International Journal of Tokat Medical Sciences

Olgu Sunumu / Case Report

Int J Tokat Med Sci
2026;18(1):65-70

An index case of multipl endocrine neoplasia type -1: Coexistence of primary hyperparathyroidism and acromegaly

Index multip endokrin neoplazi tip-1 vakası: Primer hiperparatiroidi ve akromegali birlikteliği

Merve Çatak[1,*], Sena Akça[2], Fatma Nur Esma Akdağ[2]

[1] Tokat Gaziosmanpaşa Üniversitesi, Tıp Fakültesi, Endokrinoloji ve Metabolizma Hastalıkları Anabilim Dalı
[2] Tokat Gazşosmanpaşa Üniversitesi, Tıp Fakültesi, İç Hastalıkları Anabilim Dalı

Abstract

Objective: Multiple Endocrine Neoplasia Type 1 (MEN1) is an autosomal dominant hereditary disease characterized by hyperplasia or hyperfunction of multiple endocrine glands. The parathyroid, pancreas, and anterior pituitary are commonly affected.

Case Report: A 32-year-old female patient presented to the endocrinology outpatient clinic and was diagnosed with primary hyperparathyroidism due to hypercalcemia and elevated parathyroid hormone levels while being followed for nephrolithiasis. During the etiological evaluation, ultrasonography revealed a parathyroid adenoma in the lower right region outside the thyroid parenchyma. Parathyroid scintigraphy confirmed the adenoma's location. Consequently, a lower right parathyroid adenomectomy was performed. Despite the absence of clinical symptoms, anterior pituitary hormone assays were conducted as part of MEN1 screening due to the patient's young age. The results showed elevated Insulin-like Growth Factor-1 (IGF-1) levels. Further testing with an Oral Glucose Tolerance Test (OGTT) and Growth Hormone (GH) suppression test revealed a lowest GH level of 6.53 ng/dL, leading to a diagnosis of acromegaly. Magnetic Resonance Imaging (MRI) of the pituitary gland identified a macroadenoma, and the patient subsequently underwent a transsphenoidal adenomectomy. Postoperative follow-up showed that IGF-1 levels returned to normal, and no residual tumor was detected. The patient is currently in remission and continues regular monitoring.

Conclusion: In young patients with primary hyperparathyroidism, familial forms such as MEN1 should be considered. Early screening for MEN1 can facilitate the timely diagnosis of associated neoplasias, improving patient outcomes.

Keywords: Primary hyperparathyroidism, Multipl Endocrine Neoplasia Type-1 (MEN-1), Acromegaly.

Öz

Amaç: Multipl Endokrin Neoplazi Tip 1 (MEN1), otozomal dominant kalıtılan birden fazla endokrin bezde hiperplazi ya da hiperfonksiyon ile karakterize kalıtsal bir hastalıktır. Sıklıkla paratiroid, pankreas ve ön hipofiz etkilenmektedir.

Olgu sunumu: Otuz iki yaşındaki kadın hasta, nefrolitiazis nedeniyle takip edilirken hiperkalsemi saptanmış ve endokrinoloji polikliniğine yönlendirilmiştir. Yapılan değerlendirmede parathormon yüksekliği gözlemlenmiş olup, primer hiperparatiroidizm tanısı konulmuştur. Etiyolojik değerlendirmeye yapıldığında, ultrasonografik değerlendirmede tiroid parankimi dışında sağ altta paratiroid adenomu izlendi ve paratiroid sintigrafisinde de aynı lokalizyonda tutulum saptandı. Sağ alt paratiroid adenomektomi yapıldı. Primer hiperparatiroidizm tanısı olan hastaya, genç olması nedeniyle klinik bulgusu olmamasına rağmen yapılan MEN1 eşlik eden neoplazilerin taranması amacı ile bakılan Insulin-like Growth Faktör-1 (IGF-1) düzeyi yüksek geldi. Hastaya OGTT/GH supresyon testi yapıldı, en düşük büyüme hormon düzeyi 6.53 ng/dL olarak saptandı. Hastaya akromegali tanısı koyuldu. Hipofiz MR incelemesinde makroadenom saptanan hastaya transsfenoidal adenomektomi yapıldı. Hastanın postoperatif takibinde IGF-1 düzeyi normal sınırlara indi, rezidü alan saptanmadı. Remisyonda kabul edilerek takibe devam edilmektedir.

Sonuç: Genç primer hiperparatiroidi vakalarında ailesel formların akılda tutulması gerekmektedir. MEN1'e yönelik taramaların yapılması, eşlik edebilecek neoplazilerin erken dönemde tanınmasını sağlayabilir.

