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Diagnostic challenge in parathyroid carcinoma with multiple pathological bone fracture: A case report

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Case Report

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ABSTRACT

Parathyroid carcinoma is a rare cause of primary hyperparathyroidism. It often presents with unspecified clinical manifestation that leads to misdiagnosis. We report a case of a 36-year-old woman who suffered from multiple bone tumours and recurrent bone fracture for 3 years ago, and misdiagnosis as only a giant cell tumours of the bone. Then, the patient continued to develop another mass in the neck that kept growing and the mass move on swallowing. The clinician diagnosed her as a colloid goitre based on cytological examination from fine-needle aspiration biopsy. Elevated parathyroid hormone level, hypercalcemia, and suspected parathyroid adenoma in the Sestamibi Parathyroid scan led the clinician to perform a frozen section in this patient with subsequent histopathological of diagnosis as parathyroid carcinoma. The diagnosis of parathyroid carcinoma continues to be a challenge. Understanding the pathogenesis and multidisciplinary collaboration is important to define an accurate diagnosis and treatment.

Karsinoma Paratiroid adalah penyebab yang sangat jarang pada hiperparatiroid primer. Biasanya disertai gejala klinis yang tidak khas, sehingga mengakibatkan kesalahan diagnosis. Kami melaporkan wanita berusia 36 tahun dengan tumor tulang multipel dan fraktur tulang berulang sejak 3 tahun yang lalu, dan didiagnosis sebelumnya sebagai giant cell tumor of the bone. Lalu pasien mengeluhkan adanya massa lain di leher yang terus membesar dan bergerak saat menelan. Klinisi mendiagnosis sebagai koloid goiter berdasarkan hasil biopsi aspirasi jarum halus. Peningkatan kadar hormon paratiroid, hiperkalsemi, serta pada pemeriksaan pencitraan Sestamibi paratiroid disimpulkan sebagai suatu suspek adenoma paratiroid, sehingga klinisi memutuskan untuk melakukan operasi dengan pemeriksaan potong beku, yang kemudian disimpulkan sebagai karsinoma paratiroid berdasarkan pemeriksaan histopatologi. Diagnosis karsinoma paratiroid hingga kini masih menjadi sebuah tantangan. Pemahaman yang baik mengenai patogenesisnya dan kolaborasi multidisiplin adalah hal yang penting untuk dapat menentukan diagnosis dan terapi yang tepat.

INTRODUCTION

Parathyroid carcinoma (PC) is a rare endocrine malignancy derived from parathyroid parenchymal cells. The reported incidence is from 0.5 to 5% of primary hyperparathyroidism cases in various series.[1] Putri et al. found that the incedent of PC is less than 1% of all disease in parathyroid.[2,3] Parathyroid glands are small endocrine glands, located on the posterior of the thyroid gland, usually, there are four parathyroid glands. They consist of chief cells and oxyntic cells that control the body's calcium levels.[2,4] The risk factor of PC is associated with familial hyperparathyroidism, type 1 multiple endocrine

neoplasia syndrome, chief cell hyperplasia, and radiation.[2]

The aetiology of parathyroid cancer is unknown. Retinoblastoma (Rb), p53, breast carcinoma susceptibility (BRCA2), and cyclin D1/parathyroid adenomatosis gene 1 (PRAD1) genes are oncogenes and tumour suppressor genes which might contribute to development of parathyroid carcinomas.[5] However, none of these has been assigned as a primary role in pathogenesis. Rather than clinical manifestation due to infiltration or metastases of tumour cells, hyperparathyroidism is a major symptom of parathyroid neoplasm. Patients usually presented to the hospital with a history of bone and renal disease or a hypercalcemic crisis.[3]

CASE DESCRIPTION

Our patient was a 36-year-old woman complaining about having pain and mass on both of her upper arms and right thigh. She had been through recurrent fractures for 3 years. The pain started 1 month before she was examined and got worse ever since. In the physical examination, muscle deformity, as well as muscle atrophy, were detected. Additionally, a 4x5 cm, firm, fixed, painful mass in the right humerus was also revealed. The radiological sign of right humerus showed a well-circumscribed lytic lesion suspected as a giant cell tumour (Figure 1).

