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CASE REPORT

Thyroid Sarcoidosis as a Rare Explanation of Resistance to Radioactive Iodine in Graves' Disease

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ABSTRACT

Background: Sarcoidosis is a multiorgan idiopathic inflammatory disease that involves the thyroid gland in 1 to 4.6% of the cases.

Case report: We report a case of a 36-year-old man who was diagnosed with Graves' disease and initially treated with block and replace regimen followed by radioactive iodine (RAI), both of which were unsuccessful. The patient subsequently underwent an uncomplicated total thyroidectomy. Subsequent histological evaluation of the thyroid tissue demonstrated granulomatous inflammation consistent with a diagnosis of sarcoidosis. This was the index presentation of this diagnosis with no previous symptoms or clinical manifestations related to sarcoidosis.

Conclusion: Using this case as an example, we therefore conclude that relative resistance of Graves' thyrotoxicosis to treatment may be due to a novel underlying presentation of sarcoidosis.

Clinical significance: Sarcoidosis of the thyroid gland should be considered as part of the clinical differential diagnosis in cases of treatment-resistant thyrotoxicosis.

Keywords: Case report, Graves' disease, Sarcoidosis, Thyroidectomy.

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BACKGROUND

Sarcoidosis is a severe idiopathic inflammatory disease that is characterized by granuloma formation.[1] The disease is a multiorgan process, with pulmonary sarcoidosis the most common manifestation. Endocrine dysfunction is relatively common, with pituitary infiltration or hyperprolactinemia seen in up to a third of patients.[2] Less than 10% of patients have hypercalcemia and hypercalciuria, predominantly due to extrarenal hydroxylation of vitamin D to the biologically active 1,25-dihydroxyvitamin D.[1,2] Thyroid involvement is rare and is seen in 1 to 4.6% of cases.[1,3-5]

We present a case of apparently isolated thyroid sarcoidosis manifesting as a cause of treatment-resistant Graves' thyrotoxicosis. This rare presentation of sarcoidosis is discussed on the background of current available evidence.

CASE REPORT

A 36-year-old man presented to his general practitioner with tremors, sweating, and tachycardia. He was subsequently found to have Graves' thyrotoxicosis, with elevated thyroxine (T4), suppressed thyroid-stimulating hormone (TSH), and elevated thyroid receptor antibodies. He was referred to the specialist endocrinology clinic and prescribed a block and replace regimen with high-dose carbimazole. After 9 months, he had improved clinically but had developed mild thyroid eye disease requiring selenium treatment. Antithyroid treatment was withdrawn after 10 months. Despite a period of relative quiescence, the patient suffered a recurrence of thyrotoxicosis 6 months later. Carbimazole therapy was reintroduced. At this time, his TSH was <0.01, and free T4 17.8. Carbimazole was slowly tapered and he underwent RAI therapy.

One month after RAI, his symptoms had returned, and by his follow-up clinic appointment, he was profoundly thyrotoxic once more. Carbimazole was recommenced, and he was referred for consideration for surgery. He was referred to the endocrine surgery clinic, counseled, and subsequently underwent an uncomplicated total thyroidectomy. He was discharged on the first postoperative day with normal serum calcium (2.23 mmol/L). He was commenced on 150 µg of levothyroxine postoperatively.

Subsequent histological evaluation demonstrated diffuse noncaseating well-formed epithelioid granulomata (Fig. 1), consistent with a diagnosis of thyroid sarcoidosis. This was the index presentation for sarcoidosis

