Incidence of postradioiodine immunogenic hyperthyroidism (Graves’ disease) in relation to a temporary increase in thyrotropin receptor antibodies after radioiodine therapy for autonomous thyroid disease.

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Summary

Background: Retrospective analysis of the incidence of postradioiodine (RI) immunogenic hyperthyroidism (i.e. Graves’ disease “GD”) in relation to a temporary increase in TSH-receptor antibodies (TRAb) without overt hyperthyroidism after RI therapy for autonomous thyroid disease.

Patients and Methods: A total of 1357 patients had undergone RI treatment for autonomous thyroid disease in the institution between 2000 and 2003. On pre-treatment evaluation, 565 patients (41.6%) had solitary autonomous toxic nodule (SATN), 693 patients (51.1%) a toxic multinodular goiter (TMNG), and 99 patients (7.3%) a diffuse thyroid disease (DISS). Ultrasound examinations and thyroid scintigraphy were performed before and after RI therapy. TRAb was measured using a sensitive assay with the human TSH receptor as antigen.

Results: Fifteen of 1357 patients (1.1%) developed post-RI hyperthyroidism between 1 and 13 months after RI treatment, with clinically overt hyperthyroidism and an elevation in TRAb titers. The breakdown among the patients was as follows: SATN: 8/565, 1.4%; TMNG: 6/693, 0.9%; DISS: 1/99, 1%). Patients with elevated TPO-Ab before RI therapy had an almost 10-fold higher risk of developing post-RI immunogenic hyperthyroidism (6/57; 10.5%). A total of 13 of 999 patients with TRAb measurements after RI therapy had increased titers of TRAb and, to some extent, of TPO-Ab without development of clinically overt hyperthyroidism.

Conclusions: There is an estimated 1.1% risk of a temporary increase of TSH receptor antibodies after RI therapy for autonomous thyroid disease without development of clinically overt hyperthyroidism.

Comment

When radioiodine (RI) is given for a solitary toxic adenoma or a multinodular toxic goiter, the treatment is aimed at destroying the autonomous follicular thyroid cells. These dying cells release many antigenic constituents and it is therefore understandable that a transient increase (or an onset) of thyroid autoimmunity may follow RI administration. Thus, RI treatment may lead to definitive hypothyroidism by irreversible destruction of thyroid tissue, autoimmune hypothyroidism by chronic autoimmune thyroiditis (perhaps enhanced by RI administration), and finally in rare instances to autoimmune hyperthyroidism by RI-related induction of antibodies to the TSH receptor with stimulating activity. The latter condition would logically be found more frequently when RI treatment has been given for toxic autonomous lesions (i.e. adenomas), since radioiodine
tends to destroy primarily the autonomous cells and not the ‘normal’ thyroid tissue which is usually functionally ‘dormant’. In present study, the authors showed that immunogenic hyperthyroidism (Graves’ disease) was present in 1.5% of the treated patients, with a clear-cut increase in TRAb titers and various degrees of hyperthyroidism, with abnormally elevated levels of serum free T4 and free T3 ranging up to 6.3 ng/dl and 2100 pg/dl, respectively. It is also logical that the frequency of these abnormality, induced – or aggravated – by RI administration, was significantly greater in the patients who presented already features of thyroid autoimmunity before the treatment. Finally, it should be remembered that similar cases of induced thyroid autoimmunity have also been reported in patients with differentiated thyroid cancer, who received RI therapy to ablate residual thyroid tissue or distant metastases, although such occurrence remains exceptional.

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See Figure below

**FIG. 1.** Development of postradiiodine immunogenic hyperthyroidism in a patient with unifocal thyroid autonomy. This patient developed postradiiodine immunogenic hyperthyroidism 3 months after radioiodine therapy for unifocal thyroid autonomy. The first scintigram with pertechnetate (top left) demonstrates focal uptake, which is confirmed by a post-therapy scintigram of iodine-131 (bottom left). Diffuse uptake into the thyroid is shown in a scintigram (top right), made 3 months after radioiodine therapy. At that time overt hyperthyroidism had developed and a second post-therapy scintigram of iodine-131 (bottom right) confirms this finding, this patient having received a second application of radioiodine.