Histopathological examination of the mass showed a proliferation of giant cells between

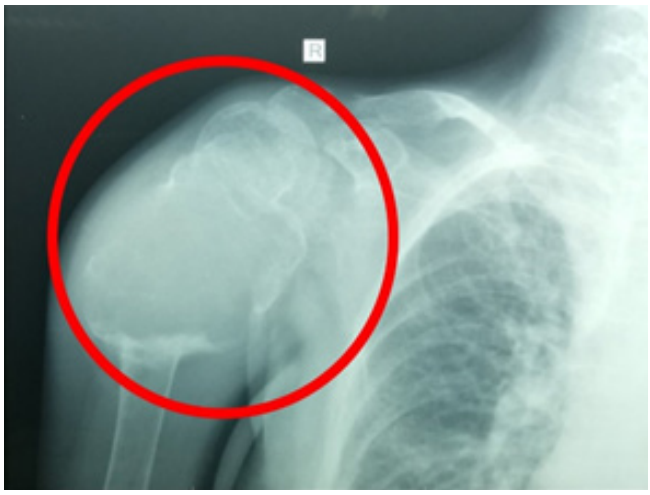

Figure 1. X-ray of right humerus showed a well-circumscribed lytic lesion suspected as a giant cell tumour.

stroma in bone lamellar. Six months after surgery, another mass continued growing. The patient underwent repeated reduction surgeries in the right elbow and humerus. Microscopically, the mass showed round, oval, and spindle cells with pleomorphic nuclei, 1-2 mitotic figures. Numerous osteoclast-like giant cells uniformly distributed throughout the tumour mass and showed positive immunohistochemical staining for CD68, and negative for LCA and Osteocalcin, these lead to giant cell tumour diagnosis (Figures 2 and 3).

She also had radiological signs of bone deformities of costa, clavicula, and bilateral scapula with decreased bone density suspected due to metabolic bone disease. There is an implant for internal fixation in the bilateral femur and left clavicula, and fracture on the right femur (Figure 4). Five-month later, the patient continued to develop another mass in the neck that keeps growing larger and the mass move on swallowing. Ultrasonography showed a

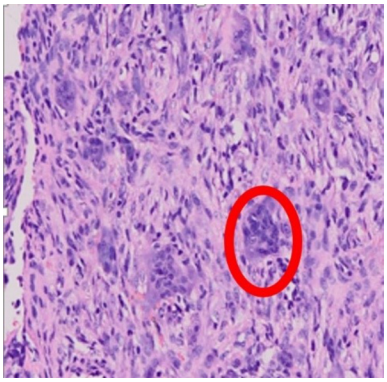

Figure 2. Hyperplasia of round, oval, and spindle cells with pleomorphic, hyperchromatic nuclei, and 1-2 mitotic figures. Osteoclast-like giant cells distributed throughout the tumour (H&E, 100x).

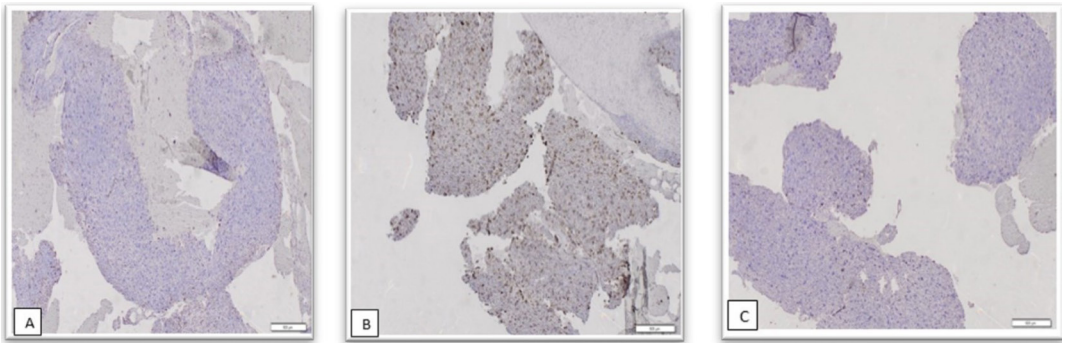

Figure 3. Immunohistochemical staining on giant cell tumor (20x): (A) LCA showed negative expression; (B) CD 68 showed positive expression; and (C) Osteocalcin showed negative expression.

