Case Report

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Pathology Section

Parathyroid Adenoma Associated with Granulomatous Inflammation- A Case Report

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ABSTRACT

Parathyroid adenoma is a benign neoplasm derived from the parenchymal cells of a parathyroid gland. Most patients present with unknown aetiology. Inflammatory disorders of the parathyroid gland are poorly defined and necrotising granulomatous inflammation of the parathyroid gland is very rare and its co-existence with a functioning adenoma of the parathyroid is indeed a unique presentation. Hereby, the author presents a case of a 47-year-old female who presented with generalised weakness and joint pain with radiological and biochemical evidence of hyperthyroidism. The patient had undergone a nuclear Tc-99m sestamibi parathyroid scan which was suggestive of parathyroid adenoma and was operated for the same. Routine histopathological examination was suggestive of parathyroid adenoma with chronic granulomatous inflammation. However, diagnostic possibilities of inflammatory aetiologies are numerous and each has presented its characteristics, and theories have always focused on disorders of the parathyroid gland which can occur probably due to autoimmune and non infectious aetiology. Hypercalcaemia can be caused by many causes. However, parathyroid adenoma with co-existent granulomatous inflammation is a rare finding. Sometimes it is not possible to find the exact cause of granulomatous inflammation as in the present case.

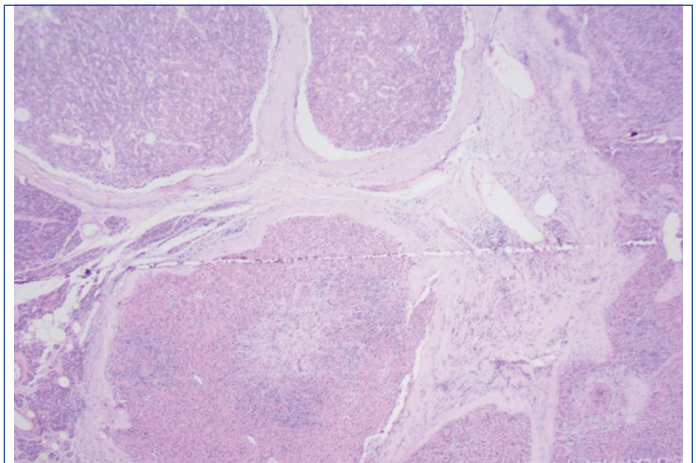
Keywords: Hypercalcaemia, Hyperparathyroidism, Hypertension

CASE REPORT

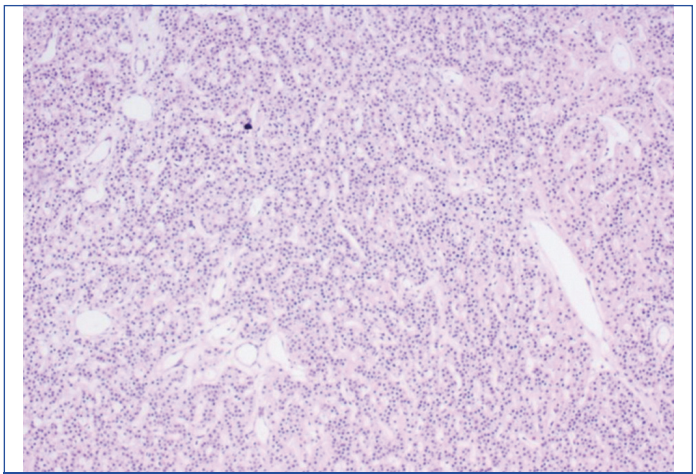
A 47-year-old female presented to the Department of Otorhinolaryngology with complaints of generalised weakness and joint pain for six to eight months. The patient was relatively asymptomatic before eight months then she developed weakness, joint pain, and weight loss of weight (10 kg). She was diagnosed with diabetes mellitus one year back, while had hypertension and hypothyroidism for five years. She was on a combination of Dapagliflozin 10 mg and Metformin 500 mg with Vildagliptin 50 mg medication for diabetes, amlodipine 5 mg for hypertension, and levothyroxine 75 µg for hypothyroidism.

