CASE REPORT

Painful acute radiation thyroiditis induced by ^{131}I treatment of Graves' diseaseKinjal K Shah,¹ Valentina Tarasova,² Michael Davidian,³ Robert J Anderson¹¹Section of Endocrinology, Diabetes and Metabolism, VA Nebraska-Western Iowa Healthcare System, Omaha, Nebraska, USA²Division of Endocrinology, Creighton University Medical Center, Omaha, Nebraska, USA³Department of Internal Medicine, Creighton University Medical Center, Omaha, Nebraska, USA**Correspondence to**

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SUMMARY

A 44-year-old woman, chronic smoker with Graves' disease was treated with radioactive iodine ablation (RAI). One week after the treatment, she presented with severe pain in the anterior neck with radiation to the angle of the jaw associated with fatigue, tremor and odynophagia. Physical examination demonstrated an asymmetric and exquisitely tender thyroid gland. There was no laboratory evidence of thyrotoxicosis. Acute radiation thyroiditis was diagnosed. Non-steroidal anti-inflammatory drugs and hydrocodone-acetaminophen started initially were ineffective for pain control. Prednisone provided relief and was continued for 1 month with a tapering dose. Symptoms completely resolved after 1 month at which time the thyroid remained diffusely enlarged and non-tender. Three months following RAI ablation she developed hypothyroid symptoms. Levothyroxine was initiated. The patient has remained asymptomatic on continued follow-up care.

BACKGROUND

Radioactive iodine ablation (RAI) has been used for the treatment of Graves' hyperthyroidism since 1946 and it is the primary recommended modality of treatment for Graves' disease in the USA. Extensive clinical experience has reaffirmed its efficacy and safety. Permanent hypothyroidism is the inevitable complication of ^{131}I therapy on long-term follow-up. The most concerning side effect of this therapy is the development or worsening of the ophthalmopathy in up to one-third of patients treated with RAI, and reports have suggested that prophylaxis with corticosteroids is effective in preventing onset or preventing worsening of Graves' orbitopathy (GO), especially in patients with pre-existing GO.^{1 2} ^{131}I -induced radiation thyroiditis, which is an inflammation of the thyroid gland, occurs in 1–5% of patients with hyperthyroid, lasts for a few weeks, and is usually painless.^{3 4} Radiation thyroiditis usually occurs when a large dose of RAI is administered as in patients with thyroid cancer with large thyroid remnants or in toxic nodular goitre. However, the occurrence of radiation thyroiditis and its course after treatment in Graves' is not well documented in the literature and most of the sparsely available quantitative data are obtained from patients treated for post-thyroidectomy remnant ablation for thyroid cancer. This case presents a unique course of an extremely painful thyroiditis without evidence of thyrotoxicosis in a patient treated with ^{131}I for Graves' disease.

CASE PRESENTATION

A 44-year-old woman, chronic smoker was diagnosed with Graves' disease 4 years earlier. She started methimazole (MMI) and remained on a stable dose of 5 mg 6 days a week for 18 months. She then opted for RAI. Her only symptom was occasional fatigue. Physical examination was significant for a diffusely enlarged, non-tender, 30 g thyroid gland. Other treatment included oral propranolol 20 mg/day. On MMI her thyroid-stimulating hormone (TSH) was 0.38 $\mu\text{IU/mL}$ (ref: 0.4–5.1) and free T4 was 0.91 ng/dL (ref: 0.7–1.6). Thyroid-stimulating immunoglobulin was not obtained due to financial constraints. The test results would not have changed her management at that point. In preparation for the radioiodine therapy, she started a low-iodine diet for 2 weeks, and stopped MMI 7 days prior to the procedure. RAI uptake was 31% (ref: 5–15%) at 4 h and 46.5% (ref: 15–35%) at 24 h (figure 1A, B). Dosimetry to allow delivery of a tailored dose for ablation was not feasible. A fixed dose of 703 MBq (19 mCi) of ^{131}I was administered orally. A prophylactic corticosteroid course was not given because she did not have GO, and the potential for developing GO was very low ($\leq 6\%$) even with smoking as a risk factor.¹ She did not develop GO post-treatment. After 1 week, she developed severe pain in the anterior neck, more on the right side, with radiation to the angle of the jaw. She had fatigue, odynophagia and tremor, likely related to her anxiety. On examination, her temperature was 96.3°F, heart rate was 88/min and blood pressure was 118/92 mm Hg. Her anterior neck was asymmetric, swollen, warm and exquisitely tender. The thyroid was enlarged on the right side, firm and non-fluctuant. Painful radiation thyroiditis was considered on clinical examination. She was advised to take 5–500 mg of hydrocodone-acetaminophen with ibuprofen every 6 h. She also took propranolol 20 mg one tablet as needed. Thyroid function tests were planned and glucocorticoids were to be added if required. Two weeks later the patient had persistent neck pain.

