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***Streptococcus agalactiae* in Relapsing Cellulitis**

TO THE EDITOR—We read with interest the report by Del Giudice et al. [1] about a case of relapsing erysipelas caused by *Streptococcus agalactiae*. Molecular analyses of the strains, which were isolated from skin and vaginal specimens during 2 episodes, revealed identical restriction patterns, leading the authors to suggest that vaginal carriage of *S. agalactiae* served as a reservoir for relapsing skin infection. Nevertheless, the detailed pathogenesis of relapsing cellulitis/erysipelas has not been fully elucidated. We report a case of fasciitis that was followed by 4 episodes of cellulitis, and we discuss an additional mechanism of recurrence.

A 38-year-old, previously healthy woman presented with fever, chills, and severe pain in the left leg. Clinical examination of the extremity revealed edematous erythema with pronounced tenderness. MRI delineated a fluid collection between the subcutaneous tissue and the fascia. Wide debridement was performed immediately, and intravenous antimicrobial treatment (amoxicillin-clavulanate, 2.2 g 3 times per day, plus clindamycin, 600 mg 3 times per day) was administered. Gram-positive cocci in chains were abundant throughout the tissue specimens, but they failed to grow on culture. Broad-spectrum PCR and blood culture results remained negative. The patient's subsequent clinical course was favorable, but lymphedema persisted at the infection site.

During the subsequent 2 years, cellulitis occurred in the same area 4 times (7, 15, 17, and 24 months after the occurrence of fasciitis). *S. agalactiae* grew in blood cultures during the first and fourth episodes of cellulitis and from a vaginal swab culture during the third episode of cellulitis. Extensive investigations, including echocardiography, gynecological, and immunological examinations, revealed neither the source of bacteremia nor evidence of primary or secondary immunosuppression. The infections resolved after 8–14 days of intravenous penicillin (plus aminoglycosides during 2 episodes). After the third episode, a 5-month prophylactic course of amoxicillin (750 mg 3 times per day) was initiated. Two months after completion of the amoxicillin regimen, the cellulitis relapsed. *SmaI* digestion of the strains isolated from the vagina (third episode) and blood (fourth episode), followed by PFGE, revealed identical restriction patterns. The patient is currently being treated with a second course of long-term oral prophylaxis.

Our case and the reported cases of relapsing cellulitis/erysipelas due to *S. agalactiae* involved a skin region affected by chronic lymphedema [1–3], which is strongly associated with recurrent streptococcal infection [4]. Lymphatic tissue alterations may lead to locally impaired immune responses and insufficient bacterial clearance. Therefore, spread from vaginal colonization may not be the only explanation for multiple relapses. In situ persistence of microorganisms in non-professional phagocytes can cause relapsing infection, as shown with *Staphylococcus aureus* [5, 6]. Furthermore, analyses of biopsy specimens obtained from persons with severe soft-tissue infection have revealed significant amounts of viable *Streptococcus pyogenes*, despite the administration of antibiotics, up to 14 days after disease onset [7]. Group B streptococci can interact with extracellular matrix components of eukaryotic cells and may invade fibroblasts and epithelial and endothelial cells [8]—find-

ings that could support our hypothesis of in situ persistence. This does not conflict with the results of the study by Del Giudice et al. [1], but it might contribute an additional possible mechanism in recurrent cellulitis/erysipelas. Intracellular persistence of viable group A streptococci in erysipelas is currently being analyzed at our center [9].

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Does the Nose Know? The Odiferous Diagnosis of *Clostridium difficile*- Associated Diarrhea

TO THE EDITOR—*Clostridium difficile*-associated diarrhea (CDAD) is a common and emerging problem in hospitals; patients present with clinical symptoms of leukocytosis and abdominal pain, and the disease is associated with significant morbidity and mortality [1]. Diagnosis relies on various modalities, including laboratory tests (e.g., tissue culture or ELISA), invasive procedures (e.g., colonoscopic examination) and, at times, clinical suspicion and response to empirical treatment [2]. An “urban legend” exists among nursing specialties that CDAD has a unique odor that would allow for olfactory diagnosis; however, this has never been scientifically tested. A majority of nurses interviewed in preparation for this study were quite confident in their ability to make a positive diagnosis of CDAD on the basis of olfactory examination.

Physician requests for stool analysis for *C. difficile* toxin were reviewed at 2 separate teaching hospitals in Dayton, Ohio, over a 6-month period. Nursing staff were interviewed, and a survey (including questions regarding nursing demographic data and specific stool-related data) was completed before stool test results were available. Nurses were included if they had the

“perceived” ability to diagnose CDAD by smell and were directly involved in the processing or examination of the patient’s stool. Nurses were excluded from the study if their patients were receiving empirical therapy with either metronidazole or oral vancomycin for >24 h. CDAD was diagnosed by standard testing in the hospital laboratory (i.e., by ELISA or tissue culture).

A total of 138 nursing staff surveys were completed. Sensitivity and specificity for the odiferous diagnosis of CDAD were 0.55 (95% CI, 0.33–0.77) and 0.83 (95% CI, 0.76–0.90), respectively. The positive predictive value and negative predictive value were 0.35 (95% CI, 0.19–0.52) and 0.92 (95% CI, 0.86–0.97), respectively. The overall accuracy of the nurses in diagnosing or excluding CDAD was 79%. Length of nursing experience did not impact the nurses’ ability to diagnose; however, stool quality (i.e., whether the stool was partially formed or formed) did impact the accuracy of the diagnosis.

This study suggests that nursing staff were able to exclude a diagnosis of CDAD with a high degree of confidence and accuracy. However, confirmation of the diagnosis on the basis of odor and stool quality was insensitive.

Results of this preliminary study, if confirmed, may have a broad impact on the approach to treatment of hospitalized patients who develop diarrhea. The odiferous characteristics associated with the stool of patients with CDAD may impact decisions regarding the initiation of empirical therapy (perhaps limiting the overuse of antibiotics, such as metronidazole), infection-control practices (limiting unnecessary patient isolation), and the necessity for stool testing for CDAD; moreover, these findings may possibly lead to new diagnostic modalities, such as an “electronic sniffer” [3].

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