Letters to the Editor

Urticaria and angioedema in a patient with Behçet's disease treated with adalimumab

Sirs,

Tumor necrosis factor α blocking agents have been demonstrated as an important therapeutic approach in different chronic inflammatory diseases. Etanercept and infliximab are both considered to be immunogenic, and different immune-mediated skin reactions have been reported. Adalimumab, however, being fully humanised, was not thought to cause significant immune response. We report a case of urticaria and angioedema in a patient with Behçet's disease following the use of adalimumab.

Adalimumab, a fully humanised anti-tumor necrosis factor (TNF) α monoclonal antibody, was not expected to cause significant immune-mediated side effects. Yet, several skin reactions have already been attributed to this anti-TNF-α agent (1-4). We report a case of urticaria and angioedema after the use of adalimumab in a 31-year-old female who had Behçet's disease diagnosed in March 2002. She had presented with recurrent and painful oral and genital aphtae, together with widespread papulopustular lesions and left ankle pain without swelling. No other system was affected. Her past medical history was unremarkable. Laboratory tests showed no abnormalities, and ANA, ENA and rheumatoid factor were all negative. Pathergy and HLA-B51 were both absent. Several therapies were tried out, including colchicine, pentoxifylline, steroids and methotrexate. In spite of that, aphtae and skin lesions kept relapsing more and more frequently. Arthralgias reappeared asymmetrically in June 2005. The patient developed arthritis in her left ankle and cutaneous vasculitic lesions in both of her lower extremities two months later. A shift in therapy was then required, and she was started on adalimumab 40 mg subcutaneously every other week. The initial response was partial, with moderate improvement in her lesions. After the third dose, she noticed a pruritic, raised, erythematous, swollen plaque at the site of injection within a few hours. It improved with topical steroids. She developed multiple equal widespread lesions following the fourth injection. They all cleared without treatment. However, after the fifth injection, new circumscribed, elevated, erythematous and pruritic swollen cutaneous lesions reappeared all over her body. Likewise, swellings of lips, tongue and pharynx developed, resulting in sore throat and dysphagia. Urticaria with associated angioedema was thus suspected, and intravenous steroids and antihistamines were administered. Wheals disappeared within 24 hours, whereas oral and pharyngeal swellings took 36 hours longer to normalise. Laboratory investigations performed - including basic blood tests, thyroid profile, C1INH, C3 and C4 levels and parasite search in stool specimens - showed no abnormalities. The patient denied having used new drugs recently except adalimumab. Therefore, adalimumab was immediately discontinued, and doses of oral steroids and methotrexate were increased. No recurrence of the cutaneous reactions has been observed ever since.

TNF-α blocking agents have proved to be an important therapeutic approach in different chronic inflammatory diseases, such as rheumatoid arthritis, psoriasis, ankylosing spondylitis, and others. Etanercept, a recombinant fusion protein, and infliximab, a chimeric monoclonal antibody, are both considered to be immunogenic. Thus, different immune-mediated skin reactions have been reported, such as discoid lupus erythematosus-like eruption, necrotising vasculitis, leucocytoclastic vasculitis, psoriasis, granuloma annulare, and others (2, 3). On the other hand, adalimumab was not thought to cause significant immune response, since it is fully humanized. Nonetheless, injection site skin reactions due to adalimumab have been reported to occur in 1.5-11% of patients with rheumatoid arthritis. Furthermore, cases of erythema multiform-like skin reaction, psoriasis, urticaria and angioedema have been reported after its use (1-4). The mechanism of these cutaneous reactions has not yet been established, but an altered cellular immunity due to TNF-α blockade has been proposed (2, 3, 5). We report a case of urticaria and angioedema in a patient with Behçet's disease following the use of adalimumab. They both disappeared when the drug was stopped, and did not recur afterwards, even though the patient continued to receive the rest of her medication. Hence, in our opinion, these reactions can be easily attributed to adalimumab.

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