PERSPECTIVE

LESS IS MORE

Balancing the Benefits and Risks of Empirical Antibiotics for Sinusitis
A Teachable Moment

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Story From the Front Lines

A man in his 70s with a history of rheumatoid arthritis being treated with infliximab presented to his primary care physician (PCP) with upper respiratory tract congestion of several days' duration. He was diagnosed as having acute rhinosinusitis and treated with cefdinir. Two days later, he developed diarrhea. After 24 hours of severe diarrhea, he discontinued taking the antibiotic, and the following day his physician prescribed the combination drug diphenoxylate hydrochloride/atropine sulfate (Lomotil; Pfizer Inc).

Five days after the initial visit, he arrived at the emergency department pale, hypotensive, and reporting an "uncountable number of episodes of diarrhea." He was aggressively treated for presumed *Clostridium difficile* infection (CDI) and was admitted in critical condition. On hospital day 2, he developed toxic megacolon and underwent small bowel resection and near-total colectomy. The patient subsequently developed multiorgan failure and required intubation, continuous venovenous hemofiltration (CVVH) and vasopressor support. Over the next week he returned to the operating room 3 more times for resection of terminal ileum, cholecystectomy, further washout, repacking, and sequential closure of his open abdomen.

Despite aggressive source control, the patient had persistent vasopressor and transfusion requirements, ongoing CVVH, and minimal improvement in mental status. Seventeen days after admission he was transitioned to comfort care, and he died shortly thereafter.

Teachable Moment

While it would be impossible to prove definitively that the administration of antibiotics in this case caused this patient's life-threatening CDI, best available evidence suggests that antibiotic exposure is an important risk factor for the development of CDI. A recent meta-analysis found that antibiotics increased the odds of community acquired CDI by a factor of 6.9.[1] Though this association was particularly pronounced with the use of clindamycin (odds ratio [OR], 20.4), it also showed increased risk (OR, 4.4) for the cephalosporins this patient received. Data are limited on how immunosuppression itself affects disease severity or progression in patients with CDI. Studies have not found an increased risk of CDI for patients taking infliximab.[2]

The important learning opportunity in this case comes from reflecting on the patient's initial diagnosis of acute rhinosinusitis and the PCP's decision to prescribe antibiotics. This is hardly an uncommon situation for PCPs and emergency medicine physicians. With an estimated 31 million cases annually in the United States, acute rhinosinusitis is one of the most common upper respiratory tract infections encountered in these settings.[3] However, epidemiologic data show that the vast majority of cases of acute rhinosinusitis are viral in nature.[3]

Therefore, the ability to differentiate bacterial from viral rhinosinusitis is paramount in providing effective and safe care. Clinical practice guidelines published in the *Journal of Otolaryngology–Head & Neck Surgery*[3] made the strong recommendation that acute bacterial rhinosinusitis should be diagnosed when maxillary tenderness in the face or teeth (especially unilateral) and purulent nasal secretions are present for more than 10 days or if symptoms worsen within 10 days after an initial improvement. However, even if the diagnosis of bacterial rhinosinusitis is made, observation without the use of antibiotics is an option for selected adults with mild illness and close follow-up.

A recent Cochrane review article evaluated 5 placebo-controlled studies including a total of 631 adult patients who had at least 2 symptoms of sinusitis lasting 7 to 30 days to gauge self-reported clinical failure at 1 to 2 weeks.[4] Overall, failure rates (defined as lack of full recovery or improvement at follow-up) were very low in both groups: 80% cured in the placebo group and 90% in the antibiotic group. The researchers found a number-needed-to-treat of 15 to prevent 1 treatment failure at follow-up. The study also found a number-needed-to-harm of 8, though the noted adverse effects identified were mild.

The essential difficulty with the present case lies in the application to an immunocompromised patient clinical guidelines designed for the general population. Current guidelines do not exist to guide the treatment of noninvasive rhinosinusitis in immunocompromised patients. A study of practice patterns among otolaryngologists[5] identifies wide variation in current management and reaches no conclusions with regard to standard care. Because this patient was taking infliximab, it is tempting for the PCP to think that the likelihood of bacterial sinusitis would be increased and thus want to empirically give antibiotics because the patient is "high risk." But it is clear that antibiotics have a benefit only when a bacterial infection is present and have no role in treating viral illness. The guidelines[3] and research[4] both suggest that antibiot-

ics should be reserved for patients who meet explicit criteria, including duration and severity of symptoms. They do not suggest a different approach for immunocompromised patients. And because the risks of unnecessary antibiotics are at least equally increased for those with immunosuppression, a reflexive lowering of the threshold for antibiotic use is not without its own risks. Thus, at this time, when no guidelines exist and viruses are still the most common cause of rhinosinusitis, the best approach for treating immunocompromised patients may still be conservative management with very close follow-up.

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