Case Report *Olgu Sunumu*

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Graves' Disease and Papillary Thyroid Carcinoma in a Patient with Active Sarcoidosis

Sarkoidozlu Bir Hastada Papiller Tiroid Kanseri ile Birlikte Seyreden Graves Hastalığı

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Abstract

Sarcoidosis is a systemic granulomatous disease of unknown etiology. In most cases, mediastinal lymph nodes and lung parenchyma are involved. In addition, the eyes, skin, abdominal organs, central nervous system or the joints might be involved during the course of the disease. Sarcoidosis has been found to be related with other autoimmune diseases such as thyroiditis. In this report, we present the case of a patient in whom hyperthroidism was found and Graves' disease and papillary thyroid carcinoma were diagnosed while being investigated with a preliminary diagnosis of sarcoidosis. A 50-year-old male patient was admitted to our chest diseases clinic with the complaints of cough with colorless sputum, joint pain, weakness, weight loss (36 kgs), palpitations, tremor of the hands and pain in the right eye. Mediastinal lympadenopathy was detected on CT scan. Laboratory tests demonstrated hypercalcemia and low levels of parathyroid hormone (PTH). Eye examination revealed uveitis. Bronchoscopy was planned to confirm the diagnosis of sarcoidosis. Thyroid function test was performed and the patient turned out to have hyperthyroidism with high free T4 and low TSH levels. TSH receptor antibody titer was 71 U/L (0- 14 U/L). Ultrasonographic examination demonstrated enlarged thyroid gland and heterogeneous parenchyma with increased blood flow pattern. 4- and 24-hour radioiodine uptakes were 30% and 60%, respectively and scintigraphy findings were compatible with diffuse toxic goiter. On Hertel exophthalmometer, the measurements of the right and left eye were 23 and 24 mm, respectively. The diagnosis of Graves' disease was made and thionamide therapy was started. Since active ophthalmopathy was present and the patient did not want to receive medical therapy for a long time, surgery was the best option for definitive therapy. The patient was prepared for the surgery with lugol solution (3x10 drops daily) and after eutyroidism was achieved, bilateral total thyroidectomy was performed. Before and after surgery, the patient was given 20 mg methylprednisolone in order to control hypercalcemia due to sarcoidosis and to control eye symptoms caused by Graves' disease. The postoperative pathology report was compatible with thyroiditis and 6 mm micropapillary carcinoma at one focal area in the right lobe. The patient received radioactive iodine therapy after thyroidectomy. Sarcoidosis occurs as a result of immune response created against environmental and genetic factors in the presence of a triggering agent. The disease can involve many organ and systems. The classical pathological finding is granulomatosis without caseification. Autoimmune thyroiditis may accompany the disease in any stage and hypo or hyperthyroidism may develop. In our case, hyperthyroidism developed during the active phase of the disease and, interestingly, papillary thyroid cancer was detected although there were no thyroid nodules found by preoperative thyroid ultrasonography. *Turk Jem 2012; 16: 72-4*

Key words: Sarcoidosis,tyroiditis, papillary cancer

Özet

Sarkoidoz etiyolojisi bilinmeyen sistemik granülomatöz bir hastalıktır. Genellikle mediastinal lenf nodları ve akciğer parankimi tutulur. Bunlara ek olarak göz, cilt, abdominal organlar, santral sinir sistemi veya eklemler de etkilenebilir. Sarkoidozun bazı otoimmün hastalıklar ile ilişkili olduğu bilinmektedir. Bu bildiride sarkoidoz ön tanısı ile tetkik edilirken hipertroidi saptanan ve Graves hastalığı ve papiller tiroid karsinomu tanısı konulan bir olgu sunulmuştur. 50 yaşında erkek hasta, bir yıldır olan öksürük, balgam, eklem ağrısı, kilo kaybı, çarpıntı, tremor, aşırı terleme ve sağ gözde ağrı yakınması ile Göğüs hastalıkları polikliniğine başvurdu. Hastanın akciğer tomografisinde mediastinal lenfadenopati saptandı. Laboratuar incelemesinde serum Ca: 12

