Case Report: A Patient with Severe Graves’ Ophthalmopathy and Follicular Carcinoma

Olgun Sunumu: Ciddi Graves Oftalmopatisi ve Folliküler Karsinoma

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Abstract
Graves' disease is the most common form of thyrotoxicosis and may occur at any age, more commonly in females. It is currently viewed as an autoimmune disease of unknown cause. Thyroid carcinoma is a relatively rare tumor, but it represents the most frequent form of cancer of the endocrine glands. The coexistence of hyperthyroidism and thyroid cancer is considered a rare event. In the present case report we describe an unusual patient with severe Graves' ophthalmopathy and after total thyroidectomy histological examination revealed the presence of follicular carcinoma. Turk Jem 2007; 11: 101-4

Key words: Graves ophthalmopathy, follicular carcinoma

Özet

Anahtar kelimeler: Graves oftalmopatisi, folliküler karsinom

Introduction
Graves' disease is the most common form of thyrotoxicosis and may occur at any age, more commonly in females. It is characterized by diffuse goiter, thyrotoxicosis, infiltrative orbitopathy, and occasionally infiltrative dermopathy. It is currently viewed as an autoimmune disease of unknown cause. Graves’ ophthalmopathy is clinically apparent in 10-25% of patients if eyelid changes are excluded, 30-45% of patients if eyelid changes are included[1]. It usually consists of chemosis, conjunctivitis, and mild proptosis. More severe lymphocytic infiltration of the eye muscles occur in 5-10% and may produce exophthalmos and sometimes diplopia due to extraocular muscle entrapment[2, 3]. The optic nerve may be compressed in severe cases. The severity of the eye disease is not closely correlated with the severity of the thyrotoxicosis.

Thyroid carcinoma is a relatively rare tumor, but it represents the most frequent form of cancer of the endocrine glands. Epidemiologically ascertained risk factors are ionising radiation, the presence of thyroid adenoma and multinodular goiter. The coexistence of hyperthyroidism and thyroid cancer is considered a rare event. Thyroid cancer was detected in 2-6% of patients after surgical treatment for hyperthyroidism[4-6]. In the present case report we described an unusual patient with severe Graves' ophthalmopathy and after total thyroidectomy histological examination revealed the presence of follicular carcinoma. This is the first report, to our knowledge, of this unique presentation in a patient with thyroid follicular carcinoma.

Case Report
The patient, a 47-year-old woman, presented to our medical center with a history of excessive sweating, palpitation, protru-
sion of the eyes and weight loss. Her past medical history had developed 4 months prior to our hospital admission. At that time she had been diagnosed as toxic diffuse multinodular goiter. Antithyroid treatment had been suggested. One month later pain and redness on the eyes had started. After the progression of the eye signs and also beginning of the vision loss, the patient admitted to our medical center and hospitalized as Graves’ ophthalmopathy in our clinic.

On physical examination, body temperature was 37°C, pulse rate was 102 beats/ min, blood pressure was 120/70 mmHg. The skin was warm and sweaty. Eyes had bilateral extremely exophthalmic appearance and also swelling and congestion of the conjunctivas were present (Picture 1). The right eye was measured as 38 mm and left eye was measured as 32 mm by Hertel exophthalmometer. According to NO SPECS she had severe ophthalmopathy. Mourits activity score was evaluated as 6. Thyroid gland was diffuse palpable and on right lobe a nodule 2x1 cm in diameter was palpated. On cardiovascular examination the heart rate was rhythmic and tachycardic.

