Mycotic aneurysm of the abdominal aorta caused by *Haemophilus influenzae* type f

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Prior to the advent of the *Haemophilus influenzae* type b vaccine, invasive infections due to *H. influenzae* type f were rarely described. However, the epidemiology of *H. influenzae* is changing. While the incidence of invasive infections due to *H. influenzae* is declining in children, such infections are becoming more common in adults, particularly in the elderly. Here, we report an unusual case of infective aortic aneurysm caused by *H. influenzae* type f that underlines the emerging clinical relevance and pathogenic capability of this organism.

**Introduction**

*Haemophilus influenzae* is a small, Gram-negative bacillus commonly found as normal flora of the human upper respiratory tract. According to its capsular polysaccharide composition, *H. influenzae* is classified into six types (a–f) and non-encapsulated strains. *H. influenzae* type b (Hib) has been considered the most pathogenic and virulent type and is associated with serious respiratory and invasive infections, including epiglottitis, pneumonia, septicemia and meningitis. The other capsular types were traditionally considered less pathogenic as they were less commonly associated with invasive disease. However, since the introduction of the highly effective Hib vaccine, the incidence of invasive non-type b *H. influenzae* infections has been increasing (Peltola, 2000).

In the 1990s, a study in the USA showed that the incidence of invasive *H. influenzae* type f disease increased from 0.5/1 000 000 in 1989 to 1.9/1 000 000 in 1994, and the percentage of all invasive *H. influenzae* disease caused by *H. influenzae* type f rose from 1 % to 17% within the same years; 72% of *H. influenzae* type f cases occurred in adults and only 26% occurred in children (Urwin et al., 1996). More recently, another study in the USA revealed that the incidence of invasive *H. influenzae* disease in adults increased from 0.4 to 1.0/100 000 between 1996 and 2004, with non-typable *H. influenzae* accounting for the greatest number of cases, followed by *H. influenzae* type f. The same study also showed that specifically in the elderly population (aged ≥65 years) the increase in incidence of invasive *H. influenzae* infections was sharper (from 1.1 to 3.9/100 000) and that *H. influenzae* type f was the most commonly isolated strain (Dworkin et al., 2007); recent European and Canadian studies have shown similar results (Adam et al., 2010; Ladhani et al., 2010, 2012). Furthermore, the disease caused by *H. influenzae* type f in individuals over 60 years of age seems to be more severe. A review of invasive *Haemophilus* disease in Sweden revealed that in that age group, 59% of invasive *H. influenzae* type f cases versus 47% of invasive non-typable *H. influenzae* cases met the criteria of severe sepsis or septic shock, and more than one-third of invasive *H. influenzae* type f cases versus one-fifth of invasive non-typable *H. influenzae* cases were admitted to intensive care units (Resman et al., 2011).

Here, we report what to our knowledge constitutes the second published case of infective aortic aneurysm caused by *H. influenzae* type f. This case highlights the emerging clinical importance of *H. influenzae* type f in the post-Hib vaccine era.

**Case report**

A 58-year-old male with a medical history significant for obesity, hypertension, hyperlipidaemia, type-2 diabetes and chronic obstructive pulmonary disease presented to an emergency department for new onset of low back and infraumbilical abdominal pain accompanied with dizziness and weakness. On imaging, a penetrating aortic ulcer at the level of the inferior mesenteric artery was noted. The patient underwent intra-aortic endograft placement, and a few days after the intervention, he was discharged home. After returning home, the patient continued having
abdominal pain, poor food intake and trouble sleeping, and later developed fever and chills. Twelve days after discharge, he returned to the emergency department. On admission, the patient was not febrile (36.9 °C), but was tachycardic (104 beats per minute) and had moderate tenderness to palpation in the periumbilical region. Blood analysis showed an elevated white cell count of 15 100 μl⁻¹ with 88 % neutrophils. A CT scan of the abdomen revealed an inflammatory aneurysm of the distal aorta involving the endograft and the right common iliac artery (see Fig. 1). The patient was then transferred to the Veterans Affairs Medical Center in Seattle for further evaluation and treatment. At the Center, he underwent laparotomy with removal of the intra-aortic graft, aortic ligation and axillibifemoral bypass. The explanted endograft was sent to the microbiology laboratory for culture, and the patient was empirically started on vancomycin 1 g intravenously every 12 h and piperacillin/tazobactam 3 g/0.37 g intravenously every 6 h.

