Hiding in clear sight: Complications of immunosuppressive therapies

Ota et al, on page 874 of this issue of the *Journal*, provide a clinical image and vignette of a woman with emphysematous cystitis and a psoas abscess. Genitourinary infections with *Escherichia coli* are well known to occasionally produce gas—especially, it seems, in people with diabetes. But I thought it valuable to publish these images to provide a reminder of this infectious complication, as well as to highlight the cloaking effect of pharmacologic immunosuppression.

The patient they describe was receiving corticosteroids for brain metastases and was thus likely receiving a high dose. She had experienced abdominal pain for 3 days before seeking medical attention, but the infectious process undoubtedly predated that. Despite receiving appropriate antibiotics for more than 3 weeks, she harbored an expanding psoas abscess that was heralded by fever after the antibiotics were discontinued. This scenario is of little surprise in an ill 69-year-old diabetic woman with metastatic cancer who was receiving high-dose corticosteroids. We have all been taught about and likely have witnessed the devastating effect of delayed diagnosis of abdominal infections in patients on high-dose steroids.

With the current explosion of new targeted therapies for systemic and organ-specific inflammatory diseases, it is hard to keep up with their names, not to mention their mechanisms of action and potential complications. Much attention has been given, highlighted by the requisite warnings in direct-to-consumer advertising, to the reactivation of tuberculosis, the occurrence of fungal infections, and the risk of malignancy in patients taking many of these drugs. The risk of cancer seems to have been overstated, at least for the anti-tumor necrosis factor (anti-TNF) agents, but there is no question that some new biologics carry a real risk of reactivating latent tuberculosis and even some viral infections. But I have seen a more common problem, one that is inadequately emphasized: the delayed diagnosis of deep-tissue infection due to a blunting of the signs of inflammation that would normally accompany the infection.

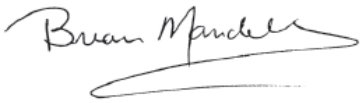
Anti-TNF therapies (eg, infliximab, etanercept, adalimumab) are being increasingly prescribed for the gamut of systemic and organ-specific inflammatory diseases, from sarcoidosis and rheumatoid arthritis to uveitis. I have no doubt that these agents suppress the inflammatory response in ways that can delay diagnosis. I have seen it happen in patients with diverticular abscess, bacterial pneumonia, epidural abscess, and bacterial septic arthritis, and I believe it is a more concerning clinical issue than any actual increase in the number of opportunistic infections.

The anti-interleukin 6 biologic agent tocilizumab, like the anti-TNF agents, not only blunts the inflammatory response and masks infection, but also seems to contribute to an increased occurrence of lower intestinal perforation.[1] This is potentially important, as it seems likely that indications for this agent will be expanded to diseases other than rheumatoid arthritis.

doi:10.3949/ccjm.83b.12016

Equal concern is likely warranted at the present time in patients receiving newer drugs such as Janus kinase (JAK) inhibitors and blockers of the interleukin 17 and 23 pathways, at least until more "real-life" patient experience is accumulated. Not all anti-inflammatory and immunosuppressive drugs have this dramatic blunting effect on findings of infection-associated inflammation (methotrexate seems not to), but we need to be wary and should perform extra-fastidious physical examinations followed by imaging studies when our patients complain of any localizing symptoms that are not readily and completely explained.

At the end of a tumultuous and divisive year, we at the *Journal* send to you, our readers, our heartfelt wishes for personal tranquility and for a universally peaceful and harmonious 2017.



BRIAN F. MANDELL, MD, PhD
Editor in Chief

1. **Strangfeld A, Richter A, Siegmund B, et al**. Risk for lower intestinal perforations in patients with rheumatoid arthritis treated with tocilizumab in comparison to treatment with other biologic or conventional synthetic DMARDs. Ann Rheum Dis 2016 Jul 12. pii: annrheumdis-2016-209773. doi: 10.1136/annrheumdis-2016-209773. [Epub ahead of print]