The blood chemistry and total blood count were unremarkable. Thyroid function tests and thyroid autoantibodies were as follows: TSH: 0.03 (normal range, 0.4-4.0 uIU/mL), FT3: 1.12 (normal range, 0.9-2.5 pg/mL), FT4: 0.74 (normal range, 0.6-2.1 ng/dL); anti TPO: 30.2 (normal range, 0-10 IU/mL), anti Tg: 34.26 (normal range, 0-10 IU/mL), TSH-R Ab: 35 (normal range, 0-10 U/L) and thyroglobulin 206.7 (normal range, 0-25 ng/mL). On the ultrasonographic examination of the thyroid gland the paranchyme was heterogeneous and in the right lobe 28x23 mm in diameter, heterogeneous, hyperechogenic solitary dominant nodule and in the left lobe 8x5mm in diameter isoechogenic, 7x5 mm hyperechogenic nodule were detected. US-guided fine-needle aspiration biopsy was performed from the dominant nodule and the cytological examination was benign. Thyroid scintiscan was evaluated as toxic diffuse multinodular goiter. The nodules were evaluated as cold nodules. Computed tomography scan of orbita demonstrated bilateral anterior bulging of bulbus oculi clearly and bilateral enlargement of medial, inferior and superior rectus muscles and also swelling of the optic nerve. In addition to antithyroid and beta blocker, for severe ophthalmopathy intravenous pulse therapy with high doses of methylprednisolone as 500 mg tapered in 24 weeks duration, diuretic treatment as spironolactone 200 mgr/bid, and octreotide LAR 30 mg 21-d intervals were administered. Also artificial tears as eyedrops, eye patches, artificial tear ointments and autogenous serum were applied to the eyes. In order to produce much more quick results, orbital decompression surgery by transsphenoidal route was performed. After medical and surgical treatments, one month later the patient could close right eyelid completely and left eyelid more than fifty percent. Once stabilized and became euthyroid, the patient underwent total thyroidectomy. In spite of surgical specimens of dominant nodule was evaluated as benign, one of the smaller nodules of gland was evaluated as follicular carcinoma (Picture 2). After regression of the eye signs 125 mCi radioactive iodine therapy was applied. No metastasis was detected. Three months later, she could close both eyelids completely and sight improvement occurred (Picture 3). The right eye was measured as 28 mm and left eye was measured as 25 mm by Hertel exophthalmometer.

The patient gave an informed consented for this case report.

Discussion

The common causes of hyperthyroidism and thyroid cancer are extremely variable. In the past it was believed that hyperthyroidism was due to an increase in thyroid hormone production by the thyroid gland caused by the presence of an autonomous thyroid tissue that was capable of producing hormones independently of the pituitary gland. In recent years, it has been recognized that hyperthyroidism may also be caused by an autoimmune disorder, Hashimoto’s thyroiditis, in which the immune system mistakenly attacks the thyroid gland and causes it to overproduce thyroid hormones. Additionally, hyperthyroidism can be caused by other conditions such as pregnancy, hyperparathyroidism, and certain medications.

In contrast, thyroid cancer is a rare condition that can occur anywhere in the thyroid gland. It is typically caused by a genetic mutation that leads to an uncontrolled growth of thyroid cells. The most common type of thyroid cancer is papillary thyroid cancer, which is usually treated with surgery, radioactive iodine therapy, and thyroid hormone replacement. Other types of thyroid cancer, such as follicular thyroid cancer and medullary thyroid cancer, may require additional treatment depending on the stage and location of the cancer.

