Case Report
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Aggravated Orbitopathy Following Remnant Ablation in a Patient with Multiple Cancers

Çoklu Kanseri Olan Bir Hastada Kalıntı Ablasyonu Sonrası Ağırlaşmış Orbitopati

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Abstract

The rate of thyroid cancer in the patients with Graves' disease is controversial. The rare incidents of multiple primary thyroid cancers in the same patient have been reported. The coexistence of multiple primary thyroid cancers in patients with autoimmune thyroiditis is even rarer. The eye findings may worsen following radioactive iodine (RAI) therapy for thyrotoxicosis in Graves' disease. In this case report, we present a patient with Graves' disease with a pathological diagnosis of papillary thyroid cancer (PTC) and follicular thyroid cancer (FTC) having aggravated orbitopathy following remnant ablation.

A 53-year-old non-smoker female was diagnosed with Graves' disease and underwent total thyroidectomy after the eye findings became more evident two months after the initiation of an anti-thyroid drug. The patient was pathologically diagnosed as having an underlying 3-cm FTC and 3-mm PTC. Furthermore, the patient received 100 mCi of RAI under steroid cover for the remnant ablation. The patient did not comply with the glucocorticoid therapy and the eye findings were aggravated, thus requiring orbital decompression therapy.

The aggravation of orbitopathy can be observed following remnant ablation for thyroid cancer in patients with Graves' disease, and glucocorticoid prophylaxis may be considered in patients with active Graves' orbitopathy.

Keywords: Graves' disease; thyroid cancer; orbitopathy

Özet

Graves hastalığı olanlarda tiroid kanseri hızı tartışmalı bir durumdur. Aynı hastada çoklu birincil tiroid kanserlerin nadir insidansı olduğu raporlanmıştır. Otoimmun tiroiditi olan kişilerde çoklu birincil tiroid kanserin eş zamanlı görülmesi daha da ender karşılaşılan bir durumdur. Graves hastalığında izlenen tirotoksikoz için yapılan radyoaktif iyodin (RAI) tedavisini takiben göz bulguları kötüleşebilir. Bu olgu sunumunda papiller troid (PTC) ve folliküler troid kanserinin (FTC) patolojik olarak tanısını almış Graves hastalığı olan bir kişide kalıntı ablasyonu sonrasında ağırlaşan orbitopati raporlanmıştır.

53 yaşında sigara içmeyen kadın hasta Graves hastalığı tanısı almış ve antitroid ilaç başlanmasından iki ay sonra göz bulgularının ağırlaşması nedeniyle total troidektomi geçirmiştir. Hasta patolojik olarak 3 cm FTC ve 3 mm PTC olarak tanı almıştır. Kalıntı ablasyonu için steroid kılıf altında 100 mCi RAI uygulanmıştır. Glukokortikoid tedavisine uyum sağlayamamış ve göz bulguları ağırlaştığı için orbital dekompresyon tedavisi yapılmıştır.

Orbitopatinin ağırlaşması Graves hastalığı olan hastalarda troid kanseri için kalıntı ablasyonunu takiben izlenebilen bir durumdur. Glukokortikoid proflaksisi aktif Graves orbitopatisi olan kişilerde düşünülebilir.

Anahtar kelimeler: Graves hastalığı; troid kanseri; orbitopati

Introduction

The rate of thyroid cancer in the patients with Graves' disease is controversial. According to several studies, the rate of malignancy in thyroid nodules varies between 2.3% and 45.8% in patients with Graves' disease (1, 2). In a retrospective study, the rate of thyroid cancer was 5.4% even in the patients with no radiologically evident thyroid nodule (2). Papillary thyroid cancer (PTC) is typically observed in patients with Graves' disease (2, 3). In a study, the rate of follicular thyroid cancer (FTC) was reported to be 5% in patients with visible nodules and 4% in those without a visible nodule (3). Rare incidents of PTC and FTC in the same patient have been reported. The coexistence of multiple primary thyroid cancers in patients with autoimmune thyroiditis is even rarer. A case report has been presented regarding both follicular and papillary cancers in a patient with underlying Hashimoto's thyroiditis (4). The radioactive iodine (RAI) ther-

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apy for thyrotoxicosis in Graves' disease may aggravate the eye findings. In patients with active Graves' orbitopathy (GO), glucocorticoid prophylaxis is essential (5). In this case report, we present a patient with Graves' disease with a pathological diagnosis of PTC and FTC having aggravated orbitopathy following remnant ablation.

