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Case Report

An unusual presentation of coexisting parathyroid carcinoma and papillary carcinoma thyroid: a case report and literature review

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ABSTRACT

Parathyroid carcinoma is the rarest endocrine cancer with aggressive behaviour. It may be presented as a feature of severe hypercalcemia, musculoskeletal involvement and a neck mass. There should be a high clinical suspicion if there is marked hypercalcemia, very high parathyroid hormone levels, palpable neck mass, recurrent laryngeal nerve palsy due to invasion and severe bone and renal symptoms. Thyroid pathology has been seen in 15-70% of patients with primary hyperparathyroidism (PHPT) especially with parathyroid adenoma. Medullary thyroid carcinoma is common with PHPT as in MEN 2 syndrome and rarely co-existed with non-medullary thyroid carcinoma. Parathyroid carcinoma and papillary thyroid carcinoma is extremely rare. Only 16 cases are reported in the literature.

Keywords: Parathyroid carcinoma, Papillary thyroid carcinoma, Hypercalcemia, PHPT

INTRODUCTION

Parathyroid carcinoma is an infrequent endocrine malignancy which attributes to 0.1% to 5% of PHPT.[1] Most of the parathyroid carcinoma cases are sporadic, whereas the remainder occur in genetic syndromes such as multiple endocrine neoplasia type 1 (MEN1) or hyperparathyroidism-jaw tumor syndrome (HPT-JT).[2] It is seen in both males and females equally and commonly occurs during the 5th decade of life. Severe hypercalcemia and very high values of parathyroid hormone levels are seen in parathyroid carcinoma. Clinical features are also due to excessive secretion of this parathyroid hormone. Diagnosis is usually done by post operative histopathology examination.

Papillary thyroid cancers (PTC) are the most common thyroid cancers which account 80-85%. It occurs predominantly in females, and during the 5th decade of life. An asymptomatic neck mass with or without cervical lymph node enlargement is usually the main clinical feature. Locally advanced papillary thyroid carcinoma can be seen in 20% of the patients.

As per the literature, 16 cases of coexisting parathyroid carcinomas and non-medullary well differentiated thyroid carcinomas have been reported. The rare presentation of contemporaneous papillary thyroid carcinoma and parathyroid carcinoma has motivated us to document this case and the literature review has been done to lay emphasis on the challenging difficulties in the management.

CASE REPORT

A 56-year-old lady with no co-morbidities presented with a history of trauma to the right forearm following a fall 6 months back which was managed conservatively. She also had an asymptomatic neck swelling which was noticed recently. On further evaluation, she was found to have hypercalcemia and the corrected calcium was 12.9 mg/dl with very high levels of parathyroid hormone and alkaline

phosphatase. Clinically, she had grade 3 goitre with a retrosternal extension on the left side. She had no symptoms of hypo or hyperthyroidism and she was euthyroid. As she had bone pain and recent history of proximal myopathy, a skeletal survey was done which showed grade 1 genant fracture along with multiple vertebrae and multiple osteitis fibrosa cystica (Figure 1 A). She was further evaluated by an ultrasound of the neck which showed multi nodular goitre with retrosternal extension on the left side. Ultrasound of the neck showed ACR TIRADS 4 nodules in both lobes, extra thyroidal lobulated nodule with few cystic areas and the calcified foci along the inferior pole of right lobe of thyroid -? parathyroid adenoma Rt inferior, was also found. A 99mTc-sestamibi imaging without single-photon emission computed tomography/computed tomography was performed, and a possible right inferior parathyroid lesion was detected (Figure 1 B). She underwent total thyroidectomy, right inferior para thyroidectomy (Figure 1 C and D) and central compartment lymph node dissection. Intra operatively, the right inferior parathyroid lesion was seen very close to the lower pole, antero-medial to the right RLN. The right superior parathyroid was normal in size, shape and consistency. The right inferior parathyroid lesion was 45×20×25 mm. After its excision IOPTH fell to 51 pg/ml from a baseline of 1899 pg/ml. The frozen section confirmed the removed gland as parathyroid.