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mg/dL, PTH: 9 pg/mL bulundu. Göz muayenesinde üveit saptanan hastaya sarkoidoz ön tanısı ile bronkoskopi planlandı. İşlem öncesi tetkiklerde hipertiroidi tespit edildi. TSH Reseptör Antikor düzeyi: 71 U/L(0- 14 U/L) idi. Tiroid ultrasonografisinde tiroid glandı parankimi heterojendi ve her iki lob boyutu artmıştı. Color-doppler incelemede tiroid glandının kanlanmasının artmış olduğu izlendi. Radyoaktif iyot up-take ölçümü 4.saatte %30, 24.saatte %60 olup artmıştı. Göz muayenesinde Hertel ölçümü sağ/sol: 23/24 mm idi. Hastaya fizik muayene, laboratuar ve görüntüleme tetkikleri sonucu Graves Hastalığı tanısı konuldu. Aktif göz tutulumu olan hasta potasyum iyodür (1 hafta süre ile 3x10 damla) ile operasyona hazırlandı ve ötiroidi sağlanınca bilateral total tiroidektomi uygulandı. Operasyon öncesi ve sonrasında sarkoidoza bağlı hiperkalsemisi olan ve PTH değeri baskılı olan hastaya 1 hafta süre ile günlük 20 mg metilprednizolon ve hidrasyon tedavisi verildi. Operasyon sonrası histopatolojik incelemede tiroidit zemininde bir odakta papiller ca saptandı. Sarkoidoz çevresel ve genetik faktörlerin bir araya gelmesi sonucu tetikleyici bir ajanın varlığında immün cevabın oluşması sonucu ortaya çıkar. Hastalık birçok organ ve sistemi tutabilir. Klasik patolojik tutulum kazeifikasyonsuz granülomlardır. Sarkoidoza hastalığın herhangi bir evresinde otoimmün tiroidit eşlik edebilir ve hipotiroidi veya hipertirodi gelişebilir. Bizim olgumuzda hipertiroidi ve sarkoidoz tanıları eş zamanlı olarak konulmuştur. İlginç olarak, tiroid ultrasonografisinde nodül olmadığı halde oftalmopati nedeniyle hipertiroidinin kalıcı tedavisine yönelik yapılan tiroidektomi sonrası parankim içinde bir odakta insidental olarak tiroid papiller karsinomuna rastlanmıştır. *Türk Jem 2012; 16: 72-4*

Anahtar kelimeler: Sarkoidoz, tiroidit, papiller kanser

Introduction

Sarcoidosis is a systemic granulomatous disorder of unknown etiology. In most cases, mediastinal lymph nodes and lung parenchyma are involved. In addition, the eye, skin, abdominal organs, central nervous system and the joints might be involved during the course of the disease (1,2). Sarcoidosis is known to be related with other autoimmune conditions such as thyroiditis (3,4). In this report we present a case in whom hyperthroidism was found and Graves disease and papillary thyroid carcinoma were diagnosed while being investigated with a preliminary diagnosis of sarcoidosis.

Case

A 50-year-old male patient, who was using oral antidiabetic agents for type 2 diabetes, was admitted to our chest diseases clinic with complaints of cough with colorless sputum, joint pain, weakness, weight loss (36 kgs), palpitations, tremor of the hands and pain in the right eye. Mediastinal lymphadenopathy was observed on CT scan. Hypercalcemia (12 mg/dl) was also detected in routine biochemistry tests whereas parathormone level was low (9 pg/ml). The patient had uveitis on the ophtalmological examination. Bronchoscopy was planned to confirm the diagnosis of sarcoidosis. Thyroid function tests were performed; thyrotoxicosis was detected with high free T4 and low TSH levels [TSH: 0.005 uIU/mL (0.27-4.2 uIU/mL) , ST3: 26 pg/mL (1.8-4.6 pg/mL), St4: 7 ng/dL (0.9-1.7 ng/dL), anti TG: 12 IU/ml(0-115 IU/ml), anti TPO: 5 IU/ml (0-34 IU/ml)]. Consultation was made and the patient was transferred to the endocrinology and metabolism clinic for the differential diagnosis and the treatment of thyrotoxicosis . TSH receptor antibody titer was 71 U/L (0- 14 U/L).On the ultrasonographic examination, thyroid gland size was found to be enlarged and parenchyma was heterogeneous with increased blood flow pattern. 4- and 24- hour radioiodine uptake were high and scintigraphy findings were compatible with diffuse toxic goiter. Soft tissue involvement and edema were noticed on the physical examination of the eyes (picture 1). Hertel measurements of the right and left eye were 23 and 24 mm, respectively. We made the diagnosis of Graves' disease and started antithyroid thionamide therapy. Since there was active ophthalmopathy and the patient did not want to receive propylthiouracil for a long time, we have decided that total thyroidectomy was the best option for definitive therapy. The patient was prepared for the surgery with lugol solution (3x10 drops daily) and, after eutyroidism was achieved, bilateral total thyroidectomy was performed. Before and after surgery, the patient was given 20mg methylprednisolone in order to control hypercalcemia due to sarcoidosis and to control eye symptoms of Graves' disease. The postoperative pathology report was compatible with thyroiditis and 6mm micropapillary carcinoma at one focal area in the right lobe. After thyroidectomy, bronchoscopy was made and the diagnosis of sarcoidosis was confirmed. Steroid therapy was discontinued and the patient received radioactive iodine therapy after surgery.