Case Report

A 53-year-old non-smoker female was referred to the Endocrinology Outpatient Clinic of our hospital with symptoms of retrobulbar pain. The TSH level of the patient was <0.05 (0.25-5.0 mIU/L) and FT4 was 67.3 pmol/L (10.6-19.4). At baseline, the visual acuity of the patient was normal and eye movements were nonpathological. The clinical activity score was 1/6. The TSH receptor antibody level was 44 U/L (>9 [+]). Thyroglobulin and thyroid peroxidase antibodies were negative. The thyroid ultrasound was compatible with thyroiditis with no visible thyroid nodule. Methimazole was initiated at a dose of 20 mg/day. The intensity of eye pain increased and periorbital edema developed two months after the initiation of the anti-thyroid drug. Total thyroidectomy was performed. Early postoperatively, eye symptoms were resolved and the clinical activity score was 0/6. The pathology report unexpectedly showed a 3-cm FTC and 3-mm PTC follicular variant in the left lobe together with lymphocytic thyroiditis despite no visible nodule was observed radiologically (Figure 1). The patient received 100 mCi RAI for remnant ablation following levothyroxine withdrawal, and glucocorticoid prophylaxis therapy was initiated. The TSH level of the patient before RAI therapy was 64 mIU/L. The post-RAI scan revealed a small focal uptake in the thyroid bed. The patient was recommended to receive 0.5 mg/kg of methylprednisolone from the day RAI was administered and the dose was tapered over 2-3 months together with levothyroxine suppression. Furthermore, the initiation of levothyroxine replacement therapy was recommended. The patient lost contact and did not comply with the glucocorticoid treatment. Thus, the patient was admitted with diplopia, bilateral exophthalmos, chemosis, periorbital edema, spontaneous retrobulbar pain, and pain on down gaze three months after RAI administration (Figures 2 and 3). The TSH level was suppressed to <0.05 mIU/L at the time of admission. Orbital MRI revealed bilateral diffuse thickening of the superior, lateral, and right medial and inferior rectus muscles and mild compression of the right optic nerve at the optic canal (Figures 4 and 5). In addition, the TSHR Ab titer was high (i.e., >100 U/L). The patient received 10 pulses of glucocorticoid therapy at a dose of 750 mg/week. As no response was detected for the glucocorticoid therapy, the patient underwent orbital decompression surgery and is still under our follow-up.

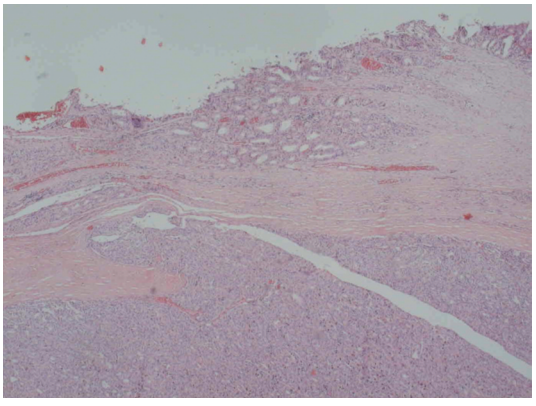

Figure 1a: The capsular invasion in follicular lesion at 10X magnification and H&E staining.

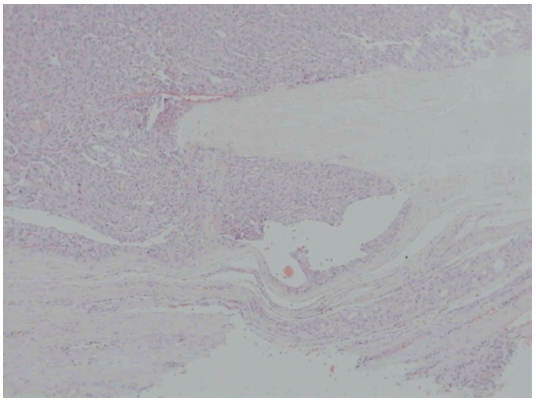

Figure 1b: The capsular invasion in follicular lesion at 20X magnification and H&E staining.

