Gonorrhoea Caused by A Mixture of Penicillinase-Positive and -Negative Gonococci : A Case Report

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Abstract: A 23-year-old unmarried man was infected with gonorrhoea from a prostitute in Fukuoka City and was treated with ampicillin which resulted in failure. By a rapid iodometric test it was found that the isolates before the treatment were penicillinase-negative. After the ampicillin treatment, however, the isolates turned to penicillinase-positive but were, in fact, a mixture of penicillinase-positive and penicillinase-negative gonococcal strains. Treatment by spectinomycin and doxycycline resulted in failure but the gonorrhoea was cured by ribostamycin.

Key words : gonorrhoea, penicillinase-producing *Neisseria gonorrhoeae*, mixed infection.

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Introduction

Penicillinase-producing *Neisseria gonorrhoeae* (PPNG) strains have been found in many countries throughout the world (Perine *et al.*, 1979; Center for Disease Control, 1982). In Fukuoka, Japan, the incidence of PPNG strains was approximately 15% in 1981 (Yoshida *et al.*, 1982; Urabe *et al.*, 1983). It has been reported by some investigators that among gonorrhoea caused by PPNG strains, there are cases caused by a mixture of PPNG and non-PPNG strains although the ratio of such cases is low (Percival *et al.*, 1976; Nayyar *et al.*, 1980; Chowdhury *et al.*, 1981). We report here such a case who at first discharged non-PPNG but discharged both PPNG and non-PPNG strains after being treated with ampicillin.

Case Report

Clinical features and treatment

A 23-year-old unmarried man was admitted because of urethral discharge. Four days before the admission he had sexual contact with a prostitute in Fukuoka City. A Gram-stained smear of urethral discharge showed many intracellular Gram-negative diplococci. Under a diagnosis of gonorrhoea, he was treated with 1.5 g of ampicillin orally per day for four days. After a 4-day treatment, however, symptom did not change so the administration of ampicillin was extended 3 more days. In the meantime the

Table 1. Minimum inhibitory concentration (MIC) of antibiotics for isolates

Date of isolation	Isolates	MIC ($\mu\text{g/ml}$)					
		PcG	AMPC	DOTC	SP	MINO	CZX
22 Nov.	Primary culture	0.10	0.20	0.39	25	0.78	
29 Nov.	Primary culture	12.5	50	3.13	25	1.56	
	PPNG	25	50	3.13	25		0.025
	non-PPNG	1.56	0.78	3.13	25		0.025
10 Dec.	Primary culture	25	50	6.25	25	3.13	

PcG : penicillin G, AMPC : amoxicillin, DOTC : doxycycline,
 SP : spectinomycin, MINO : minocycline, CZX : ceftizoxime.

pathogen isolated by the first medical examination was identified as *Neisseria gonorrhoeae* and by a rapid iodometric test (World Health Organization, 1976) its penicillinase production was found to be negative. After the 7-day therapy there was no clinical improvement, so treatment was changed to an intramuscular injection of 2.0 g of spectinomycin. The gonococci isolated on the 7th day were penicillinase-positive and the infection was shown to be due to a mixture of penicillinase-positive and penicillinase-negative strains. The spectinomycin treatment decreased the urethral discharge but the symptom recurred 4 days later. Doxycycline 200 mg per day was administered for three days but this treatment did not change the symptom. The gonorrhoea was cured at last by a daily shot of 1.0 g of ribostamycin intramuscularly over a period of 5 days. The patient denied any reinfection from the time of the first medical examination.

Minimum inhibitory concentrations of the isolates

Antibiotic susceptibility was determined by the agar dilution method for each isolate (Table 1). First isolates (22 Nov.) were fairly sensitive to penicillin G (PcG) and amoxicillin (AMPC). But after treatment by ampicillin for 7 days, the second isolates (29 Nov.) showed very high resistance to PcG and AMPC. The isolates, in fact, were a mixture of PPNG and non-PPNG strains. MICs of PcG for PPNG or non-PPNG strains were 25 $\mu\text{g/ml}$ or 1.56 $\mu\text{g/ml}$, respectively. The third isolate (10 Dec.), two days after the treatment by spectinomycin, showed very high resistance to PcG and AMPC and produced penicillinase. All isolates were sensitive to spectinomycin *in vitro* although treatment by spectinomycin resulted in failure.

Discussion

By a rapid iodometric test the gonococcus isolated from the primary culture did not show penicillinase production. The test became positive after a 7-day ampicillin therapy. The patient denied reinfection during this period. It appears likely that small numbers of PPNG mixed at first with large numbers of non-PPNG became predominant through the ampicillin therapy.

It has been reported that PPNG strains have 4.7 or 3.4 Mdal penicillinase-producing plasmid and 24.5 Mdal transfer plasmid (Sparling *et al.*, 1981). We examined the plasmid profile and confirmed that PPNG strains isolated from this patient had 4.7 and 24.5 Mdal plasmid (data not shown).

Bae *et al.* (1983) have reported a reagent-impregnated filter paper replica method to detect β -lactamase production on agar plates. By this method, mixed infection by PPNG and non-PPNG strains are easily found on the primary culture.

Mixed infection or polymicrobial infection is common in routine bacterial infection. Therefore practitioners for sexually transmitted diseases should pay close attention to gonorrhoea caused by a mixture of PPNG and non-PPNG strains, even if tests for penicillinase production are negative on the primary culture.

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ペニシリナーゼ産生淋菌とペニシリナーゼ非産生淋菌の混合感染による淋疾の一例

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要 旨： ペニシリナーゼ産生淋菌 (PPNG) は東京、大阪、福岡など各都市で prostitute を中心に定着しており、分離される割合は淋菌の 10-15% である。この報告の 23 才男性淋症患者から分離された淋菌は最初、迅速ヨード法によりペニシリナーゼ産生が陰性であったので non-PPNG 株によるものと思われた。しかし 7 日間のアンピシリン服用によって症状が改善せず再度分離した淋菌は、迅速ヨード法でペニシリナーゼ産生が陽性となった。患者は治療中の再感染を否定しているので、最初 non-PPNG 株に混じっていた少数の PPNG 株がアンピシリン治療により優位となって、迅速ヨード法が陰性から陽性に変ったと考えられる。病原菌の複合感染が最近問題となっているが、淋疾においてもこのような複合感染がみられるので治療上注意を要すると思われた。

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