

# *Haemophilus parainfluenzae* meningitis in an adult associated with acute otitis media

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## SUMMARY

A case of *Haemophilus parainfluenzae* meningitis in a woman with a 3-day history of acute otitis media is reported. Her medical history included bladder cancer surgery. Unequivocal identification of the isolate was obtained by using molecular techniques such as 16S rRNA sequencing besides to conventional culture methods. To investigate bacterial virulent traits possibly related to invasive properties, *in vitro* serum resistance of our isolate was analyzed, but it was found serum susceptible.

Our study demonstrates that *H. parainfluenzae* can be considered an opportunistic pathogen able to cause life-threatening infections not only in children but also in patients with underlying conditions.

**KEY WORDS:** *Haemophilus parainfluenzae*, Meningitis, Opportunistic pathogen

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*Haemophilus* species are normal inhabitants of the upper respiratory tract of healthy humans (Kilian 2003). However, these bacteria can cause a wide variety of diseases ranging from respiratory tract infections to potentially life threatening diseases such as meningitis. *Haemophilus influenzae* type b (Hib) was the leading cause of meningitis due to *Haemophilus* species but, since the introduction of the Hib conjugate vaccines, the incidence of Hib meningitis has dramatically decreased in developed countries (Peltola 2000). The pathogenicity of species other than *H. influenzae* is low, nevertheless they sometimes cause serious infections. *H. parainfluenzae* is occasionally involved in respiratory tract infections (Pillai *et al.*, 2000), secondary bacteremia (Chow

*et al.*, 1974), endocarditis (Das *et al.*, 1997), urethritis (Maggs *et al.*, 1994), biliary tract infections (Frankard *et al.*, 2004), hepatic abscesses (Black *et al.*, 1988; Hwang *et al.*, 2002) and meningitis (Raoult *et al.*, 1987), the latter especially in children (Frazier *et al.*, 1982; Wort 1975; Watson *et al.*, 1981). However, we recently identified a case of meningitis due to *H. parainfluenzae* in an adult with a history of acute otitis media.

On November 11, 2006, a 32 year-old woman with a 3-day history of acute otitis media of the right ear with fever was admitted to a hospital complaining of severe headache, nausea and vomiting. One day before the admission she had been given amoxicillin/clavulanic acid, orally. She had been healthy except for previous bladder cancer surgery in 2004. At admission she was not receiving anti-cancer therapy. On physical examination, she was alert, but she presented neck stiffness and other meningeal signs. Cerebrospinal fluid (CSF) cell count was  $10^3/\text{mm}^3$  with 90% polymorphonuclear leucocytes and 10% monocytes, glucose 0.3 mmol/l, total CSF-protein 1 g/l and CSF-lactate 0.3 g/l. Culture of CSF sample grew cocco-bacillary gram-negative bacteria pre-

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sumptively identified as *H. parainfluenzae*. A blood culture was performed but it showed no growth. The patient received antimicrobial therapy with intravenous ampicillin and ceftriaxone for 11 days, which was associated with dexamethasone for the first 2 days, and she recovered. The *H. parainfluenzae* isolate was sent to the national reference laboratory at the Istituto Superiore di Sanità where identification was confirmed by both conventional culture methods (Api NH system, Biomerieux, Mercy l'Etoile, France), and growth requirement for X (hemin) and V (NAD) factors and molecular techniques such as 16S rRNA sequencing. By biotyping, the isolate was classified as biotype I. By the nitrocefin identification stick test, it was  $\beta$ -lactamase negative. Antibiotic susceptibility testing was performed by E-test (AB Biodisk, Solna, Sweden), according to CLSI guidelines. *H. influenzae* ATCC 49247 and *H. influenzae* ATCC 10211 were used as quality controls. The *H. parainfluenzae* isolate was found susceptible to ampicillin (0.25  $\mu$ g/ml), cefotaxime (<0.016  $\mu$ g/ml), ceftriaxone (<0.016  $\mu$ g/ml), chloramphenicol (0.50  $\mu$ g/ml), imipenem (0.094  $\mu$ g/ml) and ciprofloxacin (0.016  $\mu$ g/ml). To detect the ability of our isolate to avoid the bactericidal effect of serum, log-phase bacteria (approximately  $5 \times 10^4$  CFU/ml) were incubated for 30 min at 37°C with increasing concentrations of normal human serum (10%, 20%, 30% and 40%) diluted in 10 mM phosphate buffered saline containing 0.1% gelatine. Percent survival of *H. parainfluenzae* isolate in 10% and 20% serum was 0.93 and 0.15, respectively, while no survival was detected in 30% and 40% serum. These values were much smaller than those found for the Hib strain Eagan (up to 73% in 40% serum) and similar to those obtained for the *H. influenzae* strain Rd, indicating that the strain was serum susceptible.

*H. parainfluenzae* is regarded as an opportunistic pathogen and only occasional cases of *H. parainfluenzae* meningitis have been reported. Most cases affect young children where, sometimes, the onset of meningitis was preceded by a diagnosis of otitis media, pneumonia or other infections of the upper respiratory tract (Watson *et al.*, 1981). Very rare *H. parainfluenzae* meningitis cases in adults have been described in the literature (Raoult *et al.*, 1987; Timmis *et al.*, 1980). To our knowledge the case described herein is the

only case of meningitis associated with acute otitis media in an adult. Notably, our patient presented an underlying disease since she had suffered from cancer in the past but she had no symptoms at time of the onset of meningitis. It might be supposed that the same *H. parainfluenzae* isolate was responsible for both meningitis and acute otitis media, although we could not prove this hypothesis since no culture of the middle ear fluid was performed.

Interestingly, the *H. parainfluenzae* isolate described herein was classified as biotype I, although this biotype was found associated with isolates from healthy carriers in a previous report (Privitera *et al.*, 1998). To investigate whether our isolate possessed unusual virulence traits possibly related to particular invasive properties, its *in vitro* serum resistance was analyzed, but it was found serum susceptible. On the other hand, our previous study we performed on nontypeable *H. influenzae* isolates from meningitis demonstrated that serum resistance is not a specific characteristic of invasive isolates other than encapsulated Hib strains (Cardines *et al.*, 2007).

In conclusion, we describe an unusual case of *H. parainfluenzae* meningitis in an adult associated with acute otitis media. Although *H. parainfluenzae* has not been considered of much clinical importance in humans, the case we describe confirms that it can be regarded as an opportunistic pathogen able to cause life-threatening infections not only in children but also in adults, especially when underlying conditions are present.

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