To the Editor:

We read with great interest the article by Mohan, et al., describing a series of 35 patients with leukocytoclastic vasculitis (LV) possibly related to tumor necrosis factor-α (TNF-α) blocking agents. The information is significant because a great number of patients presented unusual manifestations that were not observed during premarketing studies.

We would also like to describe a patient who presented some special manifestations that might complete the facts of the above series. At the same time, we would like to learn more about Mohan’s group of patients.

Our patient was a 60-year-old man with a 10-year history of seropositive and erosive rheumatoid arthritis (RA), who had been treated with gold salts and chloroquine, which were withdrawn because of inefficiency, and methotrexate, which was also withdrawn because the patient developed pulmonary fibrosis. In November 2002, because of the bad clinical evolution, etanercept 25 mg twice a week was added to his regular treatment of deflazacort 7.5 mg, calcium 500 mg, vitamin D 400 IU, and indomethacin 50–100 mg daily. At that time, laboratory examination showed antinuclear antibody (ANA) titer of 1/40; rheumatoid factor (RF) 315 IU/ml; negative dsDNA, anti-Sm, anti-SSA, and anti-SSB, and ribonucleoprotein RNP antibodies; and complement levels within normal limits. He improved markedly, but in July 2003 he developed a red rash on his legs, diagnosed as LV. His ANA titer was over 1/320, other immunological findings were normal, and RF was 320 IU/ml. His skin lesions disappeared when etanercept was decreased to once a week dosing and worsened when the dosing was increased to twice a week.

We believe that the clinical course of our patient adds interesting data to those presented by Mohan, et al. We would like to know if the TNF-α blocking agent in any patient in this series was not withdrawn. We also wonder which patients were taking leflunomide in combination with TNF-α blocking agent at the time that the LV appeared.

REFERENCES

Dr. Mohan replies

To the Editor:

In response to Juan, et al., review of available US Food and Drug Administration Adverse Events Reporting System data revealed there were 4 patients in the series that were reportedly continued on etanercept.

Correspondence
Outcomes regarding 2 of them are unknown. One patient improved on lowering the dosing to once a week and worsened again on increasing the dosage to twice a week. The other patient improved partially on discontinuation, but rechallenge one month later did not cause any worsening. Infliximab was continued in one patient with premedication with antihistamines and steroids, who was reported to be slowly improving. This suggests there may be more than one mechanism responsible for development of leukocytoclastic vasculitis (LV).

Three patients (2 on etanercept and one on infliximab) were taking concomitant leflunomide when they developed LV. One patient taking etanercept was not rechallenged, while the other had a positive rechallenge despite being on leflunomide. The patient on infliximab developed LV 4 days after the first infusion. The second infusion, which was due in 2 weeks, was held while awaiting resolution of the skin lesions. The next infusion was given 6 weeks after the first, and no recurrence of skin lesions was noted, indicating a negative rechallenge. This suggests that in these patients, leflunomide was not consistently effective against the development of drug-associated LV.

The response of Juan’s patient to leflunomide, however, adds to the possible list of interventions that one can attempt with a patient who has had a good therapeutic response to tumor necrosis factor (TNF) blockade but has unfortunately developed drug-associated LV. Other interventions include cautious rechallenge after resolution of skin lesions, premedication with antihistamines and corticosteroids, switching to another TNF blocking agent, and reducing the dosage.

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REFERENCES


Correction