Urethritis caused by *Neisseria meningitidis* serogroup C

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Neisseria meningitidis and *Neisseria gonorrhoeae* infections in humans have traditionally been distinguished by their clinical manifestations and site of isolation. *N. meningitidis* usually causes meningococcemia and/or meningitis, while *N. gonorrhoeae* usually infects the anogenital mucous membranes. Nevertheless, the ecological niches of these two species occasionally overlap, and it has been observed that *N. meningitidis* can colonize the anogenital tract in men and women, causing urethritis, proctitis and cervicitis; *N. gonorrhoeae* has been observed in the oropharyngeal mucous membranes, causing meningitis and pharyngitis [1].

Between 1974 and 1993, the majority of cases of *N. meningitidis* urethritis were caused by strains belonging to serogroups A [2–4] and B [3,5,6]; isolated cases caused by strains belonging to serogroups C [7], 29E [8], X [9] and Y [3,6] and non-groupables [9] have also been published. This either is related to the greater ability of these serogroups to colonize the urethra, or else reflects the predominant serogroups in the community. Epidemiologic studies show that in Spain a considerable increase in infections caused by *N. meningitidis* serogroup C has occurred since 1990, the serotype 2b:P1.2,5 being the most frequent [10]. In our population this increase has been happening since 1994. In this report we present a case of acute urethritis caused by *N. meningitidis* C:2b:P1.2.

In October 1996, a 42-year-old heterosexual male presented at the clinic at his health center, with purulent urethral exudate and pain during micturition during the previous 8 days. The patient reported two episodes of urethritis of unknown etiology several years previously. He had no regular partner and stated having had sexual intercourse with a prostitute, without fellatio or use of a condom, 20 days before presenting symptoms. His doctor referred him to the microbiology laboratory for examination of urethral exudate. The patient received treatment with 1 g cefonicid every 24 h for 2 days, after which he was asymptomatic.

At the time of obtaining the sample, the patient presented little exudate. On direct microscopic examination, 5–7 leukocytes/ ×400 field were observed. No Gram-negative diplococci or other microorganisms were seen on the Gram stain. The exudate was streaked on Martin–Lewis agar (Biomedics, Madrid, Spain), vaginalis agar (made with Columbia agar (Becton Dickinson, Cockeysville, USA), protease peptone no. 3 (Difco, Detroit, USA) and human blood), chocolate agar (Oxoid, Madrid, Spain) and Mycoplasma-Lyo (bioMérieux, Marcy-L'Étoile, France). Direct immunofluorescence was performed for the detection of *Chlamydia trachomatis* antigen (Syva Company, San José, USA). The plates were incubated at 37°C for 48 h in 5% CO_2. After 24 h, oxidase-positive colonies grew on Martin–Lewis agar and chocolate agar which on Gram stain had the appearance of Gram-negative diplococci. Identification was performed by the Api NH battery of biochemical tests (bioMerieux, Marcy-L'Étoile, France), with positive results for glucose oxidation and γ-glutamyl transpeptidase (GGT). The strain was not β-lactamase-producing. It was presumed to be *N. gonorrhoeae* because of the kind of infection and the sugar oxidation. The microorganism was sent to the Carlos III Institute (Majadahonda, Madrid, Spain) for biotyping. No other microorganism was isolated from the urethra. The patient underwent further tests for the serologic determination of syphilis, HIV, and hepatitis viruses B and C; the results were negative in all cases. One month later, a follow-up of the urethral exudate was performed; no leukocytes were observed on direct microscopic examination, and the culture was negative.

In the reference center, Carlos III Institute, biochemical identification with Api NH was positive for glucose oxidation and GGT production, and doubtful for maltose oxidation. Sugar oxidation was confirmed in trypticase cysteine medium, with positive results for glucose and maltose oxidation. Biotyping revealed the strain to be *N. meningitidis*. Monoclonal antibody typing identified it as *N. meningitidis* C:2b:P1.2. No crossover agglutinations with gonococci were found.

No clinical or laboratory data are available on the women with whom the patient had sexual intercourse.

N. meningitidis can be isolated from the nasopharynx in 5–15% of individuals [1], with a greater proportion being observed in confined populations or certain groups. Janda et al [11] found a prevalence of 42.5% meningococcal carriers in the nasopharynx in homosexual men attending a sexually transmitted diseases (STD) clinic.

In the general population, the proportion of *N. meningitidis* isolated from the urethra ranges from 0.05% [7] to 0.07% [12], while Conde-Glez and Calderón [5] found a rate of 0.4% in high-risk populations. In homosexual men, the proportion of meningococci isolated from the urethra ranges from 0.03% [7] to 0.7% [11]. Maini et al [12] did not isolate any meningococci from 8992 urethral samples from heterosexual males, while McKenna et al [7] isolated this microorganism at a rate of 0.03%.

Meningococci may colonize the rectum of homosexual men (1.1% [7] to 2.1% [13]) and of 0.2% of women [13], and while Maini et al [12] did not isolate any meningococci from 15 975 samples of cervical exudate, other authors report a rate of 0.03% [7]. These studies show that the presence of *N. meningitidis* in the anogenital tract ranges widely, depending on the population studied.

Despite the prevalence of *N. meningitidis* in the urethra, its capacity for producing urethritis is relatively low. The first case published was in 1942 by Carpenter and Charles [2], but the majority of the cases described accumulated between the years 1974 and 1993 [3–15]. From this date on, we have not found any cases reported in the databases consulted: Medline and Embase. Although McKenna et al [7] did not find any variation between the prevalence and incidence of non-gonococcal *Neisseria* in anogenital samples in the period pre- and post-AIDS, our not finding any case of urethritis caused by meningococci from 1993 on may be related to the public awareness of HIV infection, as has been observed with other STDs such as gonococcal urethritis, which has been decreasing in our population since 1990 [16]. This may be more obvious among homosexuals, who had a greater incidence of urethritis caused by meningococci [7,11,12] as these comprise the population group which has taken greatest measures regarding the prevention of HIV infection.