On general examination, no remarkable findings were noted. On systemic examination, no abnormalities were present in the head and neck region. Ultrasonography (USG) for the thyroid and parathyroid gland showed a well-defined hypoechoic nodule noted posterior to a mid-pole of the left lobe of the thyroid with a well-defined capsule, which was not separate from thyroid parenchyma and measured 1.3×0.7×0.5 cm. Tc-99m sestamibi parathyroid scan showed an increased area of radiotracer concentration in the region of the posterior aspect of the lower pole of the left thyroid lobe, suggestive of parathyroid adenoma involving the posterior aspect of the lower pole of the left lobe of the thyroid gland. On laboratory investigations, the complete blood count and coagulation profile were within the normal physiological range. Biochemical testing showed high Parathyroid Hormone (PTH) levels of 57.8 pg/mL and serum calcium level 10.60 mg/dL.

The patient underwent excision for the parathyroid adenoma. The histopathological analysis of the frozen section showed nodules of chief cells, oxyphil cells, and clear cells arranged in glands, trabeculae and nest pattern separated by fibrous septae. Occasional clusters showed mild nuclear atypia. After routine processing on Haematoxylin and Eosin (H&E)-stained section showed nodules of chief cells, oxyphil cells, and clear cells arranged in glands, trabeculae and nest pattern separated by fibrous bands with the presence of many well-formed granulomas compromised of epithelioid cells, histiocytes, lymphocytes, foreign body and Langhans giant cells with a central area of necrosis. The focal lobule shows infiltration of mature adipocytes in parathyroid parenchyma [Table/Fig-1-4].

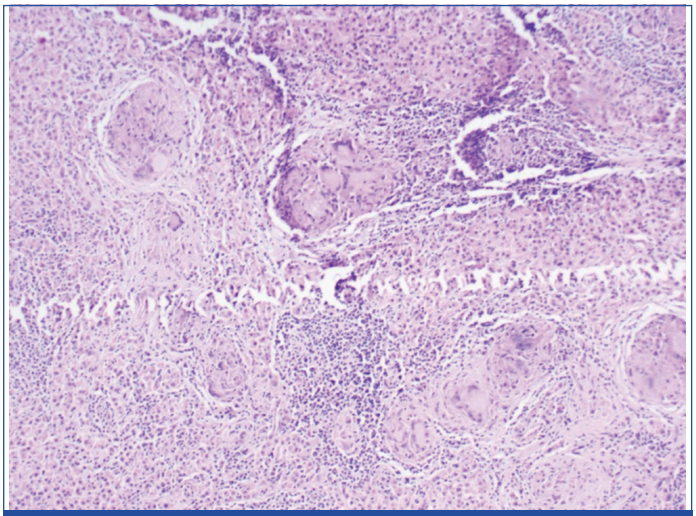


[Table/Fig-1]: Micrograph shows nodules of chief cells, oxyphil cells and clear cells arranged in glands, trabeculae and nest pattern separated by fibrous bands (40x, H&E).

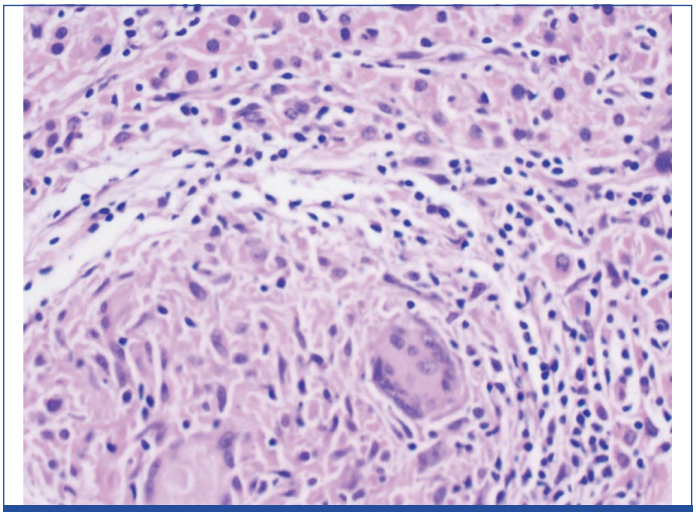


[Table/Fig-2]: Nodules of chief cells, oxyphil cells and clear cells arranged in glands, trabeculae and nest pattern and clusters show mild nuclear atypia (100x, H&E).

Thus, the final diagnosis was parathyroid adenoma with chronic granulomatous inflammation of the left lower parathyroid gland. After the excision of the gland, the PTH level was reduced to 31.0 pg/mL and the serum calcium level 8.3 mg/dL.



[Table/Fig-3]: Presence of many well-formed granulomas compromised of epithelioid cells, histiocytes lymphocytes, foreign body and Langhans giant cells with central area of necrosis. (40x, H&E).



