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Olgu Sunumu **Çolakoğlu K.**

Asemptomatik Hiperkalsemi, Normal D Vitamin ve ACE Değerleri İzlenen Primer Hiperparatiroidi ve Organ Tutulumu Olmayan Sarkoidoz Olgusu

Primary Hyperparathyroidism and Sarcoidosis without Organ Involvement in a Patient with Asymptomatic Hypercalcemia and Normal Vitamin-D and ACE Concentrations

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Özet

Burada yorgunluk ve boğaz ağrısı nedeniyle hastanemize kabul edilmiş 56 yaşında bayan hastamızı sunmaktayız. Hastanın hastanemize kabulü sırasında yapılan laboratuar incelemesinde insidental hiperkalsemi tespit edilmesi üzerine kliniğimize konsülte edildi. Yüksek plazma paratiroid seviyelerine rağmen hastanın paratiroid görüntülemesi için istenen ultrasonografi ve Tc-99m MIBI görüntülemelerinde paratiroidler izlenemedi. Ektopik bezlerin tespiti ve malignite ekartasyonu amacıyla yapılan PET BT'de ise mediastende multipl F-18 FDG tutulumları izlendi ve lezyonlar cerrahi olarak çıkarıldı. İlginç olan durum ise, hastanın preoperatif testlerinde serum $1,25(OH)_2 D_3$ ve ACE düzeylerinin normal olması ve dolayısıyla cerrahi öncesi sarkoidoz tanısı ekarte edilmiş olmasına rağmen patolojik incelemenin normal timus dokusu ve histolojik olarakta sarkoidozla uyumlu olan non-kazeöz granülomatöz lenfadenit olarak değerlendirilmesiydi.

Anahtar Kelimeler: Hiperkalsemi, hiperparatiroidi, sarkoidoz

Abstract

We present an unusual case of a 56 year old woman who admitted to our hospital with complaints of fatigue and sore throat. On admission, laboratory data showed hypercalcemia incidentally and therefore the patient consulted to our outpatient clinic. We determined high plasma parathyroid hormone level but ultrasonography and Tc-99m MIBI requested for parathyroid imaging were unremarkable for parathyroid mass. We performed PET CT scan for detecting ectopic glands and exclude malignancy at the same time and scan revealed multiple F-18 FDG involvement in mediastinum which were surgically removed. Interestingly, patients preoperative tests revealed normal $1,25(OH)_2D_3$ concentration and normal serum ACE levels that we eliminated diagnosis of sarcoidosis before surgery but surprisingly pathology results present regular thymus tissue and non-caseating granulomatous lympadenitis which histologically confirmed sarcoidosis.

Key Words: Hypercalcemia, Hyperparathyroidism, sarcoidosis

Introduction

Serum ionized calcium, vitamin D and parathyroid hormone (PTH) concentrations are effected by eachother and their regulation within a narrow range gives physician an idea about the possible diseases. Hypercalcemia is an uncharacteristic laboratory finding that is known to be caused by a variety of disease including hyperparathyroidism, vitamin A-D overdose, bone breakdown, metastatic neoplazm, myeloma, leukemia, lymphoma, berylliosis and sarcoidosis. Despite the other causes, primary hyperparathyroidism is the most common cause of hypercalcemia. While PTH induces osteoclast activity and renal absorbtion of calcium, it also induces 1,25-dihydroxyvitamin D [$1,25(OH)_2D_3$] production by stimulating 1α-hydroxylase activity in renal proximal tubular cells (1).

Hypercalcemia is also a laboratory finding of granulomatous diseases like sarcoidosis. Sarcoidosis is a systemic granulomatous disease which involves multiple systems and indeed its etiology is unknown. The association of hypercalcemia with sarcoidosis was first documented by Harrel G (2). Hypercalcemia is commonly related to high serum vitamin $1,25(OH)_2D_3$ concentrations in sarcoidosis which overproduced by sarcoid granulomata (3,4). In this situation, elevated vitamin $1,25(OH)_2D_3$ usually causes high serum calcium concentrations and correspondingly suppressed PTH levels.

In the literature, there exist numerous reports of patients revealing hyperparathyroidism in association with sarcoidosis (5,6). This patients usually represent with high PTH, vitamin $1,25(OH)_2D_3$ and serum ionized calcium levels and respond to treatment with concomitant medication and surgery. We report in the present paper on an interesting case that presented with elevated calcium and parathyroid hormon levels, normal vitamin $1,25(OH)_2D_3$ concentration and no imaging and laboratory investigations were suggestive of granulomatous disease but after overall treatment we, unexpectedly, diagnose sarcoidosis.

Case Presentation

A 56-year-old woman was evaluated at Ankara Oncology Training and Research Hospital for asymptomatic hypercalcemia. She was suffering from fatigue and sore throat while she admitted and laboratory data on her admission showed hypercalcemia incidentally without another abnormalities. The physical examination and her chest x-ray were unremarkable. She had a surgery history of cholecystectomy, appendectomy and ovarian cystectomy but no history of urolithiasis. There was no family history of granulomatous or endocrine disorders and hypercalcemia. No drug use admitted from the history.