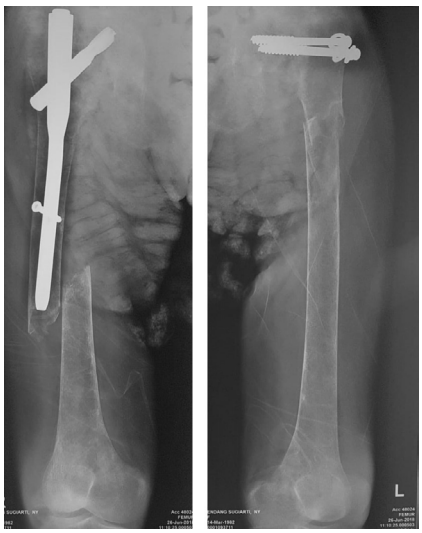

Figure 4. X-ray bilateral femur, a deformity in 1/3 right femur with internal fixation and complete fracture, as well as a deformity in the left femur with internal fixation and fracture.

benign lesion in the thyroid (TIRADS 2) (Figure 5). The result of cytopathology from fine-needle aspiration biopsy was confirmed as colloid goitre. Then the patient was treated with thyrozol, but there was no improvement. Laboratory data showed an increasing concentration of

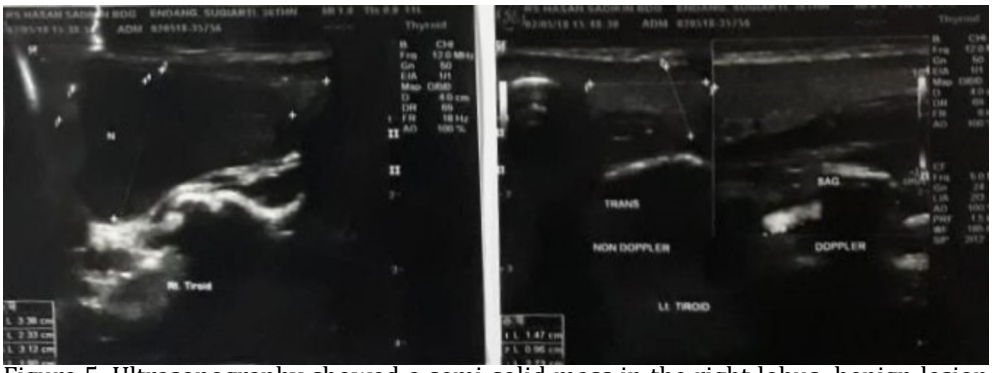

Figure 5. Ultrasonography showed a semi-solid mass in the right lobus: benign lesion (TIRADS 2)

parathyroid hormone (PTH; 1250 pg/ml [normal range 15-65 pg/mL]) and calcium (7.4 mEq/L [normal range, 4 to 5 mEq/L]). The result of the parathyroid Sestamibi scan was suggestive as a parathyroid adenoma (Figure 6).