No regional lymphadenopathy was seen. Gross examination of the surgical specimen revealed 40×30×15 mm, 12 gm brownish parathyroid mass and right lobe 40×25×35 mm, left lobe 70×30×40 mm and right lobe has had an irregular nodule of size 12x12x10 mm with calcification (Figure 2A and 2B).

Histopathological examination revealed the right inferior parathyroid lesion as parathyroid carcinoma, 40 mm with capsular invasion with extension in to adjacent fat (Figure 3B). Total thyroidectomy specimen (Figure 3A) reported as papillary carcinoma thyroid 12 mm with a central compartment lymph node showed 1/1 metastasis from papillary thyroid carcinoma. pT1b N1a Mx.

Post-operative day 1, her voice was normal and had symptoms and signs of hypocalcemia which was managed with IV and oral calcium with vitamin D supplementation. She was discharged on post-operative day (POD) 3 with oral calcium and activated vitamin D3 treatment, with a corrected calcium of 8.2 mg/dl. Her calcium was 8.6 mg/dl, 6 months after surgery. She underwent low dose radioactive iodine ablation therapy and was on suppressive dose of levothyroxine. On follow up, after a year, her stimulated thyroglobulin is 0.36 ng/ml (normal <2 ng/ml) and her corrected calcium is 8.8 mg/dl (normal).

