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EDİTÖRE MEKTUP / LETTER TO THE EDITOR

A case of normocalcemic primary hyperparathyroidism presenting with a mass in the oral cavity and accompanying incidental papillary thyroid carcinoma

Oral kavitede kitle ve eşlik eden insidental papiller tiroid karsinomu ile başvuran normokalsemik primer hiperparatiroidizm olgusu

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To the Editor,

Primary hyperparathyroidism (HPT) is the inappropriate secretion of Parathyroid hormone (PTH) accompanying hypercalcemia. Patients with overt hypercalcemia are usually complicated and symptomatic by bone and renal findings[1]. Brown tumors are rarely encountered due to the progress of laboratory examinations and early diagnosis of HPT. 4.5% of reported brown tumor cases involve facial bones. Brown tumors of the maxillofacial region are more common in women than men, with a reported female: male ratio of approximately 1.7:1, with a median age at diagnosis of 34 and are most common in the mandible[2].

In this article, we present a case of incidental papillary thyroid carcinoma with ectopic parathyroid adenoma accompanied by severe vitamin D, and diagnosed during accompanying surgery following a brown tumor was considered after primary hyperparathyroidism was detected. However, the patient was admitted with a mass in the oral cavity, diagnosed as a pyogenic granuloma with a delayed diagnosis without considering a brown tumor because it was normocalcemic. It is the first case in the literature of papillary thyroid carcinoma detected incidentally with ectopic parathyroid adenoma in the thyrothymic region.

A 30-year-old female patient applied to an external center due to a sore in the mouth four months ago and the growth and swelling of the lesion in the mouth for the last month. The biopsy taken from the intraoral lesion was evaluated as pyogenic granuloma, and the patient was referred to the medical faculty's otolaryngology (ORL) clinic for excision. In the examination of the patient, it was observed that there was a 4x3 cm painful mass in the gingiva under the left lower first molar tooth (Picture 1). In the examinations of the patient, the average albumin-corrected calcium level was 9.7 mg/dL (reference range, 8.6-10 mg/dL), phosphorus 2.08 mg/dl (reference range, 2.5-4.5 mg/dL). PTH level was 794 ng/L (reference range, 15-65 ng/L), and the patient was referred to the endocrinology clinic. The 25-hydroxyvitamin-D level was <4 ng / L (reference range, 20-70 ng / L), and the creatinine level was normal.

There were widespread bone pains and cramps in the system questioning the patient. There was no history of nephrolithiasis, and there was no family history of parathyroid disease, pituitary disease, or pancreatic disease suggestive of multiple endocrine neoplasias-1 (MEN1) and MEN2A.

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On physical examination, a 4x3 cm painful mass was observed in the mouth at the left lower first molar tooth level (Figure 1).

The biochemical evaluation revealed a high PTH level (794 ng/L), average albumin-corrected calcium level (9.7 mg/dL), low phosphorus level (2.08 mg/dL; reference range, 2.5-4.5 mg/dL), the 25-OH-D level was low (<4 ng/L) and creatinine level was average (0.4 mg/dL). The alkaline phosphatase level was high (702 units/L; reference range, 35-104 units/L). Bone densitometry T-score in the lumbar spine was -4.3 Z-score: -4.1, femoral length T-score:-2.9, Z-score: -2.6 was compatible with osteoporosis (Table-1).

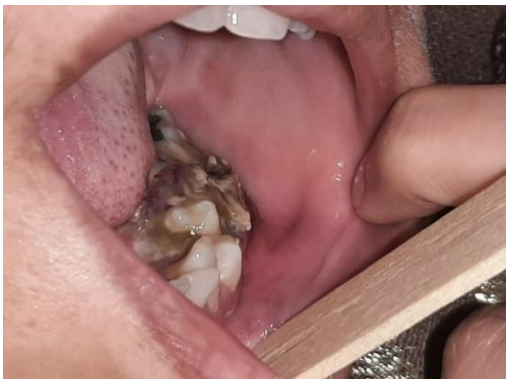

Figure 1. Intraoral mass brown tumor.