A pathological examination from the frozen section of parathyroid mass was revealed, macroscopically there were three tan-white soft masses, measuring 7x5x4cm, 1x1x0.5 and 1x0.5x0.2cm. In the cut section, the white

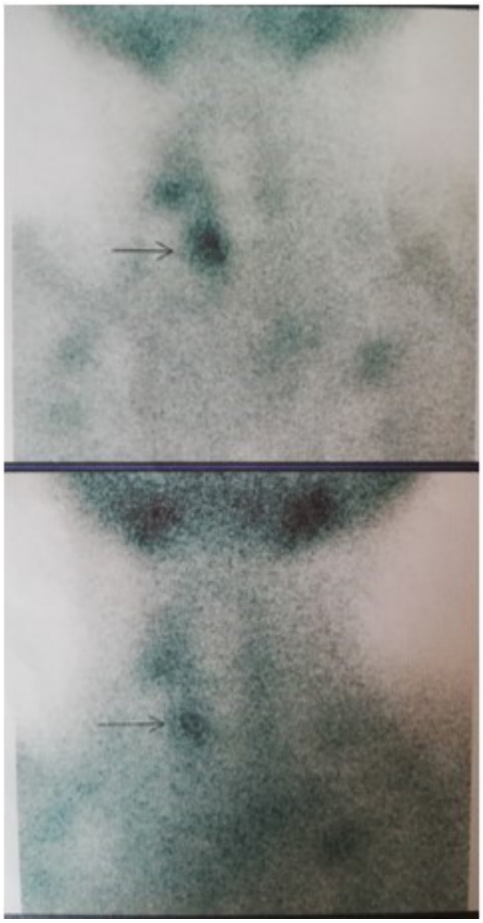

Figure 6. Suggestive parathyroid adenoma in the lower right lobe in parathyroid Sestamibi scan

mass was found. Microscopically, it consisted of round, oval cells differentiated as parathyroid cells, hyperplastic in dense form. The nucleus is pleomorphic with numerous mitotic figures. The tumour mass invaded the thyroid tissue, without any lymphovascular invasion. Thus, it was confirmed as a parathyroid carcinoma(Figure 7).

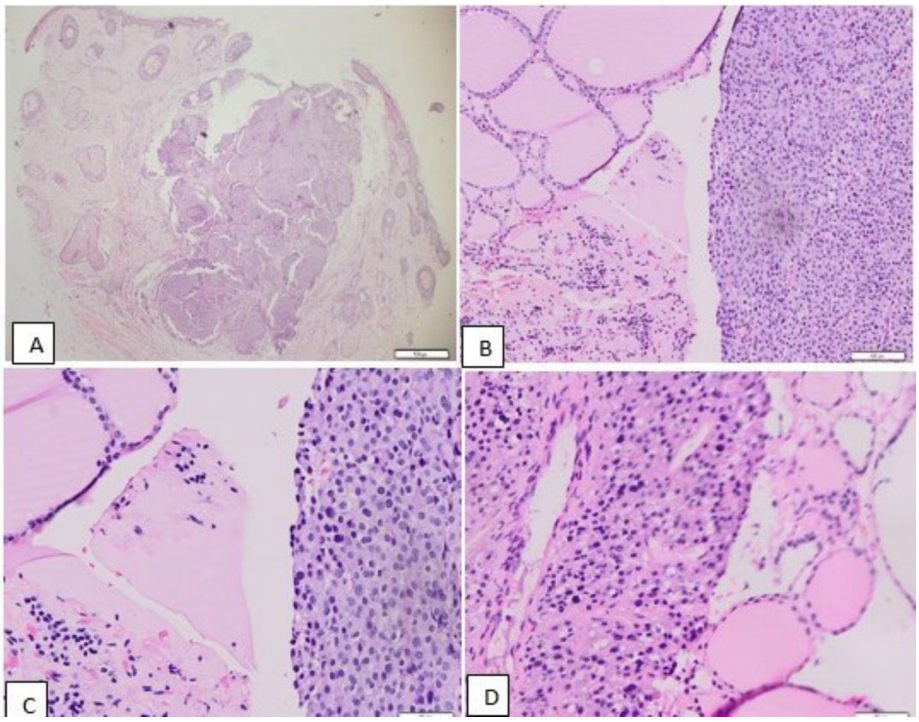

Figure 7. (A) Parathyroid tumour invading the skin (H&E, ×40).; (B) (H&E, ×100); (C) and (D) tumour cells infiltrating thyroid tissue (H&E, x200).