INVESTIGATIONS

At this time, TSH was 0.65 $\mu\text{IU/mL}$ and free T4 was 1.40 ng/dL. Prednisone 40 mg/day was started which provided relief within 1 week. Thyroid ultrasound performed after the pain resolved revealed a normal size right lobe, probably associated with the response from prednisone treatment. Heterogeneous lobes with variable solid areas, normal blood flow and no discrete nodules were also noted consistent with the

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Figure 1 (A and B) Thyroid scan (pre-RAI ablation): anterior and right anterior oblique view respectively. Planar images of thyroid demonstrate a homogenous picture with no scintigraphic evidence of hot or cold nodules. RAI, radioactive iodine ablation.

effect of the radioiodine therapy (figure 2A, B). Table 1 summarises the clinical course.

TREATMENT

Prednisone 40 mg/day with tapering dose was continued for 1 month.

OUTCOME AND FOLLOW-UP

Her symptoms resolved completely after 1 month. The thyroid remained diffusely palpable but was non-tender. She had no orbital symptoms and no worsening after ^{131}I . Three months following RAI ablation, she developed hypothyroid symptoms with a TSH of 19.66 $\mu\text{IU/mL}$ and a free T4 of 0.48 ng/dL. She has remained asymptomatic on levothyroxine.

DISCUSSION

Graves' disease is the most common cause of hyperthyroidism. Treatment options include antithyroid drugs (ATD), thyroid surgery and radioiodine therapy. The first choice of treatment differs from country to country and is guided by physician and or patient preference. The long-term quality of life following treatment for Graves' disease was found to be same in patients randomly assigned to either of the three treatment modalities.²

The prevalence of radiation thyroiditis is 1–5% in patients treated with ^{131}I therapy for hyperthyroidism with a higher prevalence reported in patients receiving RAI therapy for post-operative thyroid remnant ablation in differentiated thyroid cancer. Manifestations start a few days after and usually within 2 weeks of ^{131}I therapy. The condition is accompanied by an acutely and variably enlarged thyroid gland, neck pain, thyroid

tenderness and dysphagia. Although most of the cases are asymptomatic, mild symptoms are often elicited on careful questioning.⁵ Our patient had a remarkable presentation with an exquisitely tender thyroid swelling.

The majority of these patients also have laboratory evidence of thyrotoxicosis. In the early period after ^{131}I therapy, a transient elevation of the thyroid hormone levels can be seen, probably due to release of stored hormone from the thyroid gland. However, the exacerbation of thyrotoxicosis following ^{131}I therapy is generally not encountered in patients with Graves' who are not pretreated with ATD or in patients who are overtly hyperthyroid.⁶ The thyroid hormone levels decline a few days after therapy. Also, thyroid storm occurs only rarely following the administration of radioactive iodine. The risk of a transient worsening of the thyrotoxicosis is apparently greater in toxic nodular goitre than in Graves' disease which would support that pool of stored thyroid hormone is lower in a high turnover gland, such as Graves' disease as compared with toxic and non-toxic nodular goitre.⁶ Our patient had a unique presentation where there was no laboratory evidence of thyrotoxicosis. It might be possible that the early transient thyrotoxicosis might have been missed as thyroid function tests were done 3 weeks post-RAI treatment.