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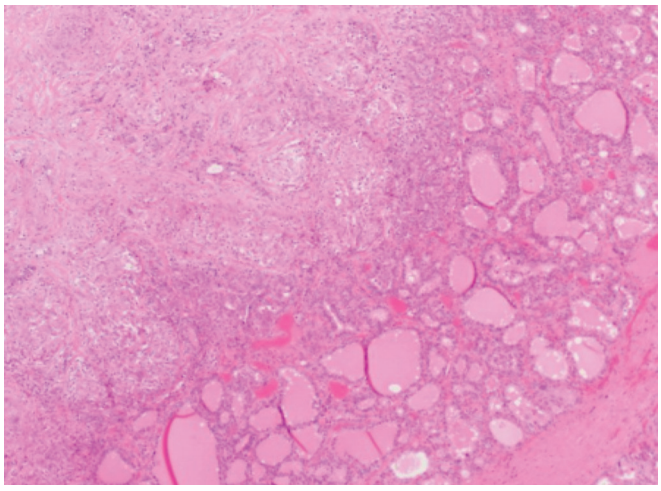

Fig. 1: A histology slide showing thyroid tissue with a well-defined, noncaseating epithelioid granuloma (×10 magnification)

in this patient, which was clinically confined to the thyroid gland.

DISCUSSION

Sarcoidosis has been reported in one study to have a statistical association with both clinical hypothyroidism, predominantly secondary hypothyroidism due to pituitary dysfunction. Both sarcoidosis and Graves' disease may be associated with higher levels of both TSH and antithyroid peroxidase antibodies.[2,6-8] An association between sarcoidosis and autoimmune thyroid disease has also been demonstrated in a literature review evaluating over 3,000 patients.[9] Thyroid involvement can take the form of a nontoxic multinodular goiter or nontoxic nodules, and in cases of sarcoidosis of the thyroid gland, fine-needle aspiration cytology is frequently nondiagnostic or unhelpful.[3,4,10] Moreover, a combination of goiter or dominant nodule with coexisting cervical lymphadenopathy can lead to thyroid sarcoidosis either mimicking, or concealing, thyroid malignancy.[11,12]

To the best of our knowledge, previous case reports of Graves' thyrotoxicosis exhibiting resistance to antithyroid treatment and RAI treatment, with a concomitant diagnosis of thyroid sarcoidosis, are rare.[12-14] In other reported cases, a preoperative demonstration of hilar lymphadenopathy with or without hepatosplenomegaly, allowed for a presumptive or confirmed diagnosis of sarcoidosis, prior to operative intervention.[12-14] The case presented here demonstrated no clinical or radiological features to suggest a preoperative diagnosis of sarcoidosis, with the diagnosis only made postoperatively following histological examination of the thyroid gland.

In one report, biochemical thyrotoxicosis only subsided following the introduction of steroid therapy, following failure of high-dose antithyroid drugs (ATDs) and two courses of RAI to achieve remission.[13] However, in this report, thyroid autoantibodies were negative and thyroid sarcoidosis was assumed, with no formal histological evaluation of thyroid tissue performed.[13] In our case, the patient had failed medical therapy with ATD, and displayed a negligible clinical response to RAI. A similar failure of ATD to control thyrotoxicosis over a period extending to 36 months prior to surgical intervention has also been reported in a patient with thyroid involvement by multiorgan sarcoidosis.[12]

Prolonged activation of proinflammatory effector cells, possibly via alternative pathways, has been postulated as a potential mechanism for the apparent resistance to ATD and RAI seen in these reports.[13] Reactivation or recurrence of sarcoidosis following RAI treatment for papillary thyroid cancer has been reported in isolated case reports, possibly due to alterations in immunological function, such as reductions in interleukin (IL)-4, IL-5, and IL-13.[15] The cellular mechanisms responsible for the apparent resistance of the thyroid to treatment are not yet clearly understood and may warrant further investigation.

CONCLUSION

Thyroid involvement in systemic sarcoidosis is a recognized but rare phenomenon, with several clinical manifestations. Relative resistance of Graves' thyrotoxicosis to treatment with ATD or RAI may suggest a novel underlying presentation of sarcoidosis.

CLINICAL SIGNIFICANCE

Sarcoidosis of the thyroid gland should be considered as part of the clinical differential diagnosis in cases of treatment-resistant thyrotoxicosis.

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