 x 10⁹/L). Agar electrophoresis showed a slightly elevated IgM fraction. Antinuclear factor, Rose-Waaler, and latex fixation tests were negative. The total hemolytic complement value was normal. Cultures of urethra and cervix yielded N gonorrhoeae. A complement fixation test against gonococci was positive; antibodies against outer membrane antigens of gonococci could be detected in the stored sera. On arthrocentesis there was only a small amount of fluid. Gram's stain and culture did not show microorganisms. Blood cultures remained sterile. The diagnosis of DGI was made, and the patient was successfully treated with 10 million units of penicillin G sodium for three days followed by ampicillin sodium, 2 g daily, and probenecid, 500 mg twice daily for seven days.

CASE 3.—A 57-year-old man was admitted to the hospital because of arthritis of his left knee in 1983. In 1978 he had had a swollen left knee after trauma; the swelling had subsided spontaneously. In 1981 he had been treated with penicillin by his physician because of urethritis. A culture for gonococci at that time was negative. The patient denied extramarital sexual contacts.

On examination the rectal temperature was 38.8°C. His left knee was red, swollen, and painful. The ESR was 80 mm/h. The white blood cell count was 10 500/mm³ (10.5 x 10⁹/L). Total hemolytic complement level was normal. A diagnostic arthrocentesis showed 90 mL of turbid yellow fluid. Gram's stain showed gram-negative diplococci. The culture showed N gonorrhoeae. A complement fixation test against gonococci was negative. Antibodies against outer membrane antigens were detectable. Blood and urine cultures remained negative. The patient was successfully treated with 6 million units of penicillin G sodium for 14 days.

CASE 4.—A 62-year-old man had been receiving treatment with lithium carbonate for several years because of manic-depressive psychosis. He was well until January 1985, when he started complaining of anorexia, weakness, and weight loss. In April 1983 he was admitted to a psychiatric hospital because lithium ion intoxication was suspected. The lithium ion concentration in the serum was elevated (1.27 mEq/L [1.27 mmol/L]). Because of anemia, a high ESR, and intermittent fever with chills and rigors, he was transferred to our hospital.

On examination the patient was tired and pale. Temperature was 38.9°C; blood pressure, 90/50 mm Hg; and pulse rate, 72 beats per minute. No abnormalities were found except for a grade 1 systolic murmur at the left sternal border and a few purpuric skin lesions on both lower extremities. Results of urinalysis were normal. The ESR was 188 mm/h; hemoglobin level, 8.7 g/dL (5.4 mmol/L); and hematocrit, 25%. The white blood cell count was 11 400/mm³ (11.4 x 10⁹/L) with a normal differential cell count.

Agar electrophoresis and immunoelectrophoresis of serum...
Characteristics of Four Elderly Patients With Disseminated Gonococcal Infection

<table>
<thead>
<tr>
<th>Patient</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y/sex</td>
<td>71/F</td>
<td>53/F</td>
<td>57/M</td>
<td>62/M</td>
</tr>
<tr>
<td>Suppurative arthritis</td>
<td>R elbow, L 1st metacarpophalangeal joint</td>
<td>L wrist, L ankle</td>
<td>L knee</td>
<td>None</td>
</tr>
<tr>
<td>Migratory arthritis</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Tenosynovitis</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Skin lesions</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Fever</td>
<td>Yes</td>
<td>Yes*</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Time to diagnosis, d</td>
<td>20</td>
<td>50</td>
<td>5</td>
<td>&gt;30</td>
</tr>
<tr>
<td>Positive cultures</td>
<td>Cervix</td>
<td>Cervix, urethra</td>
<td>Knee joint</td>
<td>Blood</td>
</tr>
<tr>
<td>Serologic tests</td>
<td>Complement fixation</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Outer membrane antigens</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

*Subsided.

showed a moderately elevated IgG value with three homogeneous components of k and l type (immunofluorescence of the bone marrow gave no evidence of monoclonal gammapathy). Total hemolytic complement level was normal; C3 and C4 values were both slightly depressed (0.63 and 0.13 mg/dL [0.0063 and 0.0013 g/L], respectively). Immune complexes were detected (C1q binding, 199 μgEq of aggregated IgG per milliliter). Echocardiography did not show vegetations.

