INTRODUCTION

Parathyroid carcinoma constitutes about 1% of all cases of primary hyperparathyroidism (PHPT). Their presentation is clinically and biochemically similar to parathyroid adenoma, especially in Indians. Pathologically, unless the parathyroid tumor satisfies the well-described criteria of malignancy, the tumor may not be labeled as carcinoma by the pathologist. Some of these adenomas are labeled as “atypical adenoma.” Even though during surgery, presence of firm, lobulated grayish-white tumor induces suspicion of malignancy, pathological confirmation is necessary for further adjuvant therapy so as to prevent recurrence. We present a case of PHPT wherein the diagnosis of parathyroid carcinoma was made after recurrence of hypercalcemia 3 years from the initial parathyroidectomy, stressing the need to include the gross features as one of the pathological criteria of malignancy in parathyroid tumors.

CASE REPORT

A 40-year-old lady presented 3 years back with recurrent fractures. There was history of pancreatitis and renal stones in the past. She was bed-ridden due to the fractures, muscle weakness, and severe fatigue. Biochemical evaluation revealed serum calcium 13.3 mg% (Range 8.4-10.5 mg%), serum phosphorus 1.8 mg% (2.5-4.2 mg%), S iPTH 1891 pg/ml (20-60 pg/ml), S alkaline phosphatase 4320 IU/L. USG neck revealed 2.38 × 1.6 5 × 1.58 cm well-defined hypoechoic lesion in the region of the left inferior parathyroid gland, which was also clinically palpable. At surgery, grayish-white, firm, left inferior parathyroid tumor was identified. The gross intra-operative features led to a suspicion of parathyroid carcinoma, even though there was no local invasion or regional lymphadenopathy. Hence, left hemithyroidectomy was also performed along with the tumor excision. Other 3 parathyroids were inspected and found to be normal in size, shape, and position. Intra-operative PTH demonstrated >80% drop in the iPTH after excision. The histopathology report was

ABSTRACT

Pathological criteria alone do not make an accurate diagnosis of parathyroid carcinoma in cases of well-defined organ contained lesion without local and distant metastasis. Intra-operative appearance of pale, grayish, firm tumor is highly suggestive of parathyroid carcinoma, even though this finding is not included in the pathological criteria for diagnosing a malignancy. Gross features of the tumor also should be added to the pathological criteria so as to ensure an accurate assessment of the biological behavior of the parathyroid tumor.

Key words: Adenoma, parathyroid carcinoma, primary hyperparathyroidism

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adenoma [Figure 1a and b]. Immunohistochemistry for malignancy (Rb protein) was not performed. She was under follow-up every 6 months. Patient was having normal serum calcium and iPTH for 3 years after surgery; however, she later developed hypercalcemia. At the second admission, her serum calcium was 15.8 mg%, S iPTH 822 pg/ml. Ultrasound neck and MIBI scans revealed the local recurrence [Figure 2a and b]. No distant uptake of MIBI was noticed, ruling out a distant metastasis. X-ray of the chest and USG abdomen also did not reveal any distant metastasis. Re-exploration revealed recurrence at the previous surgery site and hence, a wide local excision with the adjoining strap muscles was performed. The histopathology confirmed parathyroid carcinoma [Figure 3]. At a follow-up of 3 months, patient has normal calcium and iPTH levels.

**DISCUSSION**

After the first description of parathyroid carcinoma by Armstrong in 1933, several cases have been reported including case series.[4] For the optimal management of parathyroid carcinoma, it is important to diagnose it at the time of the first surgery. Parathyroid carcinoma presents with clinical features similar to all other causes of primary hyperparathyroidism, and it is extremely unusual for the parathyroid carcinoma to present with lymph nodal or distant metastasis.[1] Hence, in organ contained parathyroid carcinoma, it is vital to make a diagnosis at least during the histopathology for optimal surgical and other adjuvant therapy.

Gender and age are of no help in distinguishing between parathyroid adenoma and carcinoma.[1] Various studies have mentioned that clinical and biochemical features may help to distinguish between parathyroid adenoma and carcinoma. Serum calcium >14 mg% at diagnosis, marked elevation of iPTH are said to be suggestive of parathyroid carcinoma. [1] Palpable tumors are said to be commonly associated with carcinoma.[3] It has also been mentioned that higher incidence of symptomatic disease (95% vs. 20%), renal stones (80% vs. 18%), skeletal disease (90% vs. 5%) helps to distinguish parathyroid carcinoma from adenoma.[1] However, in a study from one of the high volume centers in India,[2] it has been observed that these clinical and biochemical features do not distinguish between parathyroid adenoma and carcinoma. Hence, clinical, biochemical features have doubtful role in the final diagnosis.

The pathological diagnosis of parathyroid carcinoma is made on the criteria proposed by Schantz and Castleman (1973), based on their findings in 70 cases of parathyroid carcinoma.[8] They mentioned presence of mitosis within parenchymal cells as the single most important criteria for carcinoma. This was observed in 81% of their cases. Presence of fibrous trabeculae with lobulated architecture was proposed as the other major criteria (90% cases). However, the authors cautioned that scarring from previous hemorrhage or surgery may appear histopathologically indistinguishable from the fibrous bands. In their series, capsular invasion and vascular invasion was seen only in 67% and 12% of cases, respectively.[8] Contrary to this, other studies have opined that capsular and vascular invasion correlates best with local recurrences.[1] Nuclear diameter is said to be greater in carcinoma. Even though mean nuclear content and aneuploidy appears to be greater in carcinoma,[8,9] the latter is also frequently seen in adenomas. Nuclear pleomorphism and macronucleoli are also said to be associated with carcinoma. None of these pathological findings were seen in our case at the time of the first histopathological examination. Since many of these...
features individually do not make a clear-cut pathological diagnosis of parathyroid carcinoma, a combination of histological findings gives a diagnosis closer to the biological behavior of the tumor.[10,11]

Since the diagnosis is difficult, especially in the setting of absence of local invasion and metastasis, only long-term follow-up can ensure that the tumor was indeed benign. Local recurrence and development of metastasis are signs of malignancy. Prognosis is said to be poor for recurrences within 2 years after first surgery.[8] However, waiting for local recurrence may rob the patient of early adjuvant therapy and/or more extensive local surgery. It has been consistently reported in various studies that the intraoperative findings of grayish, firm tumor with dense adhesions to thyroid capsule and presence of lobulations should arouse the suspicion of malignancy.[4,6,12] Figure 4 shows the gross appearances of adenoma vs. carcinoma. Once these findings are seen, an aggressive surgical strategy has to be adopted. Hemithyroidectomy and clearance of fatty tissues around the tumor is to be performed, ensuring that the local recurrences are delayed. The gross appearance and consistency of the tumor also has to be included into the present pathological criteria to predict the biological behavior more consistently.

In the present case, even though the pathological criteria of malignancy was not fully satisfied, the gross features were pointers towards malignancy, hence more extensive surgery was performed at the first operation than what was planned. Hence, the recurrence was delayed to 3 years, which would have been earlier if extensive surgery was not performed. At the second surgery for the local recurrence, further wider local excision along with strap muscles have been performed, and we further plan for local radiotherapy. Radiotherapy has been shown to decrease the recurrence.[3] Use of radiotherapy has also been controversial since some believe it to be a radio-resistant tumor.[11]

To conclude, the gross operative findings also need to be included in the pathological criteria for malignancy in parathyroid carcinoma so that appropriate adjuvant treatment is ensured.

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