中文題目：副甲狀腺癌

英文題目：When should parathyroid carcinoma be considered?

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Introduction:

Parathyroid carcinoma is a rare endocrinemalignancy, and it remains a big challenge to differentiate preoperatively benign causes of primary hyperparathyroidism frommalignant etiologies. Clinical presentations of functional parathyroid carcinoma arenot different to those with primary hyperparathyroidism which includes general weakness, depression, anxiety, obtundation, constipation, pancreatitis, decreased bone mass, renal dysfunction, hypercalciuria, nephrolithiasis, hypertension, enlarged left ventricular of heart and etc.Here, we present a case that presented initially with general weakness which was suspected to result from urinary tract infection, and subsequently foundto be caused by severe hypercalcemia related to parathyroid carcinomawith primary hyperparathyroidism.

Case Presentation:

This 74-year-old woman was admitted to Taipei City Hospital Renai Branch on May 22th of 2022, due to proximal and distal limb weakness. She had underlying disease of type 2 diabetic mellitus, hypertension, hyperlipidemia and dementia under regular follow up at outpatient department.

During hospitalizing, the laboratory data showed leukocytosis (22740 uL [3540-9060 uL]), and pyuria (WBC 6-9/HPF, [0-5/HPF]). Urinary tract infection was impressed. However, other findings indicated primary hyperparathyroidism: extremely hypercalcemia (Ca: 13.1mg/dL[8.1-10.4]), albumin (2.8 g/dl, [3.5-5.2 g/dL]), increased parathyroid hormone level (929.5pg/mL, [15.0-65.0 pg/mL]), and decreased serum phosphorus (1.9 mg/dL, [2.5-4.5 mg/dL]). Decreased level of serum vitamin D(25-OH-D 12.0 ng/mL, [deficient≦20 ng/mL]) and hypercalciuria (479 mg/24-hour, [100-320 mg/24-hour]) were noted.

Thyroid ultrasonography revealed a 0.4 x 0.34 x 0.31 cm hypoechoic nodule at right lobe, and a 1.17x1.11x1.01 cm hypoechoic lesion at left lower thyroid bed. Parathyroid lesion is suspect. The ^{99m}sestamibi parathyroid SPECT-CT revealed an extrathyroidal hot nodule inferior to the lower pole of the left thyroid lobe, which is consistent with the ultrasonography finding. Dual energy X-ray absorptiometry of bone (DXA) of lumbar spine revealed T-score -3.06. No salt and pepper skull, rugger jersey spine or distal phalangeal erosion and calcification were seen on head, neck and hands X-ray.

Simple parathyroidectomy was performed on June 27th, 2022. Enlarged tumor is found adhered to the left lower pole of thyroid gland, which was extended inferiorly to the thymus. The last histopathological report related a tumor sized 2.6x1.5x1.4 cm. The tumor involved through parathyroid capsule to adjacent fibroadipose tissue but absent of perineural and vascular invasion. The surgical margin was focally involved by tumor. The immunohistochemical analysis demonstrated positivity to cyclin D1, synaptophycin, GATA-3 and Ki-67 (15%).The angiolymphatic permeation was equivocal in CD34 stain. These findings suggested the diagnosis of parathyroid carcinoma.

Around three months after resection, she presented asymptomatic with PTH serum level of 315.9 pg/mL (15-65 pg/mL), serum total calcium level of 7.5 mg/dL (8.1-10.4 mg/dL), and serum phosphorus level of

3.9mg/dL (2.5-4.5 mg/dL). Cervical ultrasonography revealed normal right lobe in size with a nodule (3.7x3.1 mm) in the lower medial portion.

Discussion:

Primary hyperparathyroidism is usually caused by a parathyroid adenoma, primary parathyroid hyperplasia, and rarely, by parathyroid carcinomas.It is difficult to differentiate benign parathyroid disease with malignancies. Compared with patients with parathyroid adenomas, patients with parathyroid carcinomas are more likelyto be diagnosed by mass lesions with signs of malignancy observed by imaging or a tender mass with uneven margins found intraoperatively. Extremely elevated calcium levels (>14 mg/dL) and PTH levels 10 times or more than the upper limit also indicate the higher risk of malignancy. The diagnosis of parathyroid cancer is typically made by pathology finding. In some cases, it may not be diagnosed as malignancy until local recurrence or the occurrence of distal metastases at subsequent follow-up.Some geneticmutations such as germline HRPT2/CDC73 mutations are reported significant relation to sporadic parathyroid carcinoma, and genetic evaluation can play an important role in management of such patients and family members.

Surgery is the mainstaytreatment for both newly diagnosedparathyroid carcinoma andfor recurrences or metastatic disease. If parathyroid carcinoma spread widely and not suitable for surgical resection, aggressivemedical control merely on hypercalcemia can prolong survival time because the morbidity and mortality is mainly associated with severe hypercalcemia.The initial therapy for hypercalcemia of parathyroid cancer is similar to managements for that due to other cause, including IV saline infusion, bisphosphonates, and cinacalcet. Denosumab can be used in patientrefractory to both bisphosphonates and cinacalcet.Ethanol ablation may also be used for unresectable primary or recurrent disease. It helps decrease serum PTH levels and refractory hypercalcemia.Radiation therapy and chemotherapy plays no role of treatment of parathyroid cancer.

Conclusion:

Parathyroid carcinoma is a rare endocrine malignancy. Preoperative diagnosis is challenging and requires a high index of suspicion, with extremely elevated calcium or PTH levels, palpable neck mass, hoarseness, or evidence of lymphadenopathy. Mainstay of treatment with curative intent is en bloc resection with clear surgical margins. Chemotherapy and radiation therapy have a limited role in the adjuvant management of parathyroid carcinoma.