Anahtar Kelimeler: Primer Hiperparatiroidi, Multip Endokrin Neoplazi Tip-1, Akromegali

Geliş Tarihi: 27.12.2024 • **Kabul Tarihi:** 12.04.2025 • **Sorumlu Yazar:** mervebahceci@yahoo.com.tr

Introduction

Primary hyperparathyroidism (PHPT) is an endocrine disorder characterized by inappropriately elevated parathyroid hormone (PTH) levels and hypercalcemia. Hypercalcemia, resulting from increased bone resorption, can lead to complications such as osteoporosis, nephrolithiasis, and nephrocalcinosis. While PHPT can occur at any age, its incidence increases after the age of 50. Although 80% of cases are sporadic, familial forms of PHPT also exist (1). The majority of familial PHPT cases are associated with **Multiple Endocrine Neoplasia Type 1 (MEN1)**, and it is rarely seen in MEN2A and hyperparathyroidism-jaw tumor syndrome (2).

MEN1 is an autosomal dominant hereditary disorder characterized by hyperplasia or hyperfunction of multiple endocrine glands. The parathyroid glands, pancreas, and anterior pituitary are commonly affected. Guidelines recommend considering familial forms in young patients (especially those under 40 years old) with primary hyperparathyroidism affecting more than one parathyroid gland. In such cases, appropriate screening for MEN1 should be conducted to enable early diagnosis and management of associated neoplasias (3-4).

Case Report

A thirty-five-year-old female patient was referred to the endocrinology outpatient clinic after hypercalcemia was detected during urological follow-up for nephrolithiasis. The patient had no known medical conditions and was not taking any medications. Her blood pressure was 110/70 mmHg, and her pulse was 70 beats per minute. No pathological findings were observed during the physical examination.

The patient was diagnosed with primary hyperparathyroidism (PHPT) when corrected calcium level was found to be 12.5 mg/dL and parathyroid hormone (PTH) level was 321 pg/mL. Other biochemical parameters are listed in Table 1. Neck ultrasonography revealed a 20x20x15 mm lesion consistent with a parathyroid adenoma on the lower right side, outside the thyroid parenchyma. MIBI parathyroid scintigraphy also showed uptake in the same location (Figure 1). Her 24-hour urinary calcium excretion was 549 mg/day, and lumbar vertebral T-score was -2.7 as determined by bone mineral densitometry.

Table1. Laboratory parameters

	Pre-operative	Post-operative
Ca	12.5 mg/dl	9.7 mg/dl
Fosfor	2.7 mg/dl	3.4 mg/dl
25-OH-Vitamin D3	12 ng/ml	14 ng/ml
PTH	321 pg/ml	42 pg/ml
Creatinin	0.6 mg/dl	0.52 mg/dl
TSH	3.2 IU/ml	3.9 IU/ml
GH	6.21 ng/ml	0.67 ng/mL
IGF-1	560 ng/ml	190 ng/ml

Ca : corrected calcium, GH: Growth hormone, IGF-1: Insulin like growth faktör -1, PTH: Parathormone, TSH: Thyroid stimulating hormone

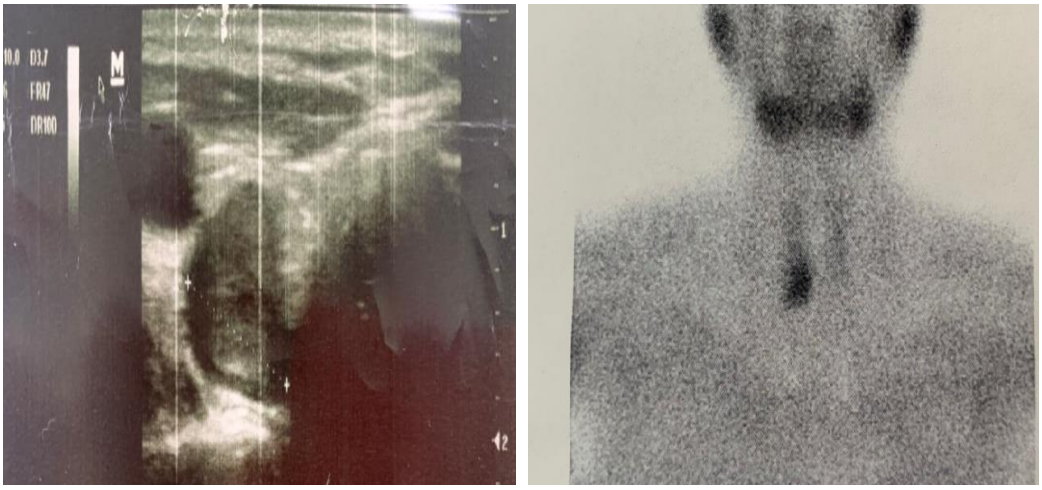

Figure 1. Ultrasonografic and scintigrafic appearence of parathyroid adenoma

Pituitary MR image Due to the presence of nephrolithiasis and osteoporosis, high 24-hour urinary calcium excretion, and her age, the patient underwent a minimally invasive parathyroid adenomectomy. Postoperatively, the patient's calcium and PTH levels normalized, and no complications were observed. Pathology results confirmed a parathyroid adenoma.

