Suppurative Lymphadenitis after Radioactive Iodine Therapy for Graves' Disease: A Rare Complication?

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Established Facts

- Radioiodine (RAI) therapy for Graves' disease is generally well tolerated.
- RAI therapy can rarely cause radiation-induced thyroiditis, but this is self-limiting and localized to the thyroid gland.

Novel Insights

- Lymphadenitis can occur in association with RAI therapy for Graves' disease.
- This can progress to abscess formation requiring surgical drainage.

Keywords

Graves' disease · Hyperthyroidism · Lymphadenitis · Lymphadenopathy · Radioiodine therapy

Abstract

Background: Radioiodine (RAI) therapy for Graves' disease is a well-accepted and effective treatment with a good side effect profile. Short-term adverse effects can occasionally include radiation-induced thyroiditis. To my knowledge, cervical lymphadenitis associated with RAI therapy for Graves' disease has not been reported before. **Case Report:** A 38-year-old woman initially presented with uncontrolled thyrotoxicosis secondary to Graves' disease. She subsequently received RAI therapy for her condition. Within a week, she developed painful bilateral cervical lymphadenopathy that progressed to abscess formation requiring incision and drainage. No other causes (neoplastic or infective)

were found. Symptomatic treatment was instituted, and within 2 months the lymphadenitis resolved completely. **Discussion:** RAI therapy for Graves' disease can sometimes cause radiation-induced thyroiditis but associated cervical lymphadenopathy or lymphadenitis has not been described. This may represent a continuum of the proinflammatory state induced by RAI manifesting as a rare but potentially morbid complication.

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Introduction

The use of radioactive iodine or iodine-131 (I-131) in the treatment of Graves' disease is well described and has been shown to have good results with an acceptable side effect profile. Radiation-induced thyroiditis can occur in 1–5% of hyperthyroid patients and usually resolves on its

Table 1. Summary of thyroid function tests and inflammatory markers trends

	9 days before RAI	Just before RAI	1 week after RAI	2 weeks after RAI	5 weeks after RAI	9 weeks after RAI	14 weeks after RAI
Thyroid-stimulating hormone (TSH), mIU/L	<0.01	0.01	<0.01	<0.01	<0.01	<0.01	16.10
Free thyroxine (fT4), pmol/L	48	50	23	35	31	13	4
Free tri-iodothyronine (fT3), pmol/L	7.5	10.6	6.0	8.8	8.3	4.2	3.4
C-reactive protein (CRP), mg/L	310.6	110	82.9	160.2	4.9	–	3.6
White blood cell (WBC) count, $\times 10^9/L$	0.5	10	12.3	12.3	4.9	–	–
Neutrophil count, $\times 10^9/L$	0.01	5.14	9.94	10.37	3.17	–	–

Reference ranges were TSH: 0.45–4.50 mIU/L; fT4: 8–16 pmol/L; fT3: 3.5–6.0 pmol/L; CRP: 0.0–5.0 mg/L; WBC count: 4.0–9.6 $\times 10^9/L$; neutrophil count: 1.90–6.60 $\times 10^9/L$.

own. It usually manifests within 2 weeks of radioiodine (RAI) administration and can be painful but is more commonly painless [1–3]. Corticosteroids have been used in the treatment of radiation thyroiditis together with symptomatic treatment. To my knowledge, there are no other reports of painful cervical lymphadenopathy associated with RAI treatment of Graves' disease. This case thus presents a unique clinical progression and potential rare complication.

Case Report

A 38-year-old Chinese woman was first diagnosed with Graves' disease in 2012. She was prescribed carbimazole for about 2 years before defaulting. In 2018, she was seen as an outpatient for symptoms of thyrotoxicosis. Her thyroid function test showed a free thyroxine (fT4) level of 100 pmol/L and thyroid-stimulating hormone (TSH) level of <0.005 mIU/L. Her TSH receptor antibody (TRAb) level was 4.7 IU/L (0.0–1.7 IU/L). Carbimazole 30 mg every morning was commenced.

One month later, she was admitted for headache, fever with tachycardia of 132 beats/minute, loss of weight, and nausea/vomiting. Laboratory investigations (Table 1) showed thyrotoxicosis and marked leukopenia and neutropenia. There was no palpable goiter or cervical lymph nodes. She was managed for possible thyroid storm and started on lithium as an interim medication. Granulocyte-stimulating factor (G-CSF) was administered for carbimazole-induced agranulocytosis. Nine days after admission, she was given 30 mCi (1,140 Mbq) of I-131 as definitive treatment for Graves' disease. She was discharged well 2 days later.

