SUMMARY

Context: The mechanism of activation of the immune system after iodine-131 (\(^{131}\)I) treatment of hyperthyroidism is still not fully clarified. Serum levels of CXCL10, a prototype of the CXC family of chemokines, are increased in several endocrine autoimmune conditions, and this chemokine plays a role at least in the initial phase of thyroid autoimmune disease and in Graves’ disease (GD).

Objective, Design, and Patients: Aim was to measure CXCL10 serum levels in 20 patients with GD and 10 patients with toxic nodular goiter (TNG) before and 6 months after \(^{131}\)I treatment, when patients had achieved euthyroidism. Forty healthy subjects and 40 patients with autoimmune thyroiditis served as the control group.

Results: Before \(^{131}\)I, mean CXCL10 was significantly higher in patients with GD and thyroiditis than controls or those with TNG. Serum CXCL10 levels significantly decreased in GD patients 6 months after \(^{131}\)I treatment, whereas they remained within normal limits in TNG patients after restoration of euthyroidism by \(^{131}\)I.

Conclusions: The results demonstrate that high serum CXCL10 levels are associated with the hyperthyroid phase of GD but not with TNG, providing further evidence for a minimal role of hyperthyroidism \textit{per se} in determining high CXCL10 levels and showing a strong association with the autoimmune process. The reduction of CXCL10 levels after \(^{131}\)I treatment in GD only shows that the thyroid gland itself is the main source of CXCL10.

COMMENT

Chemokines are a group of low-molecular weight peptides that help recruit specific leukocyte subtypes to inflammation sites. More than 50 chemokines have presently been described, that are also known to play a role in angiogenesis, tumor growth, organ sclerosis, etc. Among the four main families of chemokines, the chemokines of the CXC family (CXCL9, CXCL10, CXCL11) are inducible by interferon-\(\gamma\) and are associated with Th1-mediated immune responses.

Present study aimed at investigating the IFN-\(\gamma\) inducible status in autoimmune and nonautoimmune hyperthyroidism after treatment with radioiodine. This issue has clinical interest since CXCL10 is thought to be involved in the initial phase of Graves’ ophthalmopathy (GO), when the inflammatory process is mainly regulated.
by the T-helper lymphocyte-1 immune pheno-type. Because radioiodine treatment has been associated with worsening of GO, variations in CXCL10 levels may be important to evaluate. The results showed that CXCL10 serum levels are increased in newly diagnosed GD patients. High levels of CXCL10 were associated with markers of inflammatory activity (such as hypo-echogenicity and hypervascularity on ultrasound) but not with thyroid autoantibodies. After $^{131}$I therapy, the high CXCL10 levels in GD patients normalized almost entirely, thus suggesting that thyrocyte destruction by $^{131}$I was responsible for the immunomodulation of the inflammatory process. In patients with hyperthyroidism due to TNG, initial CXCL10 levels were less elevated than in GD patients. Furthermore, there was little change in CXCL10 levels after $^{131}$I administration in patients with TNG, two arguments that are used to consider that hyperthyroidism per se does not play a major role to explain high CXCL10 levels. Finally, present results suggest that the main source of CXCL10 production resides within the thyroid gland and that the normalization of CXCL10 levels after $^{131}$I administration in GD patients resulted from cell destruction, hence removing a large part of intrathyroidal lymphocytes and/or the thyrocytes themselves. (Daniel Glinoer, M.D.; Ph.D.)

See Figure below

![Figure 1](image.png)