In the last decades, tumor necrosis factor antagonists (anti-TNF-α) have demonstrated efficacy in the treatment of different chronic immune inflammatory disorders. Anti-TNF-α therapies seem to be safe and well-tolerated drugs, but with their increasing use and longer follow-up periods of treatment a new spectrum of adverse events, including some immune-mediated diseases, have been observed. Leukocytoclastic vasculitis, lupus-like syndrome, systemic lupus erythematosus and interstitial lung disease are the principal reported immune-mediated associated diseases, as well as paradoxical psoriasis formation. In the last 4 years, isolated cases of localized or extensive alopecia areata (AA) developing in patients under treatment with anti-TNF-α agents have been described.

**RESULTS**

Data about our five cases and the eleven reported in the literature are described in table 1. In summary, a third of the cases had a positive (personal or family) history of AA. Most of them presented with rapid extensive AA usually involving the ophasia area. Prognosis was usually poor, with slight response to treatments. In the cases where anti-TNF-α therapy was maintained, the course did not seem to change. 

**DISCUSSION**

The causality of anti-TNF-α agents in AA development is difficult to establish. Drug induced alopecia should be diagnosed if improvement of the alopecia occurs after cessation of the suspected drug, but only 2 out of the 7 cases in which anti-TNF-α therapy was discontinued showed improvement with complete regrowth of hair. In addition, considering the increased risk for autoimmune disease in these rheumatic patients, the possibility that the use of an anti-TNF-α drug and the development of AA might have been coincidental cannot be excluded. However, immune-mediated diseases induced by anti-TNF-α don’t follow the patterns of most adverse drug reactions and do not fit the classic criteria for adverse effect. A plausible hypothesis would be that TNF-α blocking switches off the primary disease inflammatory pathway but could move the unblocked proximal inflammatory response into an alternative signalling pathway. Depending on the individual genetic susceptibility, this pathway could clinically manifest as one or another immune-mediated disease states, for instance, psoriasiform paradoxical eruptions or AA.

In summary, our five cases in a short series of articular inflammatory diseases suggest that the incidence of AA might be higher than reported in this subgroup of patients. Considering that some cases had a personal or family history of AA, a complete personal and family medical history is suggested before starting an anti-TNF-α agent.

**REFERENCES**


