Disseminated gonococcal infection due to a β -lactamase-producing strain of *Neisseria gonorrhoeae*

A case report

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SUMMARY A β -lactamase-producing strain of *Neisseria gonorrhoeae* with nutritional requirements for arginine, hypoxanthine, and uracil was isolated from the knee-joint fluid, the genital tract, and the sexual partner of a woman presenting with gonococcal arthritis.

Introduction

Disseminated gonococcal infection (DGI) can occur in at least two distinct situations. The gonococcus can be serum resistant as the result of receptors on its surface that can bind IgG antibodies, which are present in the serum of normal previously uninfected persons.¹ These blocking antibodies can inhibit the bactericidal action of specific antibody and complement in normal human serum. Alternatively, the patient can be genetically deficient in complement factors C6, C7, or C8, resulting in a lack of normal serum bactericidal activity.^{2,3}

Strains of gonococci causing disseminated infections can be characterised by their in-vitro cultural requirements (auxotyping), most of them requiring arginine, hypoxanthine, and uracil.⁴

The penicillin sensitivity of gonococci has gradually decreased over the past decades. This chromosome-mediated relative resistance can still be overcome by increased doses of penicillin.⁵ However, strains of gonococci have recently been identified which contain a plasmid coding for an enzyme that inactivates penicillin by opening the β -lactam ring. These strains cannot be eradicated by high doses of penicillin.⁶

The prevalence of these strains in uncomplicated gonococcal infections differs widely in different parts

of the world. In the Netherlands a recent survey indicated that about 3% of all gonococcal strains isolated in the public health laboratories produced β -lactamase. Gonococci in disseminated infections are usually relatively sensitive to penicillin.⁷ However, since these strains can also acquire the plasmid coding for β -lactamase formation it can no longer be assumed that patients with disseminated disease will respond to the usual penicillin therapy.

Case report

CLINICAL AND LABORATORY FINDINGS

A woman, born in 1953, was admitted because of an acute monoarthritis of the right knee. Her previous history was uneventful. The day before admission she had a fever and rigors. The following day the right knee became painful and swollen. On admission her temperature was 39.6°C. The right knee was acutely inflamed but the other joints were normal. There were no skin lesions or heart murmur on auscultation. The right Bartholin's gland was inflamed, and the patient was menstruating. A purulent exudate was aspirated from the knee and contained $6100 \times 10^6/1$ granulocytes ($6100/\text{mm}^3$). A Gram-stained smear showed many intracellular Gram-negative diplococci, as did smears from the cervix and the inflamed Bartholin's gland.

DIAGNOSIS AND TREATMENT

A diagnosis of disseminated gonococcal infection was made and treatment was started with 10 megaunits of penicillin G divided into four daily doses. There was

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no clinical improvement; the patient remained febrile and the inflammation of the joint did not subside.

After two days cultures from the knee aspirate, cervix, and Bartholin's gland grew a strain of *Neisseria gonorrhoeae* which was resistant to penicillin due to β -lactamase production.

Treatment was then changed to co-trimoxazole, but because of insensitivity of the gonococcus to trimethoprim doxycycline 100 mg daily was given instead. On this regimen the patient's recovery was uneventful. She became afebrile within a few days and inflammation of the knee joint gradually subsided, although swelling of the joint and a serous effusion persisted for several weeks. Cultures from repeated aspirates remained sterile. No other joints were affected. Serum total haemolytic complement (CH50), and the concentrations of C3 and C4 were slightly raised.

The patient admitted sexual contact with a single partner only. The same gonococcal strain was isolated from him and another of his contacts.

BACTERIOLOGICAL TECHNIQUES

Specimens from the cervix, Bartholin's gland, and the knee aspirate yielded growth in Thayer-Martin medium and in GC medium with supplements. These cultures were identified by fermentation tests and growth requirements as *N gonorrhoeae*. The antibiogram of the three strains was similar and showed resistance to penicillin and ampicillin. The minimum inhibitory concentrations (MIC) were: penicillin 8-16 units/ml, ampicillin 16 μ g/ml, tetracycline 0.5 μ g/ml, and erythromycin 0.5 μ g/ml. The chromogenic cephalosporin test for β -lactamase gave a positive result for suspensions of all three strains.

The strain isolated from the knee joint was confirmed as a penicillinase-producing *N gonorrhoeae* by the National Institute of Public Health Reference Laboratory (RIV, Bilthoven, the Netherlands). Subsequent auxotyping, kindly performed by Dr Joan Knapp at the Neisseria Reference Laboratory of the United States Public Health Service Hospital, Seattle, USA, showed that the strain required arginine, hypoxanthine, uracil, and methionine; it was confirmed that it produced β -lactamase.

Discussion

This case illustrates that DGI can be caused by β -lactamase-producing gonococci. The strain isolated from our patient required arginine, hypoxanthine, and uracil and thus belonged to the auxotype most frequently involved in DGI.⁴ Dissemination was presumably due to inherent virulence factors of the micro-organism and not to a defective host-defence system in the patient. Apparently acquisition of the

plasmid inducing β -lactamase production did not alter the strain's capacity to cause invasive infection.

High-dose penicillin therapy is the treatment of choice of DGI.⁸ Although there are clear-cut alternative therapeutic regimens for uncomplicated gonococcal infections the situation in DGI is less clear. A recent treatment schedule gives spectinomycin as the treatment of choice in cases of DGI caused by β -lactamase-producing gonococci.⁹ However, lack of experience with this antibiotic made us decide to use doxycycline, which proved to be effective.

The prevalence of β -lactamase-producing gonococci in DGI is at present unknown. However, with the increasing frequency of these strains in uncomplicated infections the number of disseminated infections caused by these strains may be increased, although such a case is only incidentally mentioned in the literature.¹⁰ Penicillin can, therefore, no longer be expected to be effective in DGI. Testing for β -lactamase formation must be carried out if there is the slightest evidence of decreased resistance to penicillin from either in-vitro or in-vivo data. However, even before the results of these tests are available, an unsatisfactory response to penicillin therapy may indicate an infection with a β -lactamase-producing strain and be a reason to consider a change of antibiotic therapy.

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