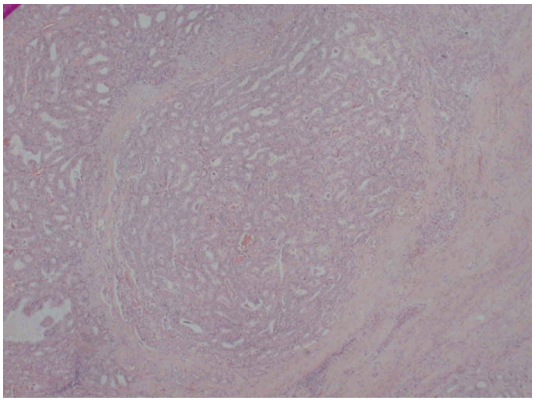

Figure 1c: Papillary microcarcinoma, follicular variant (x5 H&E Stain).

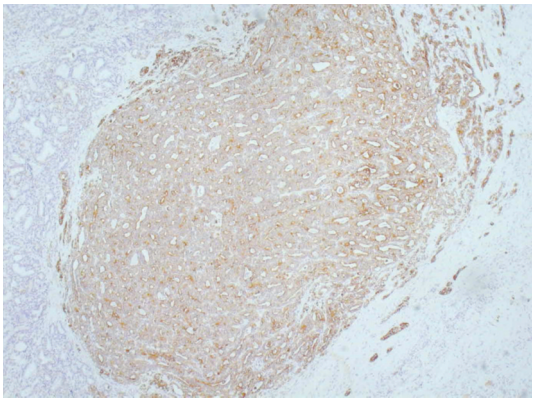

Figure 1d: Papillary microcarcinoma, follicular variant; tumor cells showing positive cytoplasmic immunohistochemical expression (x5CK19).

Discussion

Although occult micro-PTC is frequently observed in the thyroidectomy material of patients with Graves' disease, it was surprising to

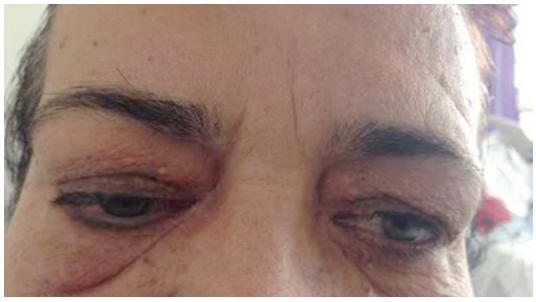

Figure 2a: The marked periorbital edema in both eyes.

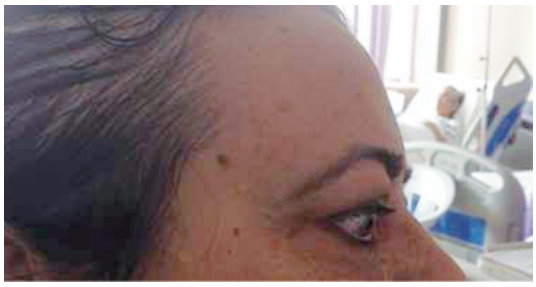

Figure 2b: Proptosis and down gaze of the right eye.

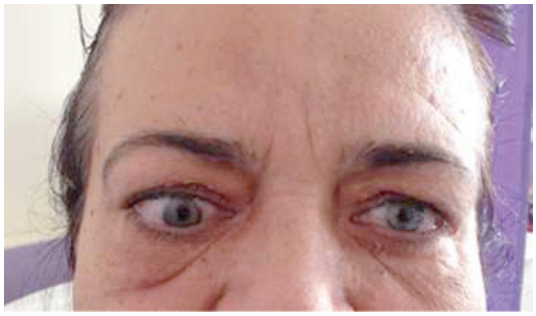

Figure 2c: Periorbital edema and strabismus.

visualize a 3-cm tumor pathologically but not radiologically. This can be explained by the heterogeneous parenchyma masking the tumor. In addition, many thyroid nodules are isoechoic on ultrasound. The FTC was of 3 cm that can usually fill a complete thyroid lobe. The isoechoic tumor may have been mistaken for the normal thyroid parenchyma by the analyst. According to a recent study, the rate of FTC was 4% in patients with Graves' disease without a radiologically visible nodule (3). In another study, thyroid cancer was visualized in 5.4% of patients with Graves' disease having no visible thyroid nodule (2). A study showed that the incidence of the tall cell variant of PTC was high in the patients with Graves' disease (6).