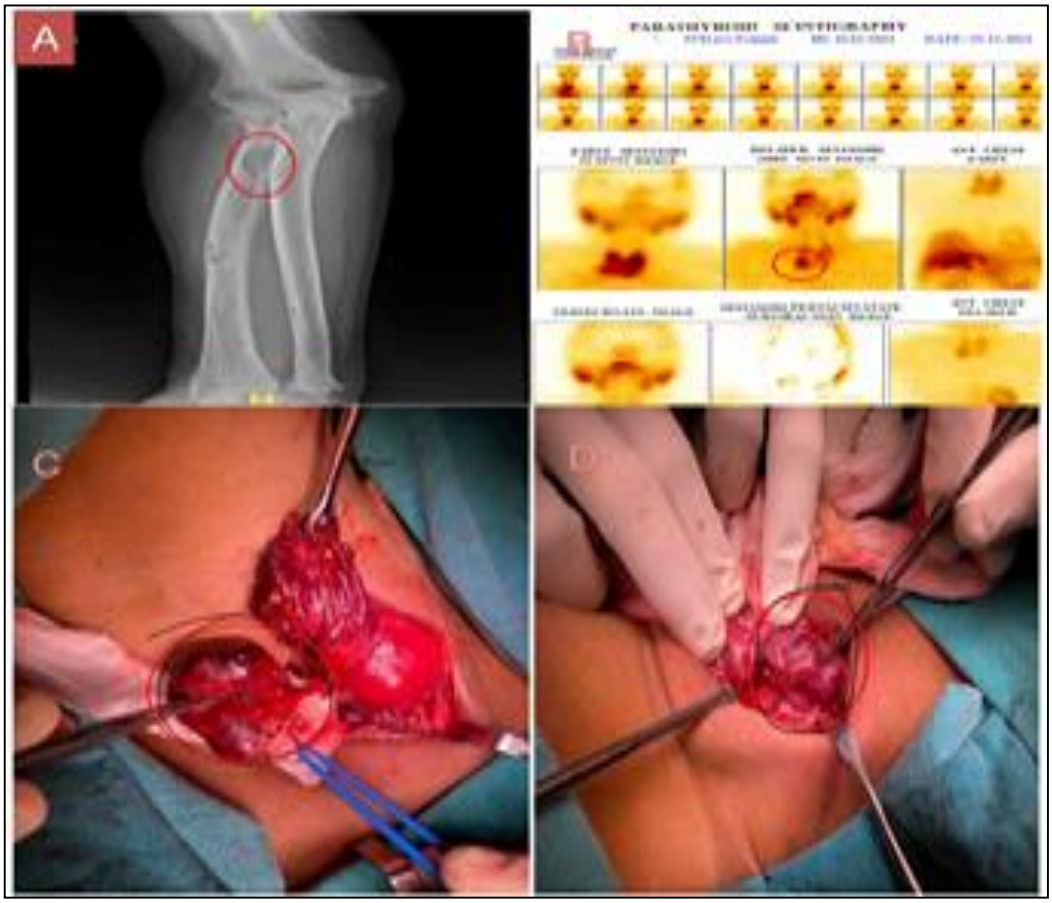

Figure 1 (A-D): X ray of elbow showing osteitis fibrosa cystica, sestamibi of right inferior parathyroid lesion, intra operative picture showing parathyroid lesion and intra-operative picture showing a thyroid nodule.

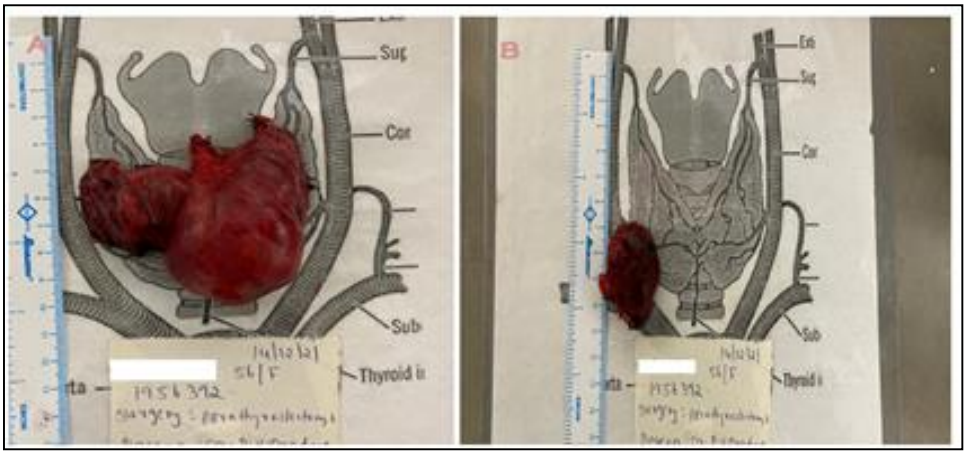

Figure 2 (A and B): Specimen picture of total thyroidectomy, specimen picture of parathyroidectomy.

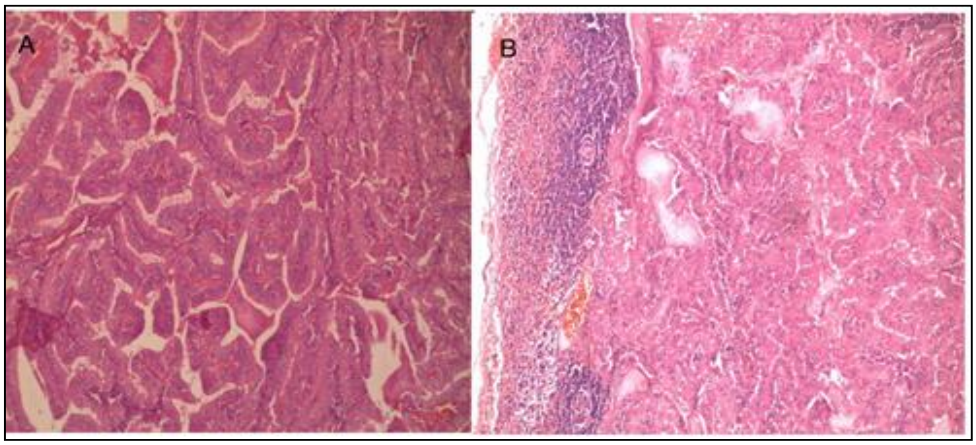

Figure 3 (A and B): Papillary thyroid carcinoma.

Table 1: Laboratory investigations.