In conclusion, hyperthyroidism and thyroid cancer are distinct conditions with different causes and treatments. Hyperthyroidism is typically caused by an increase in thyroid hormone production, while thyroid cancer is caused by a genetic mutation that leads to uncontrolled growth of thyroid cells. Understanding the underlying causes of these conditions is crucial for effective diagnosis and treatment.
roidism excluded thyroid malignancy, with only rare cases being reported[7-10]. First two cases reported by Leiter and Seldin in 1948[7]. Different frequencies of concurrent hyperthyroidism and thyroid carcinoma had been reported[11-14]. Thyroid cancer was detected in 2-6% of patients after surgical treatment for hyperthyroidism[4-6]. The frequency of thyroid carcinoma in patients with Graves' disease was 2.5 fold greater than in those with toxic adenoma[15]. Belfiore et al. had reported that thyroid carcinoma associated with Graves' disease had an aggressive course[16]. Sokal found out that in 10,839 patients treated for Graves' disease there was an incidence of 0.06% of thyroid carcinoma, the incidence was 0.75% in 2,782 patients treated for uni- or multinodular goiter[11]. Reiger et al. had studied on 1848 patients who went on thyroid operation due to hyperthyroidism, among those 1848 patients (410.76%) had a coexisting thyroid malignancy[17]. The number of patients with multinodular goiter and malignancy was 111 (6.33%), in contrast it was 310 (27%) in patients with uninodular toxic goiter, also in this study no carcinoma was detected in patients with Graves' disease[17]. The pathologic types of carcinomas were papillary carcinoma in five patients, follicular carcinoma in four patients, anaplastic carcinoma in three patients and medullary carcinoma in two patients[17]. In our patient pathological examination of the one of the smaller nodules, not the dominant nodule, revealed the follicular carcinoma. Fine-needle aspiration biopsy (FNAB) of a thyroid nodule is the best method for differentiation of benign from malignant thyroid disease. The sensitivity and specificity of this procedure is about 95%. Galvan et al. had performed 25,000 fine-needle aspiration biopsies and had reported that sensitivity of this metod was 93.4% and specificity was 82.3%[18]. In another study Giorgadze et al. had studied on 169 cases, all of these cases had been diagnosed as hurthle cell neoplasm by FNAB and then they had undergone surgical excision. The histological diagnoses had been benign in 93 (56%), 55% cases and malignant in 76 (76/169, 45%) cases. The malignant histological diagnoses had been Hurthle-cell carcinoma, 53 cases; papillary thyroid carcinoma, 19 cases; follicular carcinoma, 3 cases; and medullary carcinoma, 1 case[19]. In our patient we performed FNAB from dominant nodule which was approximately 3 cm in diameter and it was evaluated as benign. In the comparison of scanning images of nodules, hot nodules are more likely considered as benign and cold nodules are more likely considered as malignant. Rieger et al. had also compared preoperative scintiscan and pathologic diagnoses, among 14 patients with malignancy, 10 patients had cold nodules and two patients had hot nodules and the other two patients had unidentifiable due to small size[17]. Kraimps et al. reported that in patients with a cold nodule and Graves' disease, the incidence of malignancy is as high as 15%[20]. Also Carnell and Valente had reported that 19% of palpable cold nodules were malignant in a retrospective review of 468 patients with Graves' disease[21]. Scintiscan imaging of our patient was evaluated as toxic diffuse multinodular goiter. The nodule which biopsy performed was a cold nodule. Fewer than 5% of patients with Graves’ disease have severe ophthalmopathy[2, 3]. In our patient the according to NO SPECS she had severe ophthalmopathy. Available treatments for Graves’ ophthalmopathy are lubricants, protective eye patches, eyelid surgery, diuretics, radiotherapy, plasmapheresis, glucocorticoids and other immuno-modulatory drugs, decompression surgery, extraocular muscle surgery, recession of Müller’s muscle or levator tarsorrhaphy[1]. Orbital decompression surgery is another therapeutic approach for severe ophthalmopathy. Levy et al. had reported 3 patients (five eyes) who underwent endoscopic orbital decompression surgery for Graves’ ophthalmopathy[22]. The indications for surgery had been compressive optic neuropathy in three eyes, severe corneal exposure in one eye and severe proptosis not cosmetically acceptable for the patient in one case and at the procedure in all five eyes an average reduction of 5 mm in proptosis had been achieved[22]. Because of the compressive optic neuropathy, severe corneal exposure and cosmetic deformity due to proptosis, orbital decompression surgery by transsphenoidal route was performed in our patient. In Graves’ ophthalmopathy more severe lymphocytic infiltration may occur. Somatostatin analogs inhibit lymphocyte proliferation and activation. In one study octreotide-LAR was conducted in 51 patients with mild active ophthalmopathy. Clinical Activity Score scale was reduced for patients treated with octreotide-LAR, but without any significant difference with respect to patients receiving placebo, however octreotide-LAR significantly reduced propotosis measured by exophthalmometry[23]. In our patient in addition to steroid and azotiopurine therapy also octreotide-LAR 21-d intervals were performed. In summary, we report a case of severe Graves’ ophthalmopathy and follicular carcinoma. Fine-needle aspiration biopsy was performed form the dominant nodule but diagnosis of follicular carcinoma was achieved after pathological examination of the surgical specimen of one of the smaller nodules. In order to occurrence of thyroid malignancy in patients with Graves’ disease is a rare event, the presence of a cold nodule in a hyperfunctioning thyroid should be carefully evaluated to exclude the presence of concurrent malignancy.

References