Multiple primary thyroid cancers in the same patient are a rare entity. In a study reported from China, 356 patients with thyroid cancer were retrospectively analyzed and 5 patients were found to have multiple primary cancers. In two patients, the dominant tumor was PTC with an occult FTC in the contralateral lobe, and in three patients, the dominant nodule was PTC in one lobe and occult Hurtle cell carcinoma in the contralateral lobe. The prognosis of these patients was similar to those with a single primary thyroid cancer (7).

The presence of multiple primary thyroid cancers in patients with underlying autoimmune thyroiditis is even rarer. Two case reports have been presented with underlying Hashimoto's thyroiditis. One of the patients had a combination of medullary thyroid cancer with PTC, whereas the other had PTC with FTC (4, 8).

RAI is frequently used for the treatment of thyrotoxicosis in patients with Graves' disease. In patients with active GO, glucocorticoid prophylaxis is provided to protect the patient from the aggravation of orbitopathy (5). The administration of RAI after surgery was found to be more effective in the treatment of GO than total thyroidectomy alone in patients receiving glucocorticoid therapy (9, 10). Some case studies have reported that GO is triggered after remnant ablation for underlying thyroid cancer (11, 12). In addition, rhTSH was used to stimulate TSH levels in the patients, whereas the authors argued that rhTSH could be a stimulant for GO. However, we used levothyroxine withdrawal to stimulate TSH.

The patient in this case report received 100 mCi of RAI for remnant ablation after diagnosed with thyroid cancer. In addition, the patient did not comply with the glucocorticoid therapy and returned to our department with severe GO with mild optic nerve compression, thus requiring decompression therapy.

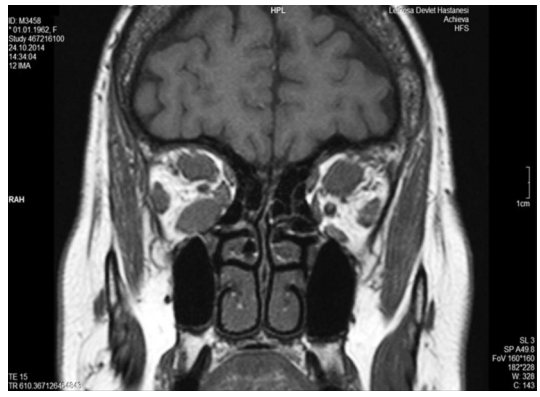

Figure 3a: Orbita MRI; coronal plane. Diffuse thickening of bilateral rectus muscles.

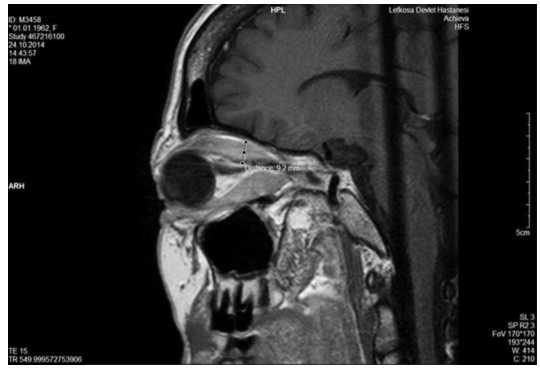

Figure 3b: Orbital MRG sagittal plane. Thickening of superior rectus muscle.

Therefore, aggravation of orbitopathy can be observed following remnant ablation for thyroid cancer in patients with Graves' disease, and glucocorticoid prophylaxis may be considered in patients with active GO.

Author Contributions

Concept: Umut Mousa, Design: Umut Mousa, Data Collection or Processing: Sebnem Aydin, Analysis or Interpretation: Hasan Sav, Literature Search: Osman Koseoglulari; Writing: Umut Mousa.

Conflict of Interest: No conflict of interest was declared by the authors.

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The written informed consent was obtained from the patient.

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