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## Fulminant Supraglottitis from *Neisseria meningitidis*

**To the Editor:** A 68-year-old Caucasian woman with non-insulin-dependent diabetes mellitus, hypertension, and peripheral vascular disease sought treatment at an emergency department after experiencing 2 days of pharyngitis and 1 day of fatigue and dysphagia for solid food. The morning of admission she noted dysphagia for solid food and liquids, dysphonia, severe anterior neck pain, neck swelling and erythema, dyspnea, and a temperature of 102.3°F (39°C). A computed tomographic (CT) scan demonstrated substantial neck soft tissue edema and narrowing of the oropharynx and hypopharynx. She received single doses of intravenous ampicillin/sulbactam, clindamycin, dexamethasone (10 mg), and methylprednisolone (125 mg) before being evacuated by air to our intensive care unit (ICU) at Walter Reed Army Medical Center. Intravenous ampicillin/sulbactam, 3 g every 6 hours, and clindamycin, 900 mg every 8 hours, were continued after the transfer. Two doses of intravenous vancomycin, 1 g every 12 hours, were given before vancomycin was discontinued.

Results of laboratory studies were the following: leukocyte count 13.3/mm<sup>3</sup> (71% polymorphonuclear leukocytes, 18% bands) and normal hematocrit, platelet count, blood urea nitrogen and creatinine concentrations, and liver-associated enzymes.

A marker pen was used to track the rapid advance of erythema overnight from her anterior, inferior chin to the top of her breasts (Figure). The infectious disease service was consulted the next morning. When she was examined, her condition had improved; she had normal vital signs, a slightly hoarse voice, and the ability to swallow some saliva. She had no headache or meningismus. The chest erythema was receding. Oral examination demonstrated erythema and an abrasion in the posterior pharynx. Her tongue was not elevated and her uvula was midline. Anterior firm edema without crepitus extended from her chin to the mid-neck. Results of her examination were otherwise unremarkable. The infectious disease consultant recommended restarting a course of vancomycin and discontinuing clindamycin.

A follow-up CT scan with contrast demonstrated anterior cervical soft tissue edema and patent airway with surrounding abnormal thickness and soft tissue density. No abscess or clot was seen. Endoscopic examination in the ICU showed diffuse erythema and generalized supraglottic edema affecting mostly the epiglottis and arytenoids. Dental examination demonstrated no acute pathologic features. Blood cultures at our hospital yielded no growth, and throat culture was negative for group A streptococci.

The patient recovered without requiring intubation (Figure). On the day of discharge, a blood culture from the referring hospital's emergency department was reported to be positive for *Neisseria meningitidis*, serogroup Y. Immediate family members and the otolaryngologists who conducted the endoscopic examina-



Figure. Top: anterior and lateral views of patient on day 1 of receiving antimicrobial drugs, demonstrating neck erythema and edema. Bottom: anterior and lateral views of patient on day 8 of receiving antimicrobial drugs, demonstrating resolution of neck erythema and edema.

tion were given postexposure prophylaxis. The patient also received terminal prophylaxis. Results of a screening CH50 for terminal complement deficiency were normal.

This patient's condition is consistent with fulminant meningococcal supraglottitis. Supraglottitis implies involvement of the epiglottis and surrounding structures and is more commonly used to describe adult infection than is epiglottitis (1). Epiglottitis has become more common in adults than in children since the introduction of the *Haemophilus influenzae* type b vaccine. Other organisms responsible for epiglottitis in adults include *H. influenzae*, *H. parainfluenzae*, pneumococci, *Staphylococcus aureus*, and group A streptococci (2).

Despite its propensity to colonize the upper respiratory tract, *N. meningitidis* has rarely been identified as a cause of supraglottitis or other deep neck infections. Only 6 cases have been reported, the first in 1995 (3–8). Previously reported cases were equally apportioned by sex, and patients were 44 to 95 years of age (3–8).

Including our patient, 3 of 7 were diabetic (6,7). None showed evidence of meningitis or fulminant meningococemia, but all had fever, pharyngitis, and airway compromise. Five required airway intervention: 3 intubations and 2 urgent tracheostomies. Two received steroids (3,4), a 54-year-old man required urgent tracheostomy before receiving steroids, and a 60-year-old man's condition "deteriorated rapidly," but the report does not indicate the interval between receipt of steroids and intubation. Although steroids have been used, their benefit is unproven, and no controlled clinical trials have been conducted (9).

Blood cultures have been positive from all reported case-patients. Two isolates were typed as serogroup B, 4 as serogroup Y, and the serotype of 1 was unreported. Meningococcal strains causing supraglottitis appear to be more locally aggressive but cause less disseminated disease, possibly due to decreased tropism for endothelial cells (8).

To our knowledge, ours is the second case of meningococcal supraglot-

titis reported with severe neck edema and cellulitis; a 44-year-old woman in a prior review had features similar to our patient (8). An 81-year-old woman with diabetes was noted to have "reddish swelling" on the right side of the neck (7), but little was described beyond that. All 3 had serogroup Y infection. We wondered whether serogroup Y might have a propensity to cause cellulitis; however, a review of 10 cases of meningococcal cellulitis included patients with multiple serogroups: C (4 cases), B (2 cases), Y (2 cases), and unknown (2 cases) (10).