DISCUSSION

Parathyroid carcinoma (PC) is a very rare disease of the parathyroid gland, it accounts for less than 0.005% of all malignancy.[2] PC is a disease of middle life and occurs equally in men and women.[2,3] In this case, the patient is only 36 years old. Ree et al. also reported CP in a 40-year-old patient.[6] There is an increased risk of PC in familial hyperparathyroidism, multiple endocrine neoplasia type 1, chief cell hyperplasia, and prior neck radiation.[2,7] This patient has no identifiable risk factors. Patient with PC often comes without any complaint of mass in the neck, but bone mass or bone pain occurs after multiple pathological fractures.[8] In this case, the patient came after bone pain and multiple fractures in bilateral femur and clavicula, then just after three years she complained of having mass in the neck that continuously grew larger. Rizky et al. and Rizwan et al., also reporting about PC case with a patient who has a major complaint of bone pain.[3,8] Bone pain and multiple recurrent bone fractures are symptoms that are caused by hyperparathyroidism, and parathyroid carcinoma is a causative factor in less than 1% of cases of hyperparathyroidism.[9,10]

PTH level in this patient increased higher (1250 pg/ml) than that reported by Fernandes et al. (301 pg/ml). Increased PTH causes the bones to release calcium into the blood by activating the osteoclast-like giant cell. Therefore, the bone will be more susceptible to fractures.[11,12] The calcium level in this patient was lower (7.4 mEq/L) than the average serum calcium level in patients with parathyroid carcinoma (15.9 mg/dL).[13]

The proliferation of osteoclast-like giant cells in histopathology of the lump in the bone of right humerus and elbow showed reactive

process due to hypersecretion of parathyroid hormone resulting in high bone resorption. Due to the lack of clinical information when the bone specimen was sent to the pathologist, the final diagnosis of the bone specimen in humerus and elbow was a giant cell tumour. After the patient had a bone scan, the result showed metabolic bone disease and suspected for brown tumour. Brown tumour is a giant cell tumour related to hyperparathyroidism.[14] Microscopically, compare to the brown tumour, giant cell tumour has more uniformly distributed giant cells, no interstitial haemorrhage, and no fibroblastic stromal cells.[2] After having a secondary review of the bone specimen and considering the patient's clinical background, the final diagnosis is multiple brown tumours.

The patient complained about mass in the neck that moved on swallowing, FNAB examination found colloid goitre but after treatment with thyrozol, the mass kept growing. The mass was not from thyroid but from parathyroid carcinoma that invaded thyroid tissue. In this case, for FNAB to have an optimal function for diagnostic, it is important to do the FNA procedure with ultrasonography guiding so pathologists will access the solid part of the mass.

None of Sestamibi scan, ultrasonography, and CT scan, can localize the parathyroid carcinoma on the patient even though the sensitivity for localizing parathyroid carcinoma in the neck using ultrasonography, 99mTc Sestamibi scan, CT and MRI were, respectively, 83%, 79%, 69% and 93%.[15] Parathyroid carcinoma case reported by Rizwan et al., even show negative for any pathology of parathyroid in the Sestamibi scan.[12] PC is a challenging diagnostic for the clinician as in the present case, it can only be made after a postoperative histopathological examination.

CONCLUSION

Parathyroid carcinoma is a rare endocrine malignancy. In this case, the patient had multiple bone fractures caused by hyperparathyroidism. This led to a twice misleading diagnosis, at first the clinician didn't recognize the increasing parathyroid hormone, only treat the repeated pathological fracture and diagnosed the bone lesion as a giant cell tumour of the bone. The second problem was when the clinician diagnosed the neck lesion as colloid goitre after FNAB in the neck mass. Regarding PC may cause unspecific major complaint, understanding the pathogenesis and multidisciplinary collaboration are important to define an accurate diagnosis and treatment.

CONFLICT OF INTEREST

There are no conflicts of interest.

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