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To cite this article: Chukwuma O Ekpebegh FMCP, Ian L Ross FCP & Naomi S Levitt MD (2006) Hyperthyroidism—an unusual feature of thyroid carcinoma, Journal of Endocrinology, Metabolism and Diabetes of South Africa, 11:2, 80-83, DOI: [10.1080/22201009.2006.10872147](https://doi.org/10.1080/22201009.2006.10872147)

To link to this article: <http://dx.doi.org/10.1080/22201009.2006.10872147>



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Published online: 12 Aug 2014.



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Hyperthyroidism – an unusual feature of thyroid carcinoma



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A 53-year-old woman presented with thyrotoxicosis, which is an unusual manifestation of thyroid carcinoma. Hyperthyroidism associated with malignancy usually occurs with well-differentiated follicular thyroid carcinoma. We show that extensive disease burden contributed to the development of hyperthyroidism, the occurrence of the Jod-Basedow phenomenon and the subsequent death of the patient. This diagnosis and treatment can be challenging.

Case description

A 53-year-old woman presented with a painless swelling of the left parieto-occipital scalp region of 6 months' duration. Painless thyromegaly had been noted a month before presentation. Besides significant weight loss, there were no overt symptoms of thyrotoxicosis. There was no personal or family history of autoimmune disease, and prior head and neck irradiation was not elicited.

Examination revealed marked cachexia, sinus tachycardia of 105/min and a non-tender, soft left parieto-occipital scalp mass measuring 10 x 12 cm. She had moderate thyromegaly (30 g), which was hard in consistency, with a bruit and lymphadenopathy of the bilateral anterior triangles of the neck. There were no features of Graves' ophthalmopathy or dermopathy. An additional finding was left lower lung consolidation.

Thyroid function test results were consistent with frank primary hyperthyroidism: free thyroxine (FT₄) 46.3 pmol/l (normal 10.3 - 21.9 pmol/l) and thyrotropin (TSH) 0.01 IU/l (normal 0.35 - 4.5 IU/l). Anti-thyroglobulin and anti-thyroid peroxidase autoantibodies were negative. A Trucut biopsy of the scalp mass was performed. Histological review demonstrated well-formed thyroid follicles with occasional nuclear atypia and pleomorphism indicating metastatic follicular thyroid carcinoma. A whole-body technetium scan revealed uptake in multiple bony sites, liver, lung parenchyma and the rim of the scalp mass but minimal uptake in the thyroid gland. The patient had received Lugol's iodine for the control of hyperthyroidism prior to the technetium scan, which interfered with the interpretation of this investigation. A chest radiograph showed infiltrations in the left lung (Fig. 1), suggestive of metastasis. Computed tomography of the skull

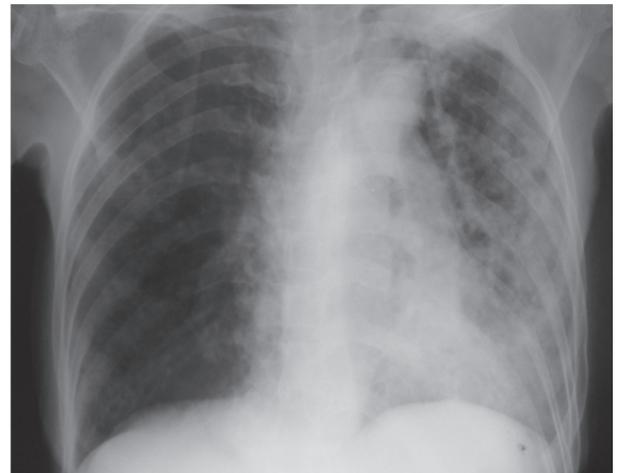


Fig. 1. Chest radiograph showing widespread infiltration in the left lung with minimal pleural effusion.

showed full-thickness erosion of the left parietal and occipital skull bones with intracranial extension of the scalp mass (Fig. 2).

The diagnosis of functional metastatic thyroid carcinoma was based on the finding of follicular carcinoma on histological examination of the scalp mass and hyperthyroidism.

Hospital course

We attempted to render the patient euthyroid to permit a safe total thyroidectomy. She was commenced on 40 mg daily of carbimazole and Lugol's iodine was initiated 6 hours after the first dose of carbimazole. A Jod-Basedow effect (induction or exacerbation of thyrotoxicosis following administration of iodine in the presence of a goitre and iodine deficiency) occurred within 5 days of commencing Lugol's iodine, with FT₄ levels surging from 46.3 pmol/l to 80 pmol/l. This response to Lugol's iodine was unexpected. In response to the dramatic

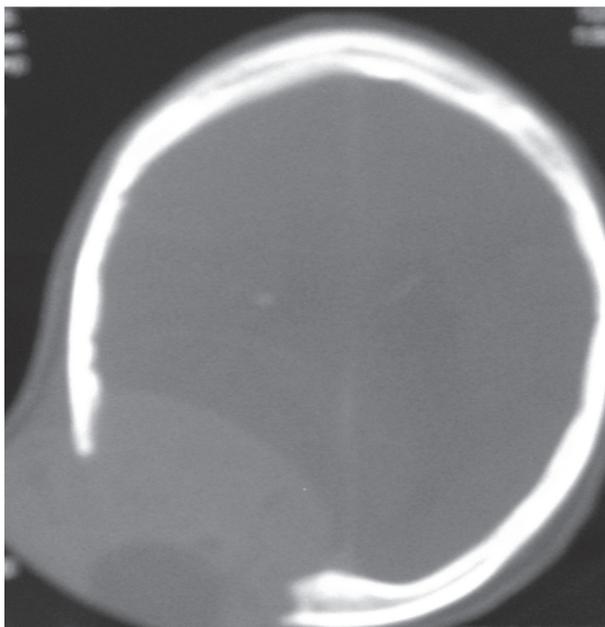


Fig. 2. CT scan showing erosion of left occipital and parietal skull bones with intracranial extension of scalp mass.