She was readmitted 1 week after RAI administration with progressively worsening bilateral neck swelling and fever. Examination revealed bilateral tender lymphadenopathy, worse on the left. Oral cavity and nasoendoscopy examination were unremarkable. Fine-needle aspiration of the left cervical lymph node showed a predominantly neutrophilic infiltrate compatible with acute inflammation. Ultrasonography (USG) of the neck showed thyroiditis and cervical lymphadenopathy, with the largest node being 2.6 $\times$ 1.5 $\times$ 0.7 cm, with no suspicious features. A core biopsy of the

left lymph node returned as inflamed granulation tissue with abscess formation. C-reactive protein during this admission reached a high of 185 mg/L but her procalcitonin levels were not significantly raised at 0.58 μ g/L.

There was progressive enlargement of the nodes despite empirical antibiotic therapy. Computed tomography (CT) of the neck was thus performed, which showed extranodal abscesses at levels II and III, again worse on the left (Fig. 1). Empirical antibiotics (Co-amoxiclav) and analgesics were given, and incision and drainage of the left neck abscess was performed.

All microbiology cultures from the blood and lymph nodes (aerobic/anaerobic, fungal, *Mycobacterium*) were negative and tests for *Cytomegalovirus*, Epstein-Barr virus, melioidosis, toxoplasmosis, *Bartonella*, and human immunodeficiency virus were all negative as well. She was discharged 5 days later with outpatient dressings to the surgical wound.

At follow-up 2 months later, her neck swelling and lymphadenopathy had resolved completely and her thyroid function test showed signs of hypothyroidism. She was commenced on levothyroxine replacement.

Discussion

RAI therapy is well established as a definitive treatment for Graves' disease. The adverse effects of RAI are a result of changes in thyroid function and size, immunological function, and the consequences of extrathyroidal irradiation [4]. A transient increase in both proinflammatory and anti-inflammatory cytokines has been reported and patients can display biochemical evidence of thyrotoxicosis in the first 2 weeks after treatment.

Post-radioactive ablation thyroiditis has been reported, with an incidence rate quoted at around 1–5% of hyperthyroid cases treated with RAI [3, 5]. These patients can present within 2 weeks after ablation with anterior neck pain and tenderness, and sometimes fever. Biochemically, evidence of thyrotoxicosis can also occur

Fig. 1. Contrast-enhanced CT of the neck 3 weeks' post-RAI therapy showing features of nodal liquefaction and extrusion of the liquid components.

transiently in these patients, likely due to the release of hormones from glandular destruction. Resolution of symptoms is observed with nonsteroidal anti-inflammatory drugs and, in some cases, steroids.

Cervical lymphadenitis post-RAI therapy, particularly complicated by suppuration and abscess formation, has not been described in the literature thus far. A possible mechanism could be RAI-induced glandular destruction, coupled with a hyperactive autoimmune response, and leading to a proinflammatory state with byproducts spreading via lymphatics to the draining cervical lymph nodes. Given the paucity of data regarding this phenomenon, other more common concomitant pathologies giving rise to lymphadenitis (such as malignancies and infections) need to be excluded. The patient in this report had extensive workup in the form of biopsies and microbiological investigations to ensure this was not the case. Although a direct causative link to I-131 has not been proven, the temporal sequence and lack of other proven causes makes I-131 therapy the likely culprit. Another contributory factor that could lead to such an exuberant inflammatory response would be the administration of GCSF. Again, there are no data concerning the interaction between GCSF and RAI and its effects.

The radiation dose absorbed by the thyroid may also play a part. A threshold of 200 Gy has been quoted for the level below which the risk of symptomatic thyroiditis is unlikely, with a corresponding increase in the risk of radiation thyroiditis for subsequent 100-Gy increments [6]. Unfortunately, a direct correlation between the dose administered and the amount absorbed is hard to ascertain. The absorbed dose is affected by the administered dose, the thyroidal volume, and the uptake of thyroidal I-131.

Using the Society of Nuclear Medicine Procedure Guideline for Thyroid Uptake Measurement radiation dosimetry [7], 1,110 MBq of I-131 roughly translates to 399.6 Gy of absorbed radiation by the thyroid. This is, however, an estimate at best. Doses of 10–15 mCi (370–555 MBq) have been reported to be adequate [8]. However, improved remission rates have been reported with increased doses of 20–30 mCi (740–1,110 MBq) [9]. The patient in this case report received 1,110 MBq of I-131; this is on the higher end of the spectrum for Graves' disease and may have been a contributing factor to her clinical presentation.

This case report highlights a unique association of RAI therapy for Graves' disease with suppurative cervical lymphadenitis. This may be a rare complication that has not been reported as of yet. Patients with poorly controlled thyrotoxicosis receiving relatively high doses of RAI may be more susceptible, particularly after recent use of GCSF. In the absence of a concomitant infective cause, there may be a role here for treatment with steroids as with radiation thyroiditis.

Statement of Ethics

This case report complies with the guidelines for human studies and was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. The patient was lost to follow-up and remained uncontactable, so informed consent could not be obtained. The author's institution domain-specific review board deemed that no consent was required as no identifiable patient information was utilized and this was a single-subject case report.

Disclosure Statement

The author has no conflicts of interest to declare.

Funding Sources

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