Table-1. Laboratory findings

Variable	Value	Reference range
Glucose	89	74-100
Creatinine	0.4	0.5-0.9
Calcium	9.7	8.6-10
Albumin	40.7	34-41.6
Phosphorus	2.08	2.5-4.5
PTH	794	15-65
ALP	702	35-104
25-0H-vitamin D	<4	20-70
BMD	L1-L4 T :-4,3 Z : -4,1 Femoral neck: T: -2,9 Z:-2,6	

In the thyroid ultrasound (USG) and parathyroid USG, a 5x5x6 mm well-circumscribed iso-hypoechoic nodule in the middle pole posterior of the thyroid gland in the right lobe and a 4x10x15 mm parathyroid adenoma outside the thyroid lodge in the left inferior posterior localization were observed. In the sestamibi scintigraphy, an involvement compatible with parathyroid adenoma was detected in a large area corresponding to the left lobe lower pole inferior part of the thyroid gland.

MEN1 and MEN2 components were scanned because of being under the age of 40. MEN 1 and MEN 2 were not considered. In the thyroid USG, a 5x5x6 mm well-circumscribed iso-hypoechoic nodule was seen in the right lobe. Due to thyroid image reporting and data system-3 (TRIADS-3), Thyroid fine-needle aspiration biopsy (TFNAB) was not considered. Primary hyperparathyroidism accompanied by normocalcemic severe vitamin D deficiency was considered in the patient.

A left parathyroidectomy was planned for the patient. During the operation, no parathyroid adenoma was found; the lesion was considered a parathyroid adenoma, and the removed lesion was studied frozen. When lymphoadenopathy (LAP) compatible with papillary ca metastasis was detected, total thyroidectomy, central lymph node dissection, and intraoral mass excision were performed. Since no intraoperative parathyroid adenoma was detected, the operation was terminated, considering it would be an intrathyroidal parathyroid adenoma. However, as the post-op PTH level was 480 ng/L. USG performed again on the first post-op day. An iso-hypoechoic formation with cystic areas of 5x15x19 mm, on the left inferior, above the sternal notch, was evaluated as a parathyroid adenoma (Figure 2). The patient was re-operated, and parathyroid adenoma was found in the left thyrothymic ligament region. A left parathyroidectomy was performed. Post-op PTH 20 ng/L was detected. In the follow-up, the patient who developed hungry bone syndrome was treated with ca and active vitamin D replacement therapy.

Calcium levels were expected in the follow-up. As a result of the patient's pathology, 1.1 cm conventional type papillary thyroid ca in the right lobe, two metastatic LAPs (0.2 cm) as a result of central lymph node dissection, (T1bN1aM0 Stage 1, low risk), parathyroid adenoma in the thymic region, the patient's intraoral lesion is giant cell granuloma was evaluated as brown tumor due to hyperparathyroidism.

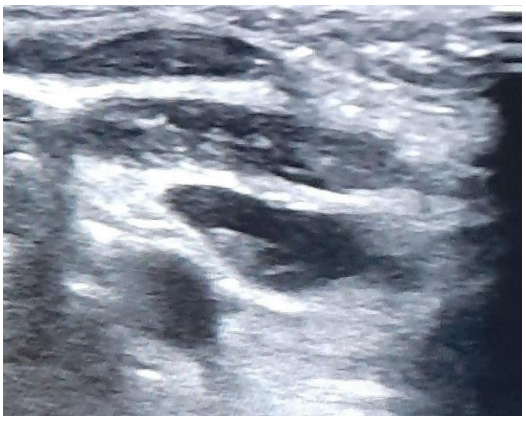

Figure-2. USG image of parathyroid adenoma.

Primary hyperparathyroidism (PHPT) with vitamin D deficiency worsens the clinical course, and average calcium values cause a late diagnosis of PHPT. They present with higher PTH levels, larger parathyroid adenomas, and bone findings than patients with PHPT alone[3].

In our patient, due to severe vitamin D deficiency accompanied by PHT, the clinical diagnosis was delayed because the calcium values were found to be expected; the mass in the oral cavity was not considered a brown tumor and was diagnosed as pyogenic granuloma. The PTH on the patient's admission to our hospital was found to be 794 ng/L. At the time of diagnosis, the patient had significant osteoporosis and a brown tumor in the mouth.

