

Dermatomyositis in Patients with Rheumatoid Arthritis During Adalimumab Therapy

To the Editor:

We read the recent letter by Brunasso, *et al*¹ with great interest. They reported that dermatomyositis (DM) developed after 4.5 years of adalimumab therapy in patients with rheumatoid arthritis (RA). We comment on development of myositis in patients with RA and whether it is actually related to anti-tumor necrosis factor (TNF) therapy.

An association of polymyositis (PM)/DM with RA has long been well known². RA can precede myositis, or it can develop after the diagnosis of PM/DM³. We previously reported 2 patients with RA who were not receiving anti-TNF therapy, but developed anti-Jo-1 antibody-positive PM and DM^{4,5}. In these 2 patients, onset of RA preceded that of DM or PM by 1 and 19 years, respectively, which suggests that PM/DM can develop at any time during the course of RA. Thus, it is possible that the patient described by Brunasso, *et al* may have developed DM incidentally, irrespective of adalimumab therapy.

TNF antagonists can induce autoantibodies and autoimmune diseases, especially vasculitis and lupus-like syndromes⁶. Antinuclear antibody becomes positive in a high percentage of patients, but most of them are asymptomatic, and the occurrence of autoimmune disease is rare. In a French national survey, the incidence of lupus syndrome was < 0.2%⁷, and lupus symptoms occurred within a mean of 9 months after subjects started infliximab and a mean of 4 months after they started etanercept. Another review of autoimmune diseases induced by anti-TNF therapy revealed that lupus-related symptoms appeared after a mean of 41 weeks⁶. Thus, the duration of adalimumab treatment (4.5 years) in the patient described by Brunasso, *et al* is quite atypical for anti-TNF-induced autoimmune disease. They also stated that there was no improvement after 6 weeks of treatment with prednisone and methotrexate, while DM improved after withdrawal of adalimumab. However, it requires longer than 6 weeks to assess whether or not treatment with corticosteroids and/or methotrexate will be effective for DM⁸.

Today, TNF antagonists are widely employed for the treatment of RA, as well as for inflammatory bowel disease (IBD), psoriasis, psoriatic arthritis, and ankylosing spondylitis. Lupus-like symptoms have been reported in patients with all of these diseases, but development of PM/DM is limited to patients with underlying RA. In general, IBD, psoriasis, and seronegative spondyloarthropathies are rarely associated with myositis compared to its occurrence in RA. If patients with these other diseases also developed myositis while receiving anti-TNF therapy, an influence of such therapy would be plausible. However, no cases have been reported to date.

We previously suggested that the occurrence of PM/DM in RA patients receiving anti-TNF therapy would increase along with the increasing use of anti-TNF therapy⁹, and such cases are actually increasing¹⁰. However, we must keep in mind that overlap of PM/DM with RA is not uncommon

and that PM/DM can develop at any stage of RA. Therefore, the association of PM/DM with anti-TNF therapy needs to be demonstrated by the detection of cases in patients without RA.

TAKAO NAGASHIMA, MD, PhD; SEIJI MINOTA, MD, PhD, Professor of Medicine, Division of Rheumatology and Clinical Immunology, Department of Medicine, Jichi Medical University, Yakushiji 3311-1, Shimotsuke, Tochigi, 329-0498, Japan.

Address correspondence to Dr. Nagashima; E-mail: naga4ma@jichi.ac.jp

REFERENCES

1. Brunasso AM, Scocco GL, Massone C. Dermatomyositis during adalimumab therapy for rheumatoid arthritis. *J Rheumatol* 2010;37:1549-50.
2. Martínez-Cordero E, León DE, Ortega LA. Association of polymyositis with rheumatoid arthritis. *Rheumatol Int* 2001;20:119-23.
3. Nagashima T, Sato H, Minota S. Destructive arthropathy associated with dermatomyositis sine myositis positive for anti-Jo-1 and anti-cyclic citrullinated peptide antibodies. *J Rheumatol* 2009;36:2133-4.
4. Nagashima T, Onishi S, Kamata Y, Minota S. Dermatomyositis associated with thyroid cancer: a paraneoplastic syndrome? *Rheumatol Int* 2009;29:1261-2.
5. Nagashima T, Iwamoto M, Minota S. Antisynthetase syndrome associated with long-standing rheumatoid arthritis. *Rheumatol Int* 2010 Mar 30. [Epub ahead of print]
6. Ramos-Casals M, Brito-Zeron P, Munoz S, Soria N, Galiana D, Bertolaccini L, et al. Autoimmune diseases induced by TNF-targeted therapies: analysis of 233 cases. *Medicine* 2007;86:242-51.
7. De Bandt M, Sibilia J, Le Loet X, Prouzeau S, Fautrel B, Marcelli C, et al. Systemic lupus erythematosus induced by anti-tumour necrosis factor alpha therapy: a French national survey. *Arthritis Res Ther* 2005;7:R545-51.
8. Callen JP. Immunomodulatory treatment for dermatomyositis. *Curr Allergy Asthma Rep* 2008;8:348-53.
9. Nagashima T, Minota S. Is polymyositis or dermatomyositis in patients with rheumatoid arthritis induced or unveiled by anti-tumor necrosis factor treatment? *Clin Rheumatol* 2010;29:819-20.
10. Klein R, Rosenbach M, Kim EJ, Kim B, Werth VP, Dunham J. Tumor necrosis factor inhibitor-associated dermatomyositis. *Arch Dermatol* 2010;146:780-4.

J Rheumatol 2011;38:3; doi:10.3899/jrheum.100947