As part of the evaluation for Multiple Endocrine Neoplasia Type 1 (MEN1) syndrome, the patient's serum insulin and gastrin levels were normal. However, in the anterior pituitary examination, insulin-like growth factor-1 (IGF-1) was elevated at 560 ng/mL, while other hormone levels remained normal. Specifically, there were no facial features suggestive of acromegaly, such as prognathism, malocclusion, enlargement of the hands and feet, or narrowing of the nasolabial folds. An oral glucose tolerance test (OGTT) showed no suppression of growth hormone, with the lowest growth hormone level recorded at 6.53 ng/mL. Consequently, the patient was diagnosed with acromegaly.

Pituitary MRI revealed a slightly indenting macroadenoma measuring 16x17.5x20 mm, causing deviation of the infundibular stalk. The adenoma was located superior to the central part of the pituitary gland, near the optic chiasm. On the T2-weighted series, it had intensity similar to white matter, and on the T1-weighted series, it resembled gray matter. After administration of a paramagnetic contrast agent, the adenoma showed very weak and slightly heterogeneous contrast enhancement compared to the gland (Figure 2). The patient underwent a transsphenoidal pituitary adenomectomy. Immunohistochemical examination of the resected tissue confirmed a pituitary adenoma, with growth hormone (GH) positive and other hormones negative.

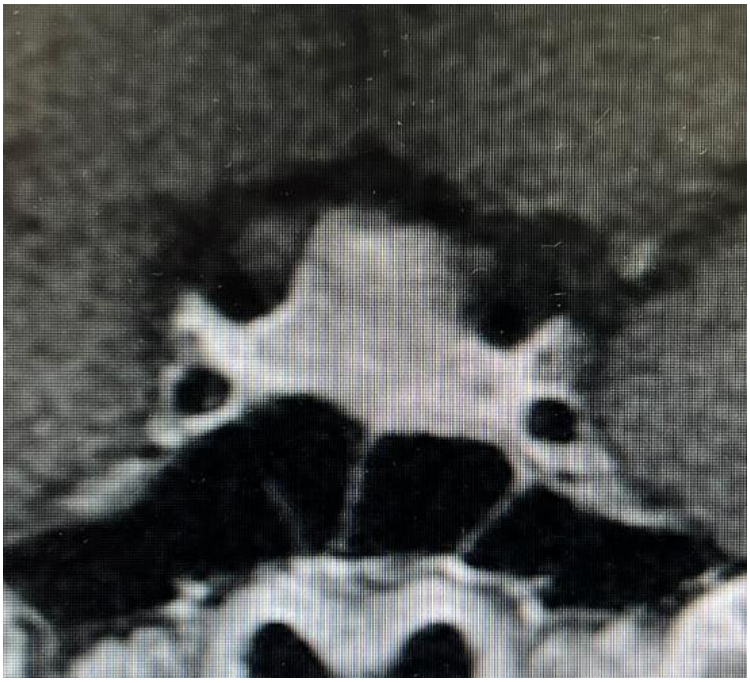

Figure 2. Pituitary MR image

Three months postoperatively, the patient's growth hormone level was 0.67 ng/mL, and IGF-1 was 190 ng/mL, indicating remission. She was followed up without medication.

Although the patient was diagnosed with MEN1, due to the correlation between ultrasonography and scintigraphy, only a right lower parathyroid adenomectomy was performed instead of removing 3-5 parathyroid glands to avoid increasing the risk of hypoparathyroidism.

Genetic testing was planned for the patient, who was clinically diagnosed with MEN1. Serum calcium and parathyroid hormone levels of her first-degree relatives were normal, and her relatives were informed of the necessity for genetic testing for MEN1.

Discussion

Multiple Endocrine Neoplasia Type 1 (MEN1) Syndrome is a hereditary disease resulting from mutations in the autosomal dominant **menin** gene. It is characterized by hyperfunction or hyperplasia in two or more endocrine glands. While the parathyroid glands, anterior pituitary, and pancreas are frequently affected, the incidence of non-functional adrenal adenomas and carcinoid tumors is also increased compared to the general population. The diagnosis can be made when two or more MEN-related tumors are present, or when a single MEN1-related tumor is identified in individuals with a clinically detected MEN1 mutation or in their first-degree relatives, regardless of genetic testing results (3-4). In our case, the patient was clinically diagnosed with MEN1 due to the presence of acromegaly accompanying primary hyperparathyroidism (PHPT).