rise in FT_4 , Lugol's iodine was withdrawn and the dose of carbimazole escalated to 65 mg daily, which was well tolerated. As she remained biochemically thyrotoxic, despite the latter intervention, we administered dexamethasone 6 mg daily in divided doses, propranolol 60 mg daily, lithium carbonate 500 mg daily and cholestyramine 4 g daily. Iopodate, which is useful for rapid restoration of euthyroidism, was considered but is not available in our setting. Euthyroidism was achieved about 39 days after initial medical therapy and a total thyroidectomy was performed. An ablative dose of radioactive iodine was planned to eradicate thyroid bed remnants and metastases, but as she had received Lugol's iodine, this intervention was to be deferred. We anticipated performing surgery and external radiation to the skeletal metastases and finally lifelong T_4 therapy aimed at suppressing serum TSH levels to < 0.1 mIU/l to reduce disease recurrence. The patient died 14 days after total thyroidectomy, before administration of radioactive iodine and surgery to the scalp mass. We believe that the cause of death was related to extensive tumour burden manifesting with extra-thyroidal and in particular intracranial metastases.

Discussion

Thyrotoxicosis is an unusual manifestation of thyroid carcinoma. It typically occurs with differentiated thyroid carcinoma, as in our patient. A review of 924 cases of thyroid carcinoma reported 19 (2.1%) with thyrotoxicosis; 15 had follicular and 4 papillary carcinoma.¹ In a 20-year audit of 223 cases of thyroid carcinoma at this institution only 2 (0.9%) were toxic, both of whom had follicular thyroid carcinoma (I L Ross – unpublished observation, 2004).

The common causes of thyrotoxicosis in thyroid malignancy are coexisting Graves' disease, nodular goitre and thyroid carcinoma *per se*.^{1,2} The presence of the bruit over the thyroid gland, a characteristic feature of Graves' disease, was the sole suggestion of this latter diagnosis; however, as the thyroid gland was hard and craggy, this diagnosis was less likely. In addition the patient exhibited no associated ophthalmopathy, dermopathy or positive antithyroperoxidase and antithyroglobulin antibodies. Thyroid autoantibodies are, however, only positive in 75 - 80% of cases.³ The assay for TSH receptor antibody, which is a much more specific marker of Graves' disease, is not available in our setting. Graves' disease as a cause of thyrotoxicosis in metastatic thyroid carcinoma is remarkable because the TSH receptor antibodies resulting from autoimmune dysregulation still retain the ability to stimulate differentiated metastatic thyroid cancer cells after a total thyroidectomy.⁴ The presence of a bruit over the thyroid gland and its hard consistency also made the diagnosis of a toxic multinodular goiter highly unlikely.

Although functional thyroid metastases may cause low thyroidal iodine uptake^{5,6} the low uptake of technetium in our patient is confounded by prior treatment with Lugol's iodine. Follicular destruction of the thyroid gland by the malignant process may also result in diminished thyroidal technetium uptake. In one series of 48 cases of toxic thyroid carcinoma,⁷ large tumour bulk is the factor most consistently associated with toxicity. The multiple sites of technetium uptake in our patient not only suggest functional metastases but are indicative of large tumour burden.

Iopodate inhibits both thyroidal uptake of iodine and release of thyroid hormones, in addition to suppressing the conversion of FT_4 to free thyroxine (FT_3).⁸ It would have represented the treatment of choice, but its lack of availability in our setting precluded its use. Dexamethasone and propranolol suppress the conversion of FT_4 to FT_3 .^{9,10} Propranolol has the additional benefit of non-selective beta-receptor blockade.¹⁰ Lithium inhibits the release of thyroid hormone from the thyroid gland¹¹ and cholestyramine interferes with the enterohepatic circulation, of FT_4 and FT_3 .¹² Radioactive iodine therapy in the excessively thyrotoxic phase is not advisable, as mortality has been reported from further exacerbation of thyrotoxicosis.¹³ The occurrence of the Jod-Basedow effect shortly after starting Lugol's iodine was unexpected, despite prior carbimazole administration. Multiple metastatic sites competing for iodine probably precipitated this.

This patient's age of over 40 years, the large size of the primary tumour and extensive metastases, in particular intracranial metastases,^{14,15} conferred an extremely poor prognosis. Brain metastasis from

thyroid malignancy is not only unusual¹⁶ but extremely ominous.¹⁷

Conclusion

Thyrotoxicosis is an unusual manifestation of thyroid malignancy and usually occurs with differentiated follicular carcinoma. It is a recognised cause of thyrotoxicosis with low thyroidal uptake of iodine on nuclear uptake scanning. A large tumour burden is the single factor most commonly associated with thyrotoxicosis. The complexities in the management of toxic thyroid carcinoma have been highlighted in this very unusual clinical presentation.

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