[Table/Fig-4]: Well-formed granuloma (400x, H&E).

DISCUSSION

Parathyroid adenoma is a benign neoplasm of the parathyroid gland, typically involving one gland. It occurs in women and men in a ratio of 3:1. They can develop at any age, but most cases occur in patients in the fourth decade. It accounts for over 85% of cases of Hyperparathyroidism (HPT) [1]. Hypercalcaemia is usually associated with either PTH-dependent or PTH-independent processes as well as infections like Tuberculosis (Tb), leprosy, disseminated candidiasis, systemic fungal infections, and non infective conditions like inflammatory bowel disease and foreign body granulomas. Granulomatous diseases can cause hypercalcaemia due to increased 1α-hydroxylase enzymatic activity in tissue macrophages which leads to elevated levels of 1,25- dihydroxy vitamin D3 (1,25(OH)2D) which is resistant to feedback control [2,3].

The index patient had PTH-mediated hypercalcaemia due to granulomatous processes involving the parathyroid gland which posed significant diagnostic challenges. Clinical research shows that parathyroid adenoma with associated granulomatous inflammation is a rare presentation, but studies have shown chronic inflammation can cause hyperfunctioning. The parathyroid gland is weakly antigenic, so it is rare to encounter granulomatous inflammation due to probable tuberculous infection of the parathyroid gland [Table/Fig-5] [4-7]. Few of them presented as chronic granulomatous inflammation and all cases with primary hyperparathyroidism presented with concomitant adenoma. Few cases reported the presence of granulomatous inflammation but special tests and special stain for acid-fast bacilli are negative which excludes sarcoidosis.

In addition, the index patient had primary hyperparathyroidism associated with end-stage renal disease and diabetes mellitus which are an immunocompromised state that explains the occurrence of chronic inflammation. Activation of osteoclasts in primary hyperparathyroidism leads to increased bone resorption associated with vitamin D 1,25(OH)2D3- mediated granulomatous disorders. However, evaluation of 1,25(OH)2D3 levels was not performed in this patient, but serum calcium decreased to 8.3 mg/dL and serum PTH decreased to 31.0 pg/mL after the removal of parathyroid adenoma. This could be explained by the causal association of granulomatous inflammation in the parathyroid gland and hyperfunctioning of the parathyroid gland associated with an immunocompromised state.

The current case presented with routine high PTH levels and calcium levels, but histopathological examination suggested associated

Variables	Present case	Granulomatous (Kabbaj DE and Oualim Z) [4]	Granulomatous (Anaforoglu I et al.,) [5]	Granulomatous (Jacob PM et al.,) [6]	Granulomatous (Singh HP et al.,) [7]
Gender	Female	Female	Female	Female	Female
Country of origin	India	Morocco	Turkey	India	India
Age (years)	47	49	50	35	43
Type of HPT	Primary	Secondary	Primary	Primary	Primary
Ca (Calcium) (mg/dL)	10.6	Normal	12	Elevated	Elevated
PTH (pg/mL)	57.8	1200	105.3	Elevated	161.4
Associated diseases	Diabetes mellitus, Hypertension, Hypothyroidism	End stage renal disease	No	No	No
Glands involved	Left inferior	None specified	Left inferior	Right inferior	Left inferior
Lymph nodes involved	No	None specified	No	No	No
Hyperplasia/adenoma (Additional findings)	Adenoma	Adenoma	Adenoma	Adenoma	Adenoma
Other glands biopsied	No	No	No	No	No
TB symptoms	No	No	No	No	No
Size of the mass (mm)	13×7×5 mm	Not specified	20×15×10	40×20×10	20×20×10
TB tests	Ziehl-Neelsen stain-Negative	Not done	PCR-PPD+QuantiFERON+	PCR-	20×20×10
Treatment	Excision of parathyroid adenoma	4-drug anti-TB treatment	Not given	Anti-TB treatment	Not given

[Table/Fig-5]: Literature review [4-7].
(Note: Normal ranges- PTH- 18.4-80.1 pg/mL, S.Calcium-8.4-10.2 mg/dL)
Values are not given in some reference articles, so they were not mentioned in table

granulomatous inflammation, which was found to have an incidental finding in microscopy.

CONCLUSION(S)

The present case sheds light on the significance of Granulomatous inflammation with parathyroid adenoma as a rare presentation. It is not clear whether parathyroid adenoma-associated hyperfunctioning contributed to the chronic inflammation, but it might show immunocompromised state can be associated with any chronic inflammation.

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