The frequency of short-term worsening of thyrotoxicosis with RAI following pretreatment with ATD therapy is not known. However, ATD is often used in elderly and those patients with comorbidities.² Although there is a decrease in the intrathyroidal hormone stores with ATD, studies have found no protection from transient thyrotoxicosis, unless the ATD was resumed after the ^{131}I .⁶ If MMI is given as pretreatment, it is recommended to

Figure 2 (A and B) Thyroid ultrasound (1 month after symptoms): transverse thyroid view. Right thyroid 4.3×1.4×1.4 cm and left thyroid 3.2×1.4×1.5 cm. Diffuse heterogeneous echotexture with normal vascularity.

Table 1 Summary of the clinical course

Clinical course	1 month prior to RAI therapy	7 days prior to RAI therapy	RAI therapy	1 week post-RAI therapy	3 weeks post-RAI therapy	7 weeks post-RAI therapy	2 months post-RAI therapy	3 months post-RAI therapy	Post LT-4*	Recent
TSH†	1.44		0.38		0.65		1.87	19.66	2.92	1.88
Free T4‡	0.91				1.40		0.67	0.48	0.85	1.1
Free T3§							2.7	2.5		
MMI		Stopped								
Pain	None			Severe	Severe	None	None	None	None	None
NSAIDs				Started						
Prednisone					40 mg	Tapered and stopped				

*LT-4: levothyroxine.

†TSH ref: 0.4–5.1 μ IU/mL.

‡Free T4 ref: 0.7–1.6 ng/dL.

§Free T3 ref: 2.5–3.9 pg/dL.

MMI, methimazole; NSAIDs, non-steroidal anti-inflammatory drugs; RAI, radioactive iodine ablation; TSH, thyroid-stimulating hormone.

discontinue 3–5 days before the administration of radioactive iodine and restarted 3–7 days later, with tapered dosing over 4–6 weeks as thyroid function normalises.² In our patient, MMI was the started at the diagnosis of the Graves' disease as the initial treatment chosen by the patient and was continued for 2 years. MMI was stopped 7 days prior to RAI therapy.

The effect of the ¹³¹I therapy generally correlates with the administered dose taken up by the thyroid, but the dose–response relationship is not linear, and large interindividual variations exist. According to the American Thyroid Association guidelines,² sufficient radiation should be administered in a single dose typically between 370 and 555 MBq (10–15 mCi) to render the patient with Graves' disease hypothyroid. Clinically significant acute radiation thyroiditis is unlikely at radiation doses below 200 Gy (approx. 555 MBq) from ¹³¹I.⁷ Acute radiation thyroiditis is estimated to develop in an additional 5% of exposed persons for each 100 Gy increment above the 200 Gy

thresholds. Cherk *et al*⁸ noted an incidence of 21% in their study of postsurgical remnant ablation in differentiated thyroid carcinoma. They used doses of 1110 and 3700 MBq (30–100 mCi) with higher incidence of radiation thyroiditis occurring in patients receiving 3700 MBq.

Symptoms of radiation thyroiditis readily respond to nonsteroidal anti-inflammatory drugs and only 5% of cases require steroid therapy.⁸ This case presents a unique course of an extremely painful thyroiditis without evidence of thyrotoxicosis in a patient treated with ¹³¹I for Graves' disease.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Learning points

- ▶ Acute painful radiation thyroiditis after radioiodine treatment for hyperthyroidism of Graves' disease is uncommon.
- ▶ Radiation thyroiditis is frequent after larger doses of ¹³¹I treatment for postsurgical remnant ablation in patients with thyroid cancer, in which case it is mostly painless and associated with transient thyrotoxicosis.
- ▶ The usual episode involves mild tenderness that quickly responds to non-steroidal anti-inflammatory drugs.
- ▶ Rarely, steroid therapy is required for non-responding cases.

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