Gram staining of the specimen demonstrated many neutrophils but no organisms. Cultures on sheep blood, MacConkey and chocolate agars yielded numerous colonies of Gram-negative rods that grew only on chocolate agar at 24 h. The organism was identified as H. influenzae based on X and V factors requirements and the API NH identification system (bioMérieux Vitek; 99.9 % probability). Biochemical testing allowed the classification of the H. influenzae as biotype I (indole, urease and ornithine decarboxylase positive), and the chromogenic cephalosporin nitrocefin disc test demonstrated the lack of β-lactamase production. Due to the unusual clinical presentation, the isolated was also analysed by 16S rRNA gene sequencing. Sequence analysis indicated that the isolate was H. influenzae type f with 100 % identity with the type strain ATCC 9833. The capsular type was confirmed to be type f by both latex agglutination and multiplex-PCR-based capsular typing.

Blood samples collected at the referring hospital were also reported positive for H. influenzae 2 days after admission. After the isolation of H. influenzae was reported, the antibiotic therapy was switched to ceftriaxone 2 g intravenously daily for 6 weeks. The patient’s condition improved progressively and he was discharged 6 days after the surgery.

**Discussion**

Mycotic aneurysm is a rare and serious infection of the arterial wall that carries significant morbidity and mortality. In the past, syphilis contributed the majority of cases of mycotic aneurysm; however, currently, infective endocarditis and trauma, either iatrogenic, accidental or from IV drug use, are the predominant causes of this infection. In the absence of infective endocarditis and trauma, sporadic mycotic aneurysms are thought to be secondary to transient bacteraemia with seeding of a previously damaged site in the lumen of the artery, most commonly an ulcerated atherosclerotic plaque. *Staphylococcus aureus* and *Salmonella* species are the most common causative agents, accounting for 28–70 % and 15–24 %, respectively, of all cases of mycotic aneurysm (Moneta et al., 1998). Other organisms occasionally isolated from mycotic aneurysms include *Streptococcus* species and *Enterococcus* species, *Mycobacterium tuberculosis*, *Clostridium* species (Moneta et al., 1998) and some Gram-negative bacilli. *H. influenzae* has been rarely implicated in this infection, with only a handful of case reports in recent years (Moneta et al., 1998; Whitfield et al., 2008), and only one other case involving *H. influenzae* type f (Adlakha et al., 1994) to our knowledge.

Historically routine clinical laboratories would have determined the capsular type of an *H. influenzae* isolate by latex agglutination with the main purpose of identifying Hib. However, in the post-Hib vaccine era, this practice has been largely abandoned not only due to the low incidence of Hib disease, but also because the test was shown to be unreliable. Several publications have demonstrated that standard slide agglutination serotyping is less accurate than 16S rRNA sequencing and PCR-based capsular typing (Sacchi et al., 2005); furthermore, standard slide agglutination serotyping fails to correctly identify strains that may have lost capsular expression after growing in *in vitro*
conditions. In this case report, after determining the identity of the isolate as *H. influenzae* type f by sequencing, we confirmed its capsular status by both latex agglutination and multiplex-PCR-based capsular typing, which has been shown to most accurately classify the capsular type (Nelson & Smith, 2010). It is of note that by 16S rRNA gene sequencing, *H. influenzae* type f strains are about 2% distant from the other *H. influenzae* capsular types; such a distance would be sufficient for some authors to classify *H. influenzae* type f as a new unique species (Clarridge, 2004). This is explained by the fact that although the 16S rRNA gene (which relates to taxonomic position) and the genes for capsule production are independent, the 16S rRNA gene sequence in *H. influenzae* strains highly correlates with the capsular type, particularly in *H. influenzae* type f (Sacchi et al., 2005).

This case underlines the emerging clinical relevance and pathogenic capability of *H. influenzae* type f in the adult population after the near elimination of invasive Hib disease. The widespread use of the Hib vaccine has reduced not only the incidence of Hib infections, but also the prevalence of Hib oropharyngeal carriage (Adegbola et al., 1998). Such a change in microbial ecology may have allowed other *H. influenzae* types and strains to fill the niche left open by Hib. However, that does not explain the overall unambiguous increase in the incidence of invasive disease caused by *H. influenzae* in southern Sweden from 1997 to 2009 shown by Resman et al. (2011). The observed increase was due to an increase in invasive disease caused by non-typable *H. influenzae* and *H. influenzae* type f, mainly in individuals >60 years of age. Ladhani et al. (2012) also found small but gradual annual increases in invasive disease from 2000 to 2009 caused by *H. influenzae* types e and f in England and Wales which they attributed to the expansion of at-risk populations such as elderly people, patients with immunosuppression and those with comorbidities. Virulence factors detected in *H. influenzae* type f strains isolated over several decades did not seem to change (Watson et al., 2013). To date, the overall incidence of invasive *H. influenzae* type f infections is still low; thus, severe infections due to the organism, such as the case presented here, remain rare. However, although the reasons for the increased incidence of *H. influenzae* type f are not certain, the epidemiology of *H. influenzae* in the post-Hib vaccine era and changing demographics of the population suggest this could change.

References