On admission, she was alert and oriented. Her vital signs were normal. Blood examination revealed marked hypercalcemia (serum Ca: 11.1 mg/dl) with normal renal functions and hyperparathyroidism (plasma PTH: 7,36 pg/ml). Plasma $1,25(OH)_2D_3$ and serum angiotensin converting enzyme (ACE) levels were both normal (35 pg/ml and 48 UI/L, respectively).

In her x-ray examination there were no sign of subperiostal absorbtion detected in her skull and hands. Imaging analysis by ultrasonography revealed a noduler isoechoic mass (23x13 mm) with calcification in the right lobe and two noduler mass lesions (7x4 mm larger one) in the left lobe of thyroid. There was no mass seen suggesting the presence of an adenoma of the parathyroid gland as in the scintigraphic examination of parathyroides with Tc-99m MIBI. Normal thyroid cells and colloid was seen in microscopic evaluation of fine needle aspiration biopsy taken from right thyroid lobe.

Cervical, thoracal and abdominal CT scan were nonpathologic but thyroid gland was bigger in shape and hipoechoic nodular lesions were detected. For detecting ectopic parathyroid glands FDG PET CT scan was performed. Multiple focal elevated F-18 FDG involvement was detected in the mediastinum but because of the excess number of involved area were detected, ectopic parathyroid gland was not expected.

According to the findings, considering her age and the risk of malignancy, our patient undergo surgery and exploration of mediastinum, thymectomy and ectopic parathyroidectomy was performed. Our postoperative histological findings were thymus tissue and sarcoidosis after all (Figure 1-2).

Figure 1. Numerous confluent non-necrotizing granulomas mainly composed of epithelioid cells in a lymph node. (x40, H-E)

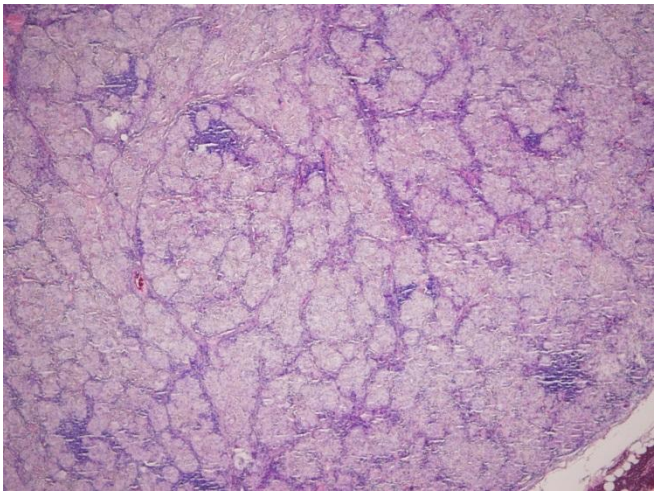
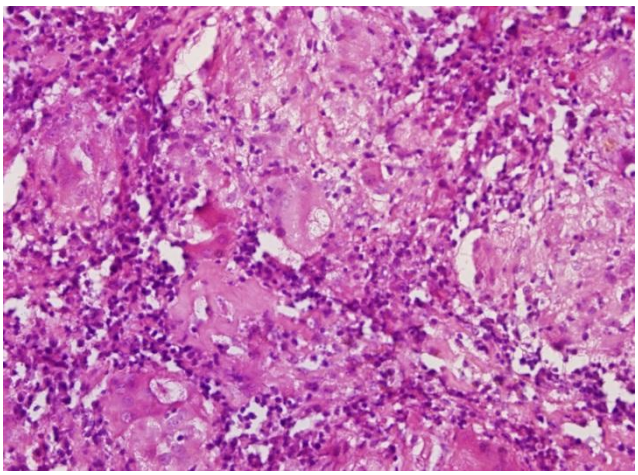


Figure 2. Asteroid body in the cytoplasm of a multinucleated giant cell in a sarcoidosis (x400, H-E).



Discussion

Hypercalcemia is a disorder which diagnosis often made incidentally in asymptomatic patients. The most common causes of hypercalcemia are primary hyperparathyroidism and malignancy. Drugs (thiazide diuretics, antacids, lithium, vitamins A-D), immobilization, renal and adrenal insufficiency, and familial hypocalciuric hypercalcemia are the other causes. Parathyroid hormone is expected to be suppressed in malignancy and elevated in primary hyperparathyroidism as in our patient. It is essential to exclude other causes before considering parathyroid surgery.

A parathyroidectomy depends on the identification and the resection of the whole of parathyroids in hyperactivity. There are two main reasons of the failure of the surgery and these are: ectopic glands and multiple parathyroid pathology not detected (7). The ^{99m} Tc- sestamibi parathyroid scintigraphy meets generally the need for detection of ectopic glands and PET CT is a reliable and accurate technique for localizing parathyroid adenomas in patients in whom conventional imaging techniques have failed (8-9).