Urethritis caused by *N. meningitidis* may be either symptomatic, generally as exudate without dysuria [8,14], or indistinguishable from gonococcal urethritis [4–6,9], or asymptomatic [12].

Probably the most common route of transmission of meningococcal urethritis among heterosexuals was orogenital [4,9], while among homosexuals transmission was both orogenital and anogenital [7,12]. In the case described here, the route of transmission of the infection could not be determined, although it is clear from the medical history either that the meningococcus was colonizing the woman's cervix or that this was not a case of STD.

The majority of cases of meningococcal urethritis described are caused by serogroup B; this may be due to it being more pathogenic in the genitoanal area, or else to it being the predominant serogroup in the population [1,10].

Cases of maltose-negative *N. meningitidis* have occasionally been published [16]. This appears to be related to the inactivation of a permease [17]. Our strain, while it did not ferment maltose in a rapid test, was positive when a more sensitive test was used.

The clinical picture, site of isolation and identification may all contribute to initial confusion over urethritis due to *N. meningitidis*, and this indicates the need for typing of genital tract isolates.

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Further increase in ciprofloxacin-resistant *Campylobacter jejuni/coli* in Styria, Austria

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Diarrhea caused by *Campylobacter jejuni/coli* is one of the most common bacterial intestinal infections in our region (province of Styria, 1.2 million inhabitants). Most of the cases appear to be mild and self-limiting, making antibiotic treatment necessary only under special conditions. Macrolides would be the recommended antibiotics for *Campylobacter*-related illness. Usually, however, ciprofloxacin is prescribed empirically in our region [1,2].

At the Institute of Hygiene, University of Graz, *Campylobacter* spp. have been tested for resistance to nalidixic acid to detect the so-called NARTC (nalidixic acid-resistant thermophilic campylobacter) since 1988. Nalidixic acid-resistant strains were rare in 1988–90, but in the summer of 1991 we found a notable increase of resistant isolates, so we started to test ciprofloxacin and erythromycin routinely in 1992. Even during the first year we found a remarkable increase in ciprofloxacin resistance [3] and this has continued until now (Figure 1).

To determine resistance patterns throughout the province of Styria, the three main Styrian laboratories have collected and evaluated data from the last 2 years (1996 and 1997). In total, 58 505 specimens of feces were examined and 1315 isolates of *Campylobacter* spp. were obtained from 1158 patients (specimen positivity 2.25%). Species differentiation of 935 first isolates from individual patients revealed 94.1% *C. jejuni* and 5.9% *C. coli*. Nearly 30% of the isolates were from patients whose diarrheal illness had necessitated hospital treatment. The age distribution showed an excess of cases among children from 0 to 10 years (30%) and a second peak among the 20–30-year-olds. Most of these infections were acquired in our region; the number of infections acquired abroad was less than 5%.

In all three laboratories, patterns of resistance of *Campylobacter* spp. to erythromycin (15 μg), nalidixic acid (30 μg) and ciprofloxacin (5 μg) were tested by disk diffusion performed on Mueller–Hinton agar (Oxoid, Basingstoke, UK) supplemented with 5% blood. All strains were incubated in a micro-aerophilic atmosphere at 42°C and read after 24–48 h. The following zone diameters (in mm) were used: erythromycin, >=23 susceptible, <=13 resistant; nalidixic acid, >=19 susceptible, <=13 resistant; ciprofloxacin, >=21 susceptible, <=15 resistant. In doubtful cases (nalidixic acid resistant and ciprofloxacin susceptible or intermediate), an additional Etest was performed according to the recommen-dations of Baker [4] for further confirmation and detection of type 2 mutants [5]. The following break-points of ciprofloxacin were used: MIC >=4 mg/L, resistant; MIC <=1 mg/L, susceptible. The results of these tests (only first isolates were used) are shown in Table 1. No connection was apparent between cipro-floxacin resistance and age or geographic distribution. A difference, however, occurred between *C. jejuni* and *C. coli*. Of 935 species-differentiated isolates, 880 were *C. jejuni* with a ciprofloxacin resistance of 27.4% and erythromycin resistance of 0.7%, while the cipro-floxacin and erythromycin resistance of 55 strains of *C. coli* reached 47.3% and 5.5%, respectively.

The reason for this development may have been a regulation of the Austrian government ('Geflügel-hygieneverordnung'), which was passed in the summer of 1991 and came into force on 1 January, 1992 with the aim of reducing the incidence of salmonellosis in Austria. This regulation laid down a number of measures, e.g. the testing of all poultry flocks for *Salmonella* spp. prior to slaughtering, with only *Salmonella*-free flocks being released for slaughter. This measure increasingly induced veterinarians to use antibiotics in the poultry industry, especially enrofloxacin (Baytril), a quinolone closely related to ciprofloxacin. This development of resistance after the introduction of enrofloxacin in veterinary medicine was first described by Endtz et al in The Netherlands [6,7]; since that time, further publications reporting similar findings have become available [8–11]. In Austria, enrofloxacin was introduced in the summer of 1989, but a large degree of overuse was initiated by the government regulation

Table 1 Susceptibility of 1149 *Campylobacter* spp. (first isolates from individual patients) to erythromycin, nalidixic acid and ciprofloxacin

	Number of isolates	Resistant to erythromycin (%)	Resistant to nalidixic acid (%)	Resistant to ciprofloxacin (%)
1996	568	1.4	25.9	25.2
1997	581	0.3	34.9	34.1
Total	1149	0.9	30.4	29.7