These findings are not specific to the brown tumor. Brown tumors are confused with giant cell tumors that appear primarily as bone metastases, giant cell granulomas, amyloid cysts, chondromas, aneurysmal bone cysts, osteosarcoma, and osteolytic lesions[4]. The presence of hypercalcemia and hyperparathyroidism should be investigated in cases whose pathology reports are "giant cell tumors." The diagnosis can be made by combining it with the hyperparathyroidism clinic. In our case, the first biopsy result from the intraoral lesion was evaluated as pyogenic granuloma (PG). PG is usually an inflammatory hyperplastic lesion. It occurs in response to irritants, dentures, trauma, hormonal changes, or certain medications. PG is more common in women in their 20s. In 75% of cases, it is located on the gingiva, tongue, and buccal mucosa[5].

Pathologically, PG and brown tumors are not lesions that can be confused. However, since the location of the lesion is close to the first molar tooth in the gingiva, it was thought to be confusing. Polymorphonuclear cells are seen pathologically in PG.

Thyroid nodules are a common disease found incidentally with PHPT on ultrasound examination of the neck. In studies conducted, accompanying thyroid nodules were found in 50-73.3% of PHPT patients[6]. The most common type of malignant thyroid lesion synchronized with PHPT is papillary thyroid cancer (PTC)[7].

In our patient, 1.1 cm classical-type papillary carcinoma was detected.

In case of the coexistence of thyroid and parathyroid pathologies, thyroid PTC should be diagnosed before surgical treatment to avoid repetitive surgery complications, ensure patient comfort, and minimize costs. TFNAB is the most accurate method for evaluating thyroid nodules. Therefore, it is crucial to detect thyroid malignancy by performing TFNAB on nodules with indications before parathyroidectomy.

The thyroid USG of our patient revealed a well-circumscribed iso-hypoechoic nodule measuring 5x5x6 mm in size in the posterior part of the middle pole of the right lobe of the thyroid gland, and TFNAB was not considered because of TRIADS-3[8]. TFNAB was not considered because parathyroid adenoma was not detected during the first operation. Total thyroidectomy and central lymph node dissection were performed after papillary carcinoma metastasis was detected in the removed central lymph node. Total thyroidectomy and central lymph node dissection were performed on the patient, who was diagnosed with intraoperative papillary thyroid cancer because parathyroid adenoma could not be found intraoperatively in the first operation, and the lymph node removed by mistaking it for parathyroid adenoma was compatible with metastatic papillary thyroid carcinoma. In the literature, papillary thyroid cancer, detected incidentally in patients with hyperparathyroidism, was found in patients who

underwent total thyroidectomy associated with intrathyroidal parathyroid adenoma[9].

It is the first case in the literature of papillary thyroid carcinoma detected incidentally with ectopic parathyroid adenoma in the thyrothymic region.

Surgical management of parathyroid adenoma can sometimes be complex because the surgeon cannot detect parathyroids in unusual locations. The glands are detected in ectopic places at a rate of 8.5%. 0.2% is intrathyroidal, 2% is located in different neck regions, 4.1% is in the upper mediastinum, and 2.2% is in the lower mediastinum[10].

In our case, the surgeon could not find parathyroid adenoma in the first surgery, and its failure led to the diagnosis of papillary thyroid cancer. The second surgery detected parathyroid adenoma in the upper mediastinum near the thyrothymic ligament. In pre-op USG and sestamibi scintigraphy, parathyroid adenoma was localized in a large area matching the left lobe lower pole inferior part of the thyroid gland.

In conclusion, even if calcium is expected, the brown tumor should be considered, and parathormone should be examined in cases presenting with a mass in the oral cavity. Calcium can be found to be expected in accompanying vitamin D deficiency. Accompanying thyroid pathologies should be considered while preoperative parathyroid USG is performed, and preoperative thyroid USG should also be performed. In case of the coexistence of thyroid and parathyroid pathologies, thyroid PTC should be diagnosed before surgical treatment to avoid repetitive surgeries. However, preoperative diagnosis of PTC can still be missed. Even if preoperative parathyroid adenoma is localized, when parathyroid adenoma is not found intraoperatively, the upper mediastinal thymus region should be examined, and it should be ensured that the adenoma is removed by performing rapid PTH intraoperatively.

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