Dr. Brunasso and Dr. Massone reply

To the Editor:

Letter

We appreciate the comments by Nagashima and Minota regarding our report¹, but we would underline some aspects of it.

First, the association between rheumatoid arthritis (RA) and dermatomyositis (DM) in a single patient seems to be infrequent and the real incidence is unknown^{2,3}. The coincidence of myopathies and RA has been previously described in case series of patients - 7 cases of DM and RA, 16 cases of polymyositis (PM) and RA, and 15 cases of unspecified DM or PM associated with RA. However, no uniform criteria or detailed case records could be found regarding these cases and only 4 detailed case reports with clear overlap between RA and DM were found^{2,3}. It is important to consider that patients with DM may also have joint manifestations that can be misinterpreted as RA, even if these manifestations rarely proceed to joint deformity and destruction². Drug-induced myositis, usually associated with chronic use of corticosteroids and chloroquine in patients with RA, can be another pitfall that might lead to the incorrect diagnosis of overlapping RA and PM¹. So it is important to emphasize that there is no clear and confirmed relation between RA and DM, even if there is a significant increase in frequency of autoimmune diseases (including RA) in first-degree relatives of patients with idiopathic inflammatory myopathies^{2,3,4}. This association between many autoimmune diseases can be explained by the fact that many disorders share genes that together act as polygenic risk factors for autoimmunity⁴.

In our patient we did not immediately suspect the relationship between the onset of DM and the use of adalimumab because of the long period of intake (4.5 years) and that is why the drug was not promptly suspended and therapy with prednisone and methotrexate was added. But after 8 weeks the persistence of the very incapacitating symptoms led us to suspend the anti-TNF-α treatment, with improvement of the clinical picture and complete remission after 2 months. The causality between DM and adalimumab in our case can be described as not dose-related and time-delayed (typical for immunological adverse reactions), and the association can be classified as probable and not confirmed (because rechallenge was not performed), but a clear improvement after withdrawal was seen⁵. In addition to the above-noted cases of myopathies associated with anti-TNF-α therapies (2 cases of PM associated with infliximab, one case of axonal neuropathy associated with adalimumab, one case of interstitial myositis with demyelinating neuropathy associated with infliximab, and one case of necrotizing myositis associated with etanercept)2,6, Ishikawa, et al7 recently reported a women who, soon after initiation of etanercept for RA, developed PM, with prompt recovery after withdrawal of the anti-TNF-α agent; Harald, et al⁸ described one case of DM associated with etanercept therapy in 2006.

In the absence of clear evidence regarding the association between RA

and DM/PM and with the recently published cases of probable DM/PM induced by TNF- α -blocking agents, we believe that clinicians should be aware that autoimmune syndromes with cutaneous and systemic manifestations, including DM, may occur in patients receiving anti-TNF- α therapies. In cases in which autoimmunity is suspected, antinuclear antibodies and anti-DNA antibodies should be determined immediately and an accurate clinical examination should be performed prior to drug withdrawal.

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