Parameters	Limit	Normal range
S. calcium (corrected) (mg/dl)	12.9	8.6-10
S. phosphorous (mg/dl)	2.6	3.5-4.5
Alkaline phosphatase (IU/l)	1127	35-129
S. creatinine (mg/dl)	0.5	0.55-1.02
Vitamin D (ng/ml)	13.77	20-30
Parathyroid hormone (Pg/ml)	1899	10-75
Post op PTH 10 min post excision (Pg/ml)	84	10-75
Post op PTH 20 min post excision (Pg/ml)	51	10-75
S. calcium post op day 1 (Corrected) (mg/dl)	8.2	8.6-10
S. calcium post op day 2 (Corrected) (mg/dl)	8.6	8.6-10
S. calcium post op day 30 (Corrected) (mg/dl)	8.2	8.6-10
TSH (mIU/l)	1.19	0.5-4.5
Prolactin (ng/ml)	10.97	<25

DISCUSSION

The co-occurring existence of parathyroid carcinoma and thyroid carcinoma is very rare with only 16 documented cases in the literature. The current case is the first case report from India. The summary of our case is described in Table 1 as compared to other case reports. As per SEER data, the base mean age for parathyroid carcinoma presentation was forty five years with almost equal distribution among genders and was seen between the 4th-5th decade of life in women.[3,4] In the reported cases, the youngest patient had Hurthle cell carcinoma which was associated with poor prognosis and higher recurrence as compared to PTC.[5] Most of the cases are functional, including our case, and only one case was non-functional parathyroid carcinoma occurring with papillary micro-carcinoma and as double parathyroid carcinoma.[6] This non-functional parathyroid carcinomas has a reduced survival, mostly because of its lack of symptoms and aggressive biology.[7] In the reported cases, most of the parathyroid carcinoma were localized to the left lower neck, whereas our case was localized to the right lower neck.

Table 2: Parameters of 16 patients with parathyroid and thyroid carcinoma.

Case reports	Age/ sex (Years)	Calcium (mg/dl)	PTH (pg/m)	Size (mm)	Location	Thyroid carcinoma	Surgery	Outcome
Kurita et al[15]	68/F	12.2	6300	42×32×24	Left lower	PTC	En bloc resection	Post op normo-calcemia
Christmas et al[16]	62/F	Hypercalcemia	Unknown	Unknown	Unknown	FTC	Unknown	Died from metastatic para-thyroid ca
Savli et al[17]	47/F	Normal	Normal	Normal	unknown	PTC	TT + para-thyroidectomy	Normo-calcemia (1 year)
Bednarek et al[18]	42/F	15.4	1655	50	Left lower	FTC	En bloc	Persistent hyper-calcemia
Schoretsanitis[19]	55/F	14.2	>1000	30×30	Left inferior	PTC	En bloc	Normocalcemia (6 year)
Kern et al[20]	54/F	Unknown	465	25×18×16	Right inferior	PTC and FTC	Right para-thyroidectomy +TT+ local lymph node resection+corticectomy in right superior frontal gyrus	Died from intra cranial metastasis from parathyroid carcinoma
Lin et al[21]	38/M	16.5	351	40×30×30	Left lower	PTC	Total thyroidectomy +left para-thyroidectomy	Normocalcemia (6year)
Goldfarb et al[22]	58/M	14.4	2023	34×33×22	Left lower	PTC	En bloc resection	Persistent hypercalcemia after resection. Normocalcemia after excision of contra lateral parathyroid adenoma (1 year)
Marcy et al[23]	42/F	14.1	383	13	Right inferior	PTC	TT+CCLND+ Rt inferior para-thyroidectomy	Normocalcemia (14 months)
Amoodi et al[24]	48/F	Unknown	186	>50	Left inferior	PTC	En bloc resection	Persistent hyper-calcemia, after completion of para-thyro-idectomy hypocalcemia
Chaychi et al[25]	79/F	10.4	89	11×12×48	Left superior	PTC	TT+left parathyroidectomy	Normocalcemia (6 months)
Zakerkish et al[26]	21/M	13	1311	Unknown	Unknown	HCC	TT+parathyroidectomy	Persistent hypercalcemia
Song et al[27]	45/F	17	1455	42.8×30. ×25.4	Left lower	PTC	Left HT+ left inf para-thyroidectomy + left neck dissection	Persistent hyper-calcemia, after left lobectomy and neck dissection normo-calcemia (6 months)
Baek et al[28]	68/F	12.8	1247	42×33×31	Left lower	PTC	Left HT+ left inf para-thyroidectomy	Normocalcemia
Kuzu et al[29]	52/F	11.4	208	Unknown	Unknown	PTC	Right parathyroidectomy and right hemi-thyroidectomy	Normocalcemia
Cesar ernesto et al[30]	50/F	13.9	1160	24x18x14	Left superior	PTC	Left inferior parathyroidectomy + Left HT	Normocalcemia
Our case	56/F	12.9	1899	40x30x15	Right inferior	PTC	Right inferior para-thyroidectomy +TT+CCLND	Normocalcemia

