CHEMOKINES CXCL9 AND CXCL11 ARE INVOLVED IN THE INITIAL AUTOIMMUNE RESPONSE OF AUTOIMMUNE THYROIDITIS

Antonelli A, Ferrari SM, Frascerra S, Di Domenicantonio A, Nicolini A, Ferrari P, Ferrannini E, Fallahi P. **Increase of circulating CXCL9 and CXCL11 associated with euthyroid or subclinically hypothyroid autoimmune thyroiditis.** J Clin Endocrinol Metab 2011;96:1859-63. Epub April 6, 2011.

SUMMARY

BACKGROUND

Chemokines induce chemotaxis of different leukocyte subtypes. In many inflammatory diseases, they recruit these leukocytes to settle at the site of injury. CXL10 is known to be inducible by interferon γ, as are CXL9 and CXL11. In a considerable percentage of patients, interferon γ therapy produces autoimmune thyroiditis, suggesting that these cytokines are playing a crucial role in the initial events of thyroid autoimmune disease and possibly also in the development of transient hyperthyroidism or hypothyroidism. They interact with one single receptor, CXCR3, that is expressed in some subgroups of T helper and T killer cells (1).

The role of one chemokine, CXL10, has been documented in thyroid cell cultures, and serum levels of CXCL10 have been shown to be increased in autoimmune thyroiditis. Moreover, in cultured thyroid cells, interferon γ and tumor necrosis factor a are able to induce other chemokines, such as CXCL9 and CXCL11. The aim of this study was to measure the blood levels of CXCL9 and CXCL11 in patients with autoimmune thyroiditis.

METHODS AND RESULTS

This study was performed in a single center, at which 141 consecutive patients with autoimmune thyroiditis were investigated; 81% of these patients had antithyroid peroxidase antibodies, 74% had antithyroglobulin antibodies, and 26% were subclinically hypothyroid. At ultrasound examination, hypoechogenicity was found in 82% and hypervascularization in only 39%. Two control groups consisted of patients with a normal thyroid or with multinodular goiter; all of these subjects had also undergone a complete thyroid workup. Any patient receiving drugs that might interfere with thyroid function was excluded.

The results for CXCL9 and CXCL11 are qualitatively very similar. The serum levels of both chemokines were increased in autoimmune thyroiditis above those found in the controls. They were higher in the presence of hypothyroidism and/or of a hypoechogenic gland. In addition, elderly patients had, in general, higher values than young patients. The difference was particularly marked in patients above 50 years of age as compared with patients below 50. It is interesting that even in the control groups there was a significant correlation between serum levels of chemokines and age.

CONCLUSIONS

CXC9 and CXL11 can now be added to the list of chemokines intimately involved in the initial immune response of autoimmune thyroiditis. When stimulated by interferon γ or other appropriate cytokines, thyrocytes from normal or pathologic specimens will respond with the production of chemokines. Obviously, some other cell types will respond similarly. The mechanism is therefore ubiquitous and not confined to the thyroid.

The authors do not propose a diagnostic value for the serum determinations of CXL9 and CXL11.

continued on next page

COMMENTARY

Another little piece is added to the mosaic pattern of the pathogenesis of autoimmune thyroiditis. It still does not answer the question of why the thyroid is so often affected by autoimmune processes. Also, one may argue that the process is not specific for the thyroid. It is possible that this frequently occurring and benign thyroid disease may help to elucidate the origin of autoimmunity in general.

—Albert G. Burger, MD

REFERENCE

1. Rotondi M, Chiovato L, Romagnan S, Serio M, Romagnani P. Role of chemokines in endocrine autoimmune diseases. Endocr Rev 2007; 28:492-520.