*N. meningitidis* may cause supraglottitis more frequently than is recognized (3). Timely drawing of blood cultures in relation to administration of antimicrobial drugs is most likely to identify this pathogen in this setting. Because of its public health implications and potential for rapid progression to airway compromise, *N. meningitidis* should be considered among the differential diagnoses of supraglottitis/epiglottitis.

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## *gyrA* Mutations in Fluoroquinolone-resistant *Clostridium difficile* PCR-027

**To the Editor:** *Clostridium difficile* is the most common cause of bacterial diarrhea in hospitalized patients (1). Antimicrobial drug therapy is the most important risk factor associated with the acquisition of *C. difficile*, and several antimicrobial agents including clindamycin, amoxicillin, and cephalosporins have been particularly associated with *C. difficile* infection (2). Acquisition of resistance to clindamycin is considered 1 mechanism whereby clonal strains emerge and predominate in healthcare environments (3). Historically, fluoroquinolone antimicrobial agents were considered low risk for *C. difficile*–

associated-disease; however, recent studies indicate a shift in the risk associated with their use (4). Furthermore, recent outbreaks in Canada and the United States have been associated with fluoroquinolone exposure (4).

Recently, several *C. difficile* outbreaks due to PCR ribotype 027 (PCR-027) and associated with increased disease severity and death have been reported worldwide (4). This strain type contains the genes for binary toxin and has an 18-bp deletion and a frameshift mutation in *tcdC* hypothesized to result in deregulated expression of toxins A and B. These strains produce 16× more toxin A and 23× more toxin B in vitro than toxinotype 0 strains (5). These isolates demonstrate universal high-level resistance to fluoroquinolones in contrast to that of PCR 027 isolates collected before 2001 (4).

We report the mechanism of fluoroquinolone resistance in a cluster (n = 5) of Irish PCR-027 *C. difficile* isolates that were characterized by using toxinotyping and 16–23S ribotyping. Amplification with PCR and sequencing was used to identify the binary toxin gene (*cdtB*) and an 18-bp deletion and a frameshift mutation at position 117 in the *tcdC* gene. Antimicrobial susceptibility to 5 fluoroquinolone antimicrobial drugs was determined with E-tests (AB-Biodisk, Solna, Sweden). The quinolone-resistance-determining region (QRDR) of *gyrA* and *gyrB* was amplified by PCR and characterized. The nucleotide sequence data for partial sequences of the *gyrA* gene were submitted to GenBank and assigned accession nos. DQ821481, DQ821482, DQ821483, and DQ821484.

PCR ribotyping profiles identified 1 cluster of *C. difficile* PCR-027 with clinical isolates that showed indistinguishable profiles to the control 027 strain. PCR identified the *cdtB*, an 18-bp deletion, and a frameshift mutation at position 117 in the *tcdC* gene in all 5 isolates. These strains were univer-

sally resistant to the fluoroquinolones tested (ofloxacin, ciprofloxacin, levofloxacin, moxifloxacin, and gatifloxacin, respectively, MIC >32 µg/mL [Table]). Control isolates were susceptible to moxifloxacin and gatifloxacin (MICs 0.3, 0.2 µg/mL, respectively); however, these strains had reduced susceptibility to levofloxacin (MIC 3 µg/mL) and were resistant to ciprofloxacin and ofloxacin (Table). Sequence analysis determined that all 5 PCR-027 isolates had a single transition mutation (C to T), resulting in the amino acid substitution Thr-82-Ile in *gyrA* (Table). No amino acid substitutions were found in the QRDR of *gyrB* (data not shown).

Mutations in the active site or the QRDR of DNA gyrase and topoisomerase IV have been associated with increased resistance to fluoroquinolones in several bacteria (6). This report identifies for the first time a mutation in *gyrA* that is associated with high-level resistance to fluoroquinolones in *C. difficile* PCR-027. In *Escherichia coli*, amino acid substitutions that occur at Ser-83 in *gyrA* have been associated with fluoroquinolone resistance (6). Thr-82 in *C. difficile* corresponds to Ser-83 in *E. coli*. Thr-to-Ile amino acid substitutions corresponding to Ser-83 have been associated with fluoroquinolone resistance in several bacteria, including *Pseudomonas aeruginosa*, *Enterobacter aerogenes*, *Campylobacter jejuni*, and *C. difficile* (6). Ackermann et al. described 2 mutations in *gyrA* that resulted in an amino acid substitution corresponding to codon 83 in *E. coli*. Thirteen of the 18 *C. difficile* isolates had the Thr-82-Ile substitution, and 1 strain had a Thr-82-Val substitution (7). Dridi et al. described this Thr-82-Ile GyrA substitution in 6 resistant *C. difficile* strains corresponding to 3 serogroups, H1, A9, and 1C (8).

Early studies investigating fluoroquinolone antimicrobial agents suggested that most *C. difficile* isolates were susceptible to these drugs.