Risk factors for PC are neck irradiation, hereditary HPT-jaw tumor syndrome, long standing secondary hyperparathyroidism and end-stage renal disease. Other molecular pathogenesis for PC include mutations in parafibromin and cyclin D1.[8] Our patient had not undergone genetic testing. In our case, it was a functioning parathyroid tumor with marked hypercalcemia and high PTH levels and renal and bone disease. Hence, we suspected PC pre operatively. As she had concomitant retrosternal goitre with ACR TIRADS 4 score, total thyroidectomy was also done. Post operatively she was diagnosed to have parathyroid carcinoma and papillary thyroid carcinoma.

Histopathological criteria to diagnose PC consist of local or distant metastasis, capsular or vascular invasion with extension to adjacent tissues. Criteria for diagnosis were initially described by Shantz and Castleman in 1973 which includes lobular architecture separated by fibrous trabeculae, cytonuclear atypia and mitotic figures.[9] In our case, parathyroid lesion had capsular invasion with extension in to adjacent fat tissue.

Radical surgery is the best possibility of a cure. There was no difference in the overall survival for a localized PC in local resection or radical surgery.[10] More than 50% of the patients have persistent or recurrent disease. If the recurrent disease is resectable, that will give a better outcome. Morbidity and mortality related to parathyroid carcinoma depend upon the severity of hypercalcemia and not on the tumor burden.[11] Adjuvant treatment like chemotherapy or external beam radiotherapy will not affect the overall survival in parathyroid carcinoma.[12] Patients with tumor >3 cm and metastatic disease have worse cancer specific survival.[13]

Concomitant thyroid disease is not uncommon in patients with PHPT. A pathological association between thyroid disease and parathyroid disease has been reported in various studies. Recent studies found that the prevalence of differentiated thyroid malignancy with PHPT is 2-28%.[14] Papillary micro carcinoma is commonly associated with PHPT. In concomitant DTC and PHPT, DTC will have high risk features as compared to DTC in the general population. Treatment for DTC includes total thyroidectomy, radioactive iodine (I^{131}) ablation, TSH suppression therapy and follow up with thyroglobulin and anti-thyroglobulin.

CONCLUSION

Concomitant papillary thyroid carcinoma and parathyroid carcinoma is a very rare malignancy. There should be a high clinical suspicion if there is marked hypercalcemia, very high parathyroid hormone levels, palpable neck mass, recurrent laryngeal nerve palsy due to invasion, severe bone and renal symptoms. The histological diagnosis can be challenging and capsular invasion and metastasis are strong pathological indications of carcinoma. En bloc resection at the earliest is the optimal treatment unlike non-surgical treatments like chemotherapy and radiotherapy which are not satisfactory. Long-term follow up is required as recurrence can occur many years after apparently successful treatment. Further multicentric studies are also needed to standardize the overall management.

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