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ID CASE

Breech at the Border: An Atypical Case of Invasive *Haemophilus influenzae* in a Patient on a Novel Immunotherapeutic

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Haemophilus influenzae rarely causes pyogenic infections in the female genital tract, and even less commonly does this lead to systemic infections. Novel monoclonal antibody therapies targeting interleukin-17 may impair mucosal immunity, but increased risk for *H. influenzae* infections has not been documented. Here, we describe a case of *H. influenzae* bacteremia associated with pyosalpinx and hypothesize that immunomodulatory treatment for psoriasis predisposed our patient to this infection.

Keywords. *Haemophilus influenzae*; interleukin-17; pelvic inflammatory disease; pyosalpinx; secukinumab.

CASE REPORT

A 42-year-old female with history of psoriatic arthritis presented to the hospital with 1 day of bilateral lower abdominal pain, radiating to the back and associated with chills. She had no significant medical history apart from psoriatic arthritis. She had previously tried numerous disease-modifying antirheumatic drugs and had initiated secukinumab 18 months before. She reported a penicillin allergy but had previously tolerated amoxicillin. She was sexually active with men and had intercourse with a condom 2 months before admission. Her review of systems revealed urinary urge incontinence but no dysuria or vaginal discharge. On exam, she was febrile to 38.5°C. Her abdomen was soft, nondistended, and tender to deep palpation in the bilateral lower quadrants. The pelvic exam revealed cervical motion tenderness. She had a white blood cell count of 12.9×10^9 cells/L, normal renal function, and a contaminated urinalysis. An abdominal and pelvic computed tomography scan showed a thin-walled, tubular structure likely representing a hydrosalpinx or pyosalpinx. A pelvic ultrasound confirmed an echogenic tubular structure suggesting pyosalpinx (Figure 1). She was admitted for pelvic inflammatory disease (PID). Both admission blood cultures grew *H. influenzae*. Urine culture was negative. Her symptoms improved over several days, and repeat blood cultures were negative. She initially received empiric gentamicin and metronidazole, which was narrowed to ceftriaxone and metronidazole upon discharge. A pelvic ultrasound done 3 weeks later showed resolution of the pyosalpinx.

DISCUSSION

H. influenzae is a gram-negative coccobacillus. Serotype B (Hib) previously caused significant infant morbidity and mortality, but the majority of invasive infections now are caused by nontypeable *H. influenzae* (NTHi), almost 30 years after the advent of the Hib conjugate vaccine [1, 2]. According to the Centers for Disease Control and Prevention and the Emerging Infections Program population surveillance, the 2015 incidence of invasive NTHi infections for ages 35–49 (our patient's age) was 0.59 cases per 100 000 population [3].

NTHi commonly colonize the upper respiratory tract. However, *H. influenzae* can also inhabit the genital tract, ranging from 0.3% of asymptomatic pregnant females to 6% of males and females presenting to sexual health clinics [4, 5]. Although uncommon, NHTi PID is reported, including cervicovaginitis, endometritis, and salpingitis [6, 7]. NHTi biotype IV may exhibit predilection for genital mucosa over the oropharynx; however, this remains unclear [4–6, 8]. Serologic and molecular typing of our patient's isolate identified a NTHi biotype V. Invasive biotype V strains frequently contain an IS*1016* insertion sequence, which is often found in encapsulated *H. influenzae* [9]. These strains may represent a unique subset of NHTi with invasive capacity but have not been previously associated with genitourinary infections [4–6, 9, 10].

To our knowledge, this is the first report of an invasive *H. influenzae* infection in a patient taking secukinumab, an anti-interleukin-17 (anti-IL-17) monoclonal antibody approved to treat plaque psoriasis, psoriatic arthritis, and ankylosing spondylitis [11]. IL-17 is produced by a subset of CD4+ helper T cells (Th17) and mediates immunity to multiple bacterial and fungal pathogens. Through pleiotropic effects on multiple cells types, IL-17 induces expression of cytokines and innate antimicrobial peptides at mucosal sites and drives neutrophil recruitment [12, 13]. Patients with hyper IgE syndrome—caused by defective STAT3 signaling and poor Th-17 differentiation—illustrate the importance of this immune pathway as they suffer frequent staphylococcal and candidal skin and lung infections [12].

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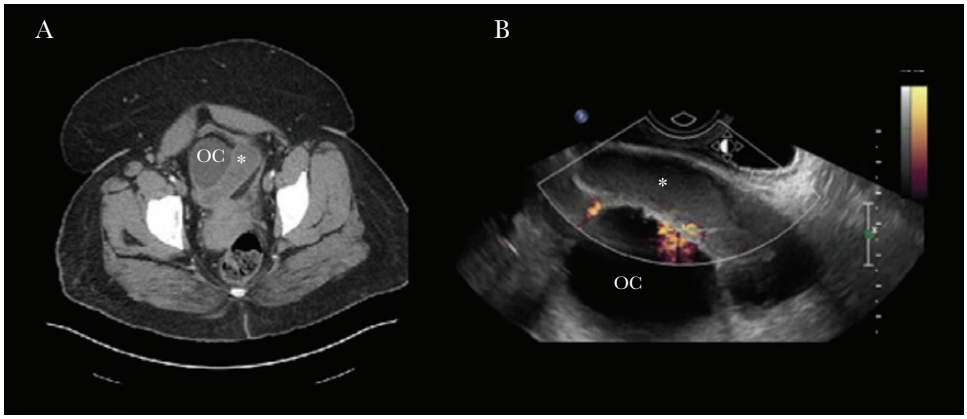

Figure 1. A, Computed tomography scan showing the presumed pyosalpinx (asterisk). B, Pelvic ultrasound showing the pyosalpinx as a hyperechoic tube with wall vascularity (asterisk). In both images, you can also see a simple ovarian cyst (OC).

The armamentarium of biological therapeutics is expanding, with more than 30 completed or ongoing trials targeting the IL-17 pathway (https://clinicaltrials.gov/). The burgeoning success of these agents has increased their use and allows for a better understanding of associated infectious complications. Nasopharyngitis and upper respiratory tract infections (URIs) are the most common infections reported in clinical trials with anti-IL-17 therapies. Similar to patients with hyper IgE syndrome, an increase in mucocutaneous candida infections (incidence rates, 2%–4.4%) has also been observed [11]. Given the increased incidence of URIs, it is tempting to speculate that *H. influenzae* may be a common bacterial culprit in patients taking secukinumab; however, detailed microbiological data on URIs have not been reported.

Lastly, we are just beginning to understand the role of IL-17 in vaginal mucosal immunity. In animal models, IL-17 plays an important function in controlling vaginal colonization of *Candida* and *Streptococcus* [14, 15]. We hypothesize that secukinumab dysregulated our patient's immune system, compromising her vaginal mucosal defense and ultimately contributing to an invasive *H. influenzae* infection.

CONCLUSION

In summary, this is the first case of an invasive *H. influenzae* infection associated with anti-IL-17 therapy. NTHi can colonize the vaginal tract, and we suspect that the monoclonal antibody disrupted this patient's mucosal barrier, increasing her risk for an invasive *H. influenzae* infection that would otherwise be extremely rare in her demographic.

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