

diagnosis from reactive lymphoproliferative processes has been the subject of some controversy since its classification as a form of cutaneous lymphoma. The simultaneous appearance of this lesion in 2 sisters supports a reactive origin, given the possibility of exposure to similar environmental factors, as well as a possible influence of as-yet-unknown genetic factors.

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Adalimumab-Induced Neutropenia in a Man With Hidradenitis Suppurativa[☆]



Neutropenia inducida por adalimumab en un paciente con hidradenitis supurativa

To the Editor:

Anti-tumor necrosis factor (TNF) agents are among the drugs used to treat hidradenitis suppurativa. These treatments are generally well tolerated, but patients must be monitored closely when taking them. Hematologic complications are an uncommon adverse effect of anti-TNF therapy and have only rarely been described in the literature. We report a case of severe neutropenia (< 500/mm³) in a man with hidradenitis suppurativa. The complication developed within 3 months of his starting anti-TNF therapy.

Case Description

The patient was a 21-year-old man who had been diagnosed with hidradenitis suppurativa (Hurley stage 3) in adolescence. He had been treated with acitretin (50 mg/d), rifampicin (600 mg/d) combined with clindamycin (300 mg/d) and adjuvant intralesional corticosteroids (triamcinolone) in succession, without experiencing improvement. There were no other relevant aspects of his medical history; nor was he on other medications. Treatment with adalimumab began at an initial dose of 160 mg the first week, followed by 80 mg the second week and 40 mg every 2 weeks after that. The previous treatments with rifampicin and clindamycin were suspended 3 weeks before adalimumab was started, and the patient was taking no analgesics or other medications. Before treatment his white blood cell count was 5450/mm³ (neutrophils, 1980/mm³). Later blood tests showed gradually decreasing neutrophil counts, to 1540/mm³ at 1 month and 480/mm³ at 2 months after the first injection of adalimumab. Hemoglobin, red blood cell, lymphocyte, and platelet counts were normal, and no infections could be demonstrated during this period. The patient had no signs or symptoms of infection at any time, and serology for syphilis and human immunodeficiency

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virus, Epstein-Barr virus, parvovirus, and enterovirus infection were all negative, as they had been at the start of treatment.

Adalimumab was suspended 8 weeks after it was started, due to the neutropenia and because the skin lesions had only partially improved at that point. The neutrophil count quickly became normal and had reached 2760/mm³ a month after the last injection of adalimumab.

Discussion

A finding of fewer than 1500 neutrophils per cubic millimeter of blood defines neutropenia.¹ Mild neutropenia is defined by a neutrophil count of 1000–1500/mm³, moderate neutropenia by a count of 500–1000/mm³, and severe neutropenia by a count under 500/mm³.

Neutropenia is sometimes an adverse effect of medication and confers high risk of infection. An adverse drug effect can be established when there are no other concomitant medications being taken or other symptoms that could explain the event. The diagnosis is clear if the effect appears when a drug is introduced and resolves when it is withdrawn, as occurred in the case we report.

Neutropenia is a rare adverse effect of anti-TNF therapy. The agents most often implicated are infliximab and etanercept.^{2–5} The development of moderate neutropenia after exposure to etanercept, and successive recurrences after reexposure to the same agent and later exposure to infliximab have been described,⁶ suggesting that the adverse effect is related to anti-TNF agents as a group. Also described are cases of neutropenia induced by adalimumab in patients with rheumatoid arthritis.⁷ A systematic review of the literature describing hematologic complications of anti-TNF therapy found that the incidence of neutropenia was greater in patients treated with etanercept (72.8%), followed by infliximab (18.5%) and adalimumab (9%). Rajakulendran et al⁸ reported that neutropenia developed in 14.3% of their patients on anti-TNF therapy and Hastings et al⁹ reported an incidence of 18.8% in theirs; the agents implicated were adalimumab, infliximab, and etanercept.

When seriously low neutrophil counts (<500/mm³) are detected, treatment must be suspended and other secondary causes of neutropenia investigated. Possible causes include exposure to other drugs; infections (especially viral); nutritional deficiencies (folic acid or vitamin B₁₂); hematologic, congenital, or chronic diseases; systemic lupus erythematosus or other autoimmune diseases; and Felty syndrome. Serology for antineutrophil antibodies should be ordered.

Evidence suggests that the frequency of this adverse effect might be underestimated, so regular monitoring of leukocyte counts is recommended for patients on anti-TNF agents, whether alone or in combination with methotrexate or other drugs used routinely to treat rheumatoid arthritis and inflammatory bowel disease.¹⁰

As far as we know, this is the first case report of severe neutropenia due to the use of adalimumab to treat hidradenitis suppurativa. Dermatologists and other physicians who use adalimumab to manage this or other diseases should be aware of the possibility of the adverse event we report and the need for differential diagnosis.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

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