Graves' Disease, Rheumatoid Arthritis, and Anti-Tumor Necrosis Factor-α Therapy

To the Editor:

We read with interest the letter by van Lieshout, *et al*[1], describing a 70-year-old woman who developed Graves' disease while being treated with anti-tumor necrosis factor-α (anti-TNF-α; 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-α[1].

We previously reported an association of Henoch-Schonlein purpura and Graves' disease[2], but immunosuppression itself (e.g., cyclosporine) might also be a precipitating factor for the development of Graves' disease[3]. 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[4].

Although there are no extensive studies in patients with RA treated with anti-TNF-α, Allanore, *et al*[5] recently described a 37-year-old woman who developed transient hyperthyroidism while being treated with anti-TNF-α (etanercept) for active RA, and this case may be very similar to that described by van Lieshout *et al*[1]. 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.[5]

Therefore, careful thyroid-function monitoring would be necessary during immunosuppressive or anti-TNF-α therapy, and further studies should be performed to elucidate the pathogenesis of Graves' disease in patients receiving anti-TNF-α therapy.

JAE IL SHIN, MD; MIN JUNG KIM, MD; JAE SEUNG LEE, MD,
Department of Pediatrics, Yonsei University College of Medicine, Severance Children's Hospital, Seoul, Korea. Address reprint requests to Dr. J.S. Lee, Department of Pediatrics, Yonsei University College of Medicine, 250 Sungsan-Ro, Seodaemun-Ku, 120-752, CPO Box 8044, Seoul, Korea. E-mail: jsyonse@yuhs.ac

REFERENCES

1. van Lieshout AW, Creemers MC, Radstake TR, Elving LD, van Riel PL. Graves' disease in a patient with rheumatoid arthritis during treatment with anti-tumor necrosis factor-α [letter]. J Rheumatol 2008;35:938-9.
2. Shin JI, Park JM, Kim JH, et al. Association of Henoch-Schonlein purpura and Graves' disease. Nephrol Dial Transplant 2006;21:2997.
3. Shin JI, Park JM, Lee JS, Kim DH, Jeong HJ. Development of Graves' disease during cyclosporin treatment for severe Henoch-Schönlein nephritis. Nephrol Dial Transplant 2005;20:2014-5.
4. Hofle G, Moncayo R, Baldissera I, Pfister R, Finkenstedt G. Endocrine ophthalmopathy in a patient under continuous immunosuppressive therapy after cardiac transplantation. Thyroid 1995;5:477–80.
5. Allanore Y, Brémont C, Kahan A, Menkès CJ. Transient hyperthyroidism in a patient with rheumatoid arthritis treated by etanercept. Clin Exp Rheumatol 2001;19:356-7.

J Rheumatol 2009;36:2; doi:10.3899/jrheum.080725