

# Letter to the Editor

## An Effusion of Blood and Phlegmon Secondary to Anakinra Injection

To the Editor:

A 52-year-old man with reported psoriatic arthritis treated with anakinra (100 mg administered subcutaneously every 24 hours) for one month presented with 2 black ulcerations, surrounding erythema, and induration on his right knee. He denied any fever. The patient received an escharectomy and one dose of oral levofloxacin (750 mg) without improvement. He was started on topical retapamulin ointment 1%, but cultures later showed no growth of bacteria. He was switched to methylprednisolone tablets with some improvement in erythema and induration but returned one week later with an increase in swelling. Upon aspiration, copious sanguineous purulence was removed (Figure 1). Cultures were again negative for bacteria growth. Magnetic resonance imaging of the bilateral thighs showed fluid or phlegmon within the subcutaneous tissue. Clinical findings represented an abscess or phlegmonous inflammation. There was no evidence of osteomyelitis. Over the following 3 weeks, a total of 26 mL of purulent material was aspirated from areas of fluctuance (Figure 2). Cultures were obtained and showed no growth of bacteria. Ultrasonography of the right knee showed the presence of a well-defined area of echo-free fluid collection in the subcutaneous region. The lesion measured 3.8×1.1×1.0 cm. The left thigh showed another small spot of fluid collection in front of the knee joint that measured 2.2×0.4×0.5 cm. There was no evidence of joint effusions in either side. The patient was started on potassium aminobenzoate and a topical emulsion, and was doing much better. The adverse reaction was reported to the manufacturer.

Anakinra is a recombinant methionyl human IL-1 receptor antagonist that competes for the IL-1 receptor with IL-1 and thus prevents IL-1 signaling. It is indicated for the reduction in signs and symptoms and slowing the progression of structural damage in moderately to severely active rheumatoid arthritis.<sup>1</sup> IL-1 also has been implicated in the pathogenesis of psoriatic arthritis because of increased levels measured in synovial fluid of patients with psoriatic arthritis compared to osteoarthritis,<sup>2</sup> which has led to the off-label use of anakinra in patients with psoriatic arthritis.

Safety studies on the use of anakinra for rheumatoid arthritis report that the most common adverse event leading to withdrawal is injection site reaction, most commonly erythema, ecchymosis, inflammation, and pain. It is the only side effect that appears to be closely related to the administration of anakinra.<sup>3</sup> More than 50% of patients using anakinra will develop injection site reactions, leading to cessation of the drug in 5%.<sup>4,5</sup> Other adverse events reported from anakinra safety studies in patients with rheumatoid arthritis include progression of disease; leukopenia; infection; and malignancy, most commonly squamous cell carcinoma, malignant melanoma, breast carcinoma, and malignant lymphoma. A decrease in neutrophils is attributable to the anti-inflammatory action of anakinra and likely increases the risk for infection. However, these adverse events are confounded by the additional risk factors inherent in patients with rheumatoid arthritis and a correlation to anakinra



**Figure 1.** Right knee (superior aspect) induration draining copious sanguineous purulence.



**Figure 2.** Left thigh fluctuance containing purulent material.

has yet to be determined.<sup>3,4</sup> In summary, we find this complication to anakinra noteworthy given the severity of the injection site reaction.

Sincerely,  
Arisa E. Ortiz, MD  
Cole M. Fulwider, MD  
Irvine, California

Jashin J. Wu, MD  
Los Angeles, California

The authors report no conflict of interest.

## REFERENCES

1. Jiang Y, Genant HK, Watt I, et al. A multicenter, double-blind, dose-ranging, randomized, placebo-controlled study of recombinant human interleukin-1 receptor antagonist in patients with rheumatoid arthritis: radiologic progression and correlation of Genant and Larsen scores. *Arthritis Rheum.* 2000;43:1001-1009.
2. Partsch G, Steiner G, Leeb BF, et al. Highly increased levels of tumor necrosis factor- $\alpha$  and other proinflammatory cytokines in psoriatic arthritis synovial fluid. *J Rheumatol.* 1997;24:518-523.
3. Nuki G, Bresnihan B, Bear MB, et al; European Group of Clinical Investigators. Long-term safety and maintenance of clinical improvement following treatment with anakinra (recombinant human interleukin-1 receptor antagonist) in patients with rheumatoid arthritis: extension phase of a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum.* 2002;46:2838-2846.
4. Fleischmann RM, Tesser J, Schiff MH, et al. Safety of extended treatment with anakinra in patients with rheumatoid arthritis. *Ann Rheum Dis.* 2006;65:1006-1012.
5. den Broeder AA, de Jong E, Franssen MJ, et al. Observational study on efficacy, safety, and drug survival of anakinra in rheumatoid arthritis patients in clinical practice. *Ann Rheum Dis.* 2006;65:760-762.