

Graves' Disease, Rheumatoid Arthritis, and Anti-Tumor Necrosis Factor- $\alpha$  Therapy

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## Graves' Disease, Rheumatoid Arthritis, and Anti-Tumor Necrosis Factor- $\alpha$ Therapy

To the Editor:

We read with interest the letter by van Lieshout, *et al*<sup>1</sup>, describing a 70-year-old woman who developed Graves' disease while being treated with anti-tumor necrosis factor- $\alpha$  (anti-TNF- $\alpha$ ; adalimumab) for active rheumatoid arthritis (RA). They suggested an association of autoimmune thyroid disease with various autoimmune diseases including RA, but could not conclude whether there is a relationship between symptoms of Graves' disease and anti-TNF- $\alpha$ <sup>1</sup>.

We previously reported an association of Henoch-Schonlein purpura and Graves' disease<sup>2</sup>, but immunosuppression itself (e.g., cyclosporine) might also be a precipitating factor for the development of Graves' disease<sup>3</sup>. Hofle, *et al* had also showed that immunosuppressive therapy consisting of cyclosporin A and prednisolone could cause development of Graves' disease in a transplant recipient by abnormal modulation of the immune system<sup>4</sup>.

Although there are no extensive studies in patients with RA treated with anti-TNF- $\alpha$ , Allanore, *et al*<sup>5</sup> recently described a 37-year-old woman who developed transient hyperthyroidism while being treated with anti-TNF- $\alpha$  (etanercept) for active RA, and this case may be very similar to that described by van Lieshout *et al*<sup>1</sup>. Allanore, *et al* speculated that the production of (1) non-neutralizing antibodies directed against the etanercept molecule (16% of patients taking the drug), (2) anti-double-stranded DNA antibodies (15% of treated patients) or antinuclear antibodies (11%), and (3) anti-animal antibodies might cause an autoimmune reaction through cross-reactive immunogenicity to the thyroid gland, which seems to be very sensitive to autoimmunity.<sup>5</sup>

Therefore, careful thyroid-function monitoring would be necessary during immunosuppressive or anti-TNF- $\alpha$  therapy, and further studies

should be performed to elucidate the pathogenesis of Graves' disease in patients receiving anti-TNF- $\alpha$  therapy.

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