To our surprise, three blood cultures were positive for *Neisseria gonorrhoeae* on the fifth day. The strain was typed as a serogroup W1, serovar IA-5. The gonococcus was penicillin sensitive and on auxotyping it was shown to be proline dependent. A complement fixation test for serum antibodies against gonococci was negative. However, antibodies against cell-envelope antigens of homologous gonococcal strain (lipo polysaccharide, protein I, protein II, protein III, and 45 K outer membrane protein) were demonstrated by enzyme-linked immunosorbent assay and gel immunoradioassay using isolated outer membranes as antigenic material.

Sexual contacts were denied. Lithium carbonate therapy was stopped and the patient was treated with 6 million units of penicillin G sodium per day. The temperature fell but did not return to normal. On the tenth day of penicillin therapy the patient developed a generalized hemorrhagic rash. *Neisseria gonorrhoeae* could not be recovered from the skin lesions. On biopsy a perivascular polymorphonuclear cell infiltrate with a few eosinophils was observed. The rash and the persistent elevation of the body temperature made us suspect allergy to penicillin, but persistent infection could not be ruled out. Therefore, treatment with this drug was stopped, and treatment with rifampin (to which the gonococcus was sensitive) was given for another four days. The drug was stopped, and treatment with rifampin (to which the gonococcus was sensitive) was given for another four days. The patient was treated with 6 million units of penicillin G sodium per day. The temperature fell but did not return to normal. On the tenth day of penicillin therapy the patient developed a generalized hemorrhagic rash.

Sexual contacts were denied. Lithium carbonate therapy was stopped and the patient was treated with 6 million units of penicillin G sodium per day. The temperature fell but did not return to normal. On the tenth day of penicillin therapy the patient developed a generalized hemorrhagic rash. *Neisseria gonorrhoeae* could not be recovered from the skin lesions. On biopsy a perivascular polymorphonuclear cell infiltrate with a few eosinophils was observed. The rash and the persistent elevation of the body temperature made us suspect allergy to penicillin, but persistent infection could not be ruled out. Therefore, treatment with this drug was stopped, and treatment with rifampin (to which the gonococcus was sensitive) was given for another four days. The temperature normalized and the skin lesions disappeared. After four weeks the patient was discharged in a fairly good condition. On follow up, his condition had improved. The abnormal protein bands, which probably were a reflection of the high antibody response to the gonococcus, had disappeared.

**COMMENT**

To our knowledge, DGI has not been reported in elderly patients before. In our hospital, we have seen four elderly patients suffering from DGI in the last ten years, suggesting that it is a rare disease in the elderly. However, the diagnosis may be missed if cultures are not taken from the involved sites.

The clinical picture in our patients varied considerably, ranging from fever and atypical skin lesions in patient 4 to migratory arthralgia and suppurative arthritis in the other three patients. It is of interest that patient 2 was afebrile when she was finally admitted to our hospital.

Only one of our patients admitted extramarital sexual contact. To obtain information on sexual activities in the elderly age group is probably still difficult. With the exception of patient 2, we were not informed of the most likely time of acquisition of the gonococcus. In patient 2, the time between the last sexual contact and the first symptoms seems to be longer than in most cases of DGI. Usually premenopausal women do not carry gonococci asymptptomatically for longer than a month because of the propensity to disseminate at the time of menstruation. It could be that postmenopausal women are able to carry gonococci for longer periods. In two of our patients (1 and 2), gonococci could not be isolated only from genital sites; in patient 2 the synovial fluid culture was positive for gonococci. In the literature, it is a common finding that gonococci cannot be isolated from the suppurative synovial fluid; according to Holmes et al, such patients should be classified as having probable DGI. An underlying disease or defect of host defense (especially of the complement system) was not found in any of our patients.

Serologic tests were performed in all patients. With the complement fixation test, antibodies were demonstrated in only two of our patients; high antibody titers against the outer membrane proteins were detected in all patients by enzyme-linked immunosorbent assay and further analyzed by gel immunoradioassay. The diagnostic value of these tests is not known at present. The paradox between high antibody levels and prolonged gonococcal infection (as in patient 4) without any sign of defect of host defense is an intriguing problem. The induction of nonprotective antibodies is the most likely explanation, probably also explaining why some people experience several gonococcal infections during their lives.

In conclusion, these case reports show that DGI should be suspected in elderly patients with arthritis, arthralgia, tenosynovitis, skin lesions, and fever despite a history that does not suggest such a diagnosis.

Serotyping in case 4 was done by Joan S. Knapp, Seattle.

**References**