

Urinary tract infection caused by nontypable *Haemophilus influenzae* in the elderly

Since the introduction of the *Haemophilus influenzae* serotype b (Hib) vaccine, the decrease in invasive Hib disease predominantly affecting children and the relative increase in nontypable *H. influenzae* (NTHi) infections have been well documented in many parts of the world. The increasing trend in the number of cases, especially among older adults, deserves attention (Heath *et al.*, 2001; De Almeida *et al.*, 2005; Dworkin *et al.*, 2007; Tsang *et al.*, 2007).

H. influenzae has been rarely implicated as the causative agent of urinary tract infections in adults. The isolation of *H. influenzae* from a urine sample was first reported in 1898 when Kretz recovered influenza bacillus from the urine sample of a 36-year-old man with haematuria and polyuria (Wright, 1905). Since then, fewer than 30 cases of this bacterium as the cause of adult urinary tract infections have been reported (Reichman, 1999; Papaioannides *et al.*, 2002). In Sweden, a study over a 24-year period showed 36 children with *Haemophilus* species infection (Hansson *et al.*, 2007).

We report a rare case of NTHi urinary infection in an 87-year-old man and discuss the possible underestimation of the true incidence of *H. influenzae* in urinary tract infections. The patient was admitted to an emergency hospital with aorto-iliac-femoral artery disease and renal artery stenosis. Twenty-four hours after surgical angioplasty, the patient showed a temperature of 38 °C. Urine was collected for urinary sediment analysis and culture. At the hospital laboratory, the urine was routinely cultured on cysteine–lactose–electrolyte–deficient (CLED) agar (Oxoid). After inoculation, the urine sample was stored under refrigeration (4–8 °C). Microscopic examination and Gram stain of a clean voided urine specimen revealed 30–40 white blood cells per oil immersion field and the presence of Gram-negative coccobacilli. In view of these findings, a

urine sample was cultured on brain heart infusion chocolate agar (Difco) enriched with 10% defibrinated rabbit blood at 37 °C for 24 h, and bacterial growth was detected after 24 h. Gram staining of bacterial colonies was performed, showing abundant pleomorphic Gram-negative rods suggesting *Haemophilus* species. The culture was sent to the National Institute for Quality Control in Health – FIOCRUZ (INCQS) for additional identification and typing tests such as slide agglutination for serotype determination, biotyping, antimicrobial sensitivity and PCR capsular typing as previously described (Falla *et al.*, 1994; Campos, 1999). Urine culture collected after surgery inoculated on CLED agar was negative after 48 h. Treatment was initiated with i.v. 3 g/6 h ampicillin–sulbactam (1 g sulbactam + 2 g ampicillin) for 8 days, since the initial suspected aetiological agent of the infection was *H. influenzae*. After culture confirmation, the antibiotic therapy was parenteral 8 g/1 g per day (4 g/500 mg/12 h) for 8 days of piperacillin–tazobactam (Wagenlehner *et al.*, 2003). Negative slide agglutination for serotyping, biotyping and negative PCR capsular typing confirmed NTHi biotype VIII as the causative agent of infection. The NTHi strain isolated was nalidixic acid resistant (MIC >256 µg ml⁻¹), β-lactamase-negative, and sensitive to ampicillin and fluoroquinolones (ciprofloxacin, levofloxacin, lemofoxacin, moxifloxacin). After antibiotic therapy, the patient showed complete resolution of symptoms, return of normal function and normalization of blood parameters.

There are few reports of urinary tract infection caused by *Haemophilus* species. The inability of *Haemophilus* species to grow in standard media commonly used for culture of uropathogens suggests that the true frequency of these strains as a cause of urinary tract infections is underestimated. *H. influenzae* has rarely been implicated as the causative agent in

urinary tract infections in adults, with most cases afflicting men with anatomical or functional genito-urinary abnormalities. The true incidence of *H. influenzae* genito-urinary infection is unknown. The apparent rarity of *H. influenzae* urinary tract infection may be ascribed to three factors: (i) bacteriological media for recovery of uropathogens do not support the growth of *H. influenzae*; (ii) the organism is not generally part of the genitoperineal flora; and (iii) growth of *H. influenzae* is inhibited by urine even when it is supplemented with the necessary growth factors (Gabre-Kidan *et al.*, 1984).

H. influenzae may be a more common uropathogen in adults than previously recognized. We should consider the use of more sensitive culture techniques and greater physician awareness of the genito-urinary pathogenicity of this bacterium, particularly in male elderly patients with anatomical or functional genito-urinary abnormalities, to enhance the detection of *H. influenzae* urinary tract infection. Therefore the nalidixic acid resistance of *H. influenzae* should be investigated according to the age of patients (Pérez-Vázquez *et al.*, 2004). Prompt institution of therapy with antibiotics active against *H. influenzae* following sensitivity studies could prevent systemic septic complications in this group of frail patients.

Clearly, further studies are required to characterize the impact on pathogenicity and virulence of NTHi in unimmunized adult patients and the epidemiology of such micro-organisms. Also, nalidixic acid resistance may be useful as a baseline for future studies to monitor antimicrobial susceptibilities including susceptibility to fluoroquinolones.

To our knowledge, this is the first report of urinary tract infection caused by NTHi in adults in Brazil after the introduction of the Hib conjugate vaccine.

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