In our patient, examination of parathyroides with Tc-99m MIBI did not marked an adenoma of the parathyroid gland. PET CT correctly locates abnormal parathyroid glands in the majority of patients with hyperparathyroidism in whom conventional non-invasive nuclear medicine imaging has failed (10). But PET CT examination did not expected ectopic parathyroid adenoma in our patient. Seki K et al (11) reported a 24 year old patient with classic severe primary hyperparathyroidism in whom both Tc-99m MIBI

scintigraphy and FDG-PET failed to detect the parathyroid tumor.

Honestly we performed surgery because of our patients age and the risk of ectopic parathyroid tissue and malignency marked on PET CT scan and unexpectedly find out sarcoidosis. High serum calcium levels are seen in about 10% of patients with sarcoidosis. Tuberculosis, fungal granulomas, berylliosis, and lymphomas are other conditions that are associated with disorders of calcium metabolism. These rare abnormalities of calcium metabolism are due to dysregulated production of $1,25(OH)_2D_3$ (calcitriol) by activated macrophages trapped in pulmonary alveoli and granulomatous inflammation (12). Hypercalcemia is known to be caused by overexpression of 1 α-OHase in the macrophage of the granulomatous tissues. But, unexpectedly, plasma $1,25(OH)_2D_3$ level was normal in our patient.

In 2007, Falk S et al (13) reported a patient with sarcoidosis-induced hypercalcemia in the setting of normal serum concentrations of 1,25-OH vitamin D and there are some report of cases with coexisting primary hyperparathyroidism and sarcoidosis and high serum vitamin D concentrations (14). To our knowledge we reported the first patient with coexisting primary hyperparathyroidism and sarcoidosis with high serum calcium levels and normal serum vitamin D concentrations.

We, the authors state that; we have no financial or other conflict of interest.

Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Kaynaklar

1. Bilezikian JP, Brandi ML, Rubin M, Silverberg SJ. Primary hyperparathyroidism: new concepts in clinical, densitometric and biochemical features. J Intern Med. 2005;257(1): 6-17.

2. Harrel G, Fisher S. Blood chemical changes in Boeck's sarcoid with particular reference to protein, calcium and phosphatase values. J Clinic Invest. 1939;18(6):687-93.

3. Adams JS, Gacad MA. Characterization of 1 alpha-hydroxylation of vitamin D3 sterols by cultured alveolar macrophages from patients with sarcoidosis. J Exp Med. 1985;161(4):755-65.

4. Nishimura M, Hara A, Nojima H, Noda S, Mashimo M, Hori Y. Possible role of the hormonal form of vitamin D_3 in the granuloma-associated angiotensin-converting enzyme activity. Sarcoidosis. 1987;8(2):101-4.

5. Sandler LM, Winearls CG, Fraher LJ, Clemens TL, Smith R, O'Riordan JL. Studies of the hypercalcaemia of sarcoidosis: effect of steroids and exogenous vitamin D3 on the circulating concentrations of 1,25-dihydroxy vitamin D3. Q J Med. 1984;53(210):165-80.

6. Ghose RR, Woodhead JS, Brown RC. Incomplete suppression of parathyroid hormone activity in sarcoidosis presenting with hypercalcemia. Postgrad Med J. 1983;59(695):272-4.

7. Levin KE, Clark OH. The reasons for failure in parathyroid operations. Arch Surg. 1989;124(8):911-915.

8. Haber RS, Kim CK, Inabnet WB. Ultrasonography for preoperative localization of enlarged parathyroid

glands in primary hyperparathyroidism: comparison with (99m)technetium sestamibi scintigraphy. Clin Endocrinol (Oxf). 2002;57(2):241-9.

9. Beggs AD, Hain SF. Localization of parathyroid adenomas using 11C-methionine positron emission tomography. Nucl Med Commun. 2005;26(2):133-6.

10. Cook GJ, Wong JC, Smellie WJ, Young AE, Maisey MN, Fogelman I. [11C]Methionine positron emission tomography for patients with persistent or recurrent hyperparathyroidism after surgery. Eur J Endocrinol. 1998;139(2):195-7.

11. Seki K, Hashimoto K, Hisada T, Maeda M, Satoh T, Uehara Y, Matsumoto H, Oyama T, Yamada M, Mori M. A patient with classic severe primary hyperparathyroidism in whom both Tc-99m MIBI scintigraphy and FDG-PET failed to detect the parathyroid tumor. Intern Med. 2004;43(9):816-23.

12. Sharma OP. Hypercalcemia in granulomatous disorders: a clinical review. Curr Opin Pulm Med. 2000;6(5):442-7.

13. Falk S, Kratzsch J, Paschke R, Koch CA. Hypercalcemia as a result of sarcoidosis with normal serum concentrations of vitamin D. Med Sci Monit. 2007;13(11):CS133-6.

14. Yoshida T, Iwasaki Y, Kagawa T, Sasaoka A, Horino T, Morita T, Hashimoto K. Coexisting primary hyperparathyroidism and sarcoidosis in a patient with severe hypercalcemia. Endocr J. 2008;55(2):391-5.