Discussion

Sarcoidosis occurs as a result of immune response created against environmental and genetic factors in the presence of a triggering agent. The disease can involve many organ and systems. The classical pathological finding is granulomatosis without caseification (4).In the granulomatous tissue, active form of vitamin D is produced and as a result of that hypercalcemia and hypercalciuria develop. The endocrine organs can also be involved. When the hypothalamus and hypophysis are affected, polydipsia, diabetes insipidus, hypogonadism, hypoadrenalism, hypothyroidism and, less frequently, hyperprolactinemia might be seen. Rarely, adrenal glands and thyroid gland involvement and hypofunction can develop. In addition to that, autoantibodies produced against self-antigens play a major role in the pathogenesis of the disease (5), and this phenomenon explains the co-occurrence of other autoimmune diseases (6,7).

Autoimmune thyroiditis might accompany sarcoidosis at any stage and hypo or hypertyrodism might develop. Although the incidence of hyperthyroidism is considered rare (11), one study (12) showed a significantly higher prevalence of Graves' disease in sarcoidosis patients than in matched controls. In a study (8), 10 autoimmune thyroiditis cases were reported among 348 cases of sarcoidosis. Six of ten patients developed Hashimoto's thyroiditis, 3 Graves' disease and one had postpartum thyroiditis. In one patient, tyroditis had developed ten years before the diagnosis of sarcoidosis was made. In the other 5 patients, thyroiditis occurred 4-17 months after the diagnosis of sarcoidosis. In

another study reported by Papadopoulos et al., 13(%16) thyroiditis was detected among 78 sarcoidosis patients and the incidence of thyroid dysfunction was significantly higher compared to controls (9). Nakamura et al. (10) have reported that 17 of 62 patients with sarcoidosis had high levels of serum thyroid autoantibodies. However, only 7 of all autoantibody positive patients had Hashimato's thyroiditis.

Concomitant occurrence of papillary cancer, Graves' disease and thyroid sarcoidosis had been reported before by Zimmermann-Belsing et al. (13). Their patient, known to have sarcoidosis, underwent total thyroidectomy because of inadequate control of hyperthyroidism with thiamazole treatment in the course of Graves' disease (the goiter gradually enlarged). Thyroid sarcoidosis and papillary cancer of the gland with metastases to the lymph nodes were incidental findings in histological examination. The difference between our case and that patient is the absence of sarcoid reaction within the gland. Therefore, we should keep in mind that sarcoidosis may coexist with thyroid cancer and sometimes papillary cancer might mimic sarcoid infiltration and make it difficult to interpret fine needle aspiration cytology (14).

Usually autoimmune thyroid disease does not develop during the period of activity of sarcoidosis (8). In our case, the diagnosis of sarcoidosis and Graves' disease were synchronous. Graves' disease occurred during the active phase of the disease, unlike the previous reports. TSH receptor antibody titers were high in our patient and there was eye involvement (Graves' ophthalmopathy). In most of the other cases, sarcoidosis was with the symptoms of Lofgren syndrome (arthritis, erythema nodosum, bilateal hilar lymphadenopathy) whereas there was more systemic involvement in our case. Our patient had no family history of thyroid disease.

In conclusion, the presence of other autoimmune diseases should be considered in patients with sarcoidosis. In addition, a careful physical examination of the thyroid gland as well as thyroid function tests and thyroid antibody testing should be performed. We should be careful before starting potassium iodide therapy for erythema nodosum because it can trigger hyperthyroidism in patients with thyroiditis, especially in iodine deficient cases.

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