Approximately 1-18% of PHPT cases are associated with MEN1 syndrome. While sporadic PHPT is more common in individuals over the age of fifty, primary hyperparathyroidism is observed in more than 90% of cases by the age of forty in MEN1 syndrome (5). In sporadic PHPT, typically a single parathyroid gland is affected, whereas in MEN1 syndrome, multiple parathyroid glands are usually involved (6). Therefore, MEN1 screening is recommended when PHPT is detected before the age of forty or when more than one parathyroid adenoma is identified. Following an assessment for pancreatic and pituitary

tumors, evaluations of insulin, gastrin, and anterior pituitary hormones should be conducted. In our case, although the patient was asymptomatic due to her young age, an elevated insulin-like growth factor-1 (IGF-1) level was detected during anterior pituitary hormone evaluation, leading to a diagnosis of acromegaly after further assessments.

Pituitary tumors are observed in 30-40% of MEN1 cases, with prolactinomas being the most common. Growth hormone-secreting adenomas are rarer, occurring in approximately 5% of cases (7-8). Studies comparing the aggressiveness and recurrence rates of MEN1-related acromegaly with isolated acromegaly have yielded varying results. Trouillas et al. reported that MEN1-related acromegaly cases were younger, more aggressive, and had higher relapse rates compared to isolated acromegaly. Conversely, Wu et al. found no significant differences in relapse rates and aggressiveness between MEN1-related and isolated acromegaly cases (9-10). Although our patient is young, she is in remission three months postoperatively, thanks to surgery performed at an experienced center, and will continue to be monitored for any recurrence.

Familial forms of PHPT, particularly MEN1, should be considered, especially in patients under the age of forty. Screening for MEN1 can facilitate the early diagnosis of associated neoplasias, improving patient management and outcomes.

Written Consent for Publication: Written consent to publish was obtained from the patient.

Funding: No funding was utilized for this manuscript.

Ethics Committee Approval: The patient signed a written informed consent form.

Authors' Contributions: All authors contributed equally

References

1. Gardner DG, Shoback D. Greenspan's Basic & Clinical Endocrinology. 9th ed. New York: McGraw-Hill; 2011. Chapter 8, p. 244-246.
2. Blau JE, Simonds WF. Familial Hyperparathyroidism. Front Endocrinol (Lausanne). 2021 25;12:623667.
3. Thakker RV, Newey PJ, Walls GV, Bilezikian J, Dralle H, Ebeling PR, et al. Endocrine Society. Clinical practice guidelines for multiple endocrine neoplasia type 1 (MEN1). J Clin Endocrinol Metab. 2012 Sep;97:2990-3011.
4. Kamilaris CDC, Stratakis CA. Multiple Endocrine Neoplasia Type 1 (MEN1): An Update and the Significance of Early Genetic and Clinical Diagnosis. Front Endocrinol (Lausanne). 2019;11: 10:339.
5. Brandi ML, Marx SJ, Aurbach GD, Fitzpatrick LA. Familial multiple endocrine neoplasia type I: a new look at pathophysiology. Endocr Rev. 1987 Nov;8:391-405.
6. Rizzoli R, Green J 3rd, Marx SJ. Primary hyperparathyroidism in familial multiple endocrine neoplasia type I. Long-term follow-up of serum calcium levels after parathyroidectomy. Am J Med. 1985 Mar;78(3):467-74.
7. disease in MEN type 1 (MEN1): data from the France-Belgium MEN1 multicenter study. J Clin Endocrinol Metab. 2002 Feb;87(2):457-65.
8. Burgess JR, Shepherd JJ, Parameswaran V, Hoffman L, Greenaway TM. Spectrum of pituitary disease in multiple endocrine neoplasia type 1 (MEN 1): clinical, biochemical, and radiological features of pituitary disease in a large MEN 1 kindred. J Clin Endocrinol Metab. 1996 Jul;81(7):2642-6.
9. Trouillas J, Labat-Moleur F, Sturm N, Kujas M, Heymann MF, Figarella-Branger D, et al. Groupe d'études des Tumeurs Endocrines. Pituitary tumors and hyperplasia in multiple endocrine neoplasia type 1 syndrome (MEN1): a case-control study in a series of 77 patients versus 2509 non-MEN1 patients. Am J Surg Pathol. 2008 Apr;32(4):534-43.

10. Wu Y, Gao L, Guo X, Wang Z, Lian W, Deng K, et al. Pituitary adenomas in patients with multiple endocrine neoplasia type 1: a single-center experience in China. Pituitary. 2019 Apr;22(2):113-123.