Case Report

Parathyroid Carcinoma in A Young Adult Parathyroid Carcinoma

Mintegui Gabriela¹*, Ronco Alvaro² and Mendoza Beatriz³

¹Associate professor, Clinic of Endocrinology and Metabolism, Hospital of Clinics, Uruguay
²Associate Professor of Oncology, CLAEH Faculty of Medicine, Uruguay
³Professor director Clinic of Endocrinology and Metabolism, Hospital of Clinics, Uruguay

Abstract

A 21-year-old woman with no pathological history, who consults for a routine check-up. Neck examination revealed a 2-centimeter hard cervical swelling and shoulder tumor was palpated. Laboratory: hypercalcemia, Parathyroid Hormone (PTH) very high at 1312pg/ml, that is, more than 15 times normal. Technetium-99m-sestamibi scintigraphy showed an area of abnormal MIBI fixation on the right lower parathyroid projection. Right upper and lower parathyroidectomy with right lobectomy and surrounding adipose tissue was performed. The postoperative course was marked by normalization of serum calcium and PTH. The pathology was in favor of a parathyroid carcinoma. The diagnosis of parathyroid carcinoma is usually established by the combination of radiological and histological signs. The severity of this pathology is due to severe hypercalcemia and the risk of recurrence and distant metastasis that justify prolonged surveillance.

Introduction

Parathyroid carcinoma is a rare neoplasm that presents in more than 90% of cases as Primary Hyper Parathyroidism (PHP) but constitutes between 0.5% and 5% of these patients [1-3]. It occurs with equal frequency in men and women, between the 4th-5th life decades, with a tendency to local invasion [4]. The W.H.O. diagnostic criteria for this tumor are: presence of distant metastasis, vascular, perineural, or capsular tumor, associated with characteristic histopathological changes such as fibrous trabeculae or mitotic figures [5]. Most parathyroid carcinomas are functional and calcium and PTH levels are usually higher than in benign PHP [6].

Some clinical characteristics may indicate that it is a parathyroid carcinoma [4,7].

- Pulppable cervical mass, unilateral paralysis of the vocal cords, calcemia >14mg/dl
- Plasma PTH levels 10-15fold the normal value
- Renal and skeletal disease simultaneously accompanied by markedly elevated plasma PTH [7].

The histological definition of parathyroid carcinoma to OMS [5] still requires one of the following findings:

- Vascular invasion (vascular invasion) characterized by tumor invading through a vessel wall and associated thrombus, or intravascular tumor cells admixed with thrombus
- Lymphatic invasion
- Perineural (intraneural) invasion,
- Local malignant invasion into adjacent anatomic structures, or
- Histologically/cytologically documented metastatic disease.

In parathyroid carcinomas, the documentation of mitotic activity and Ki67 labelling index is recommended. The genomics' alterations identified in this carcinoma are mainly represented by mutations in the CDC73 gene [8]. CDC73 mutation testing is recommended for all individuals diagnosed with parathyroid carcinoma. Up to 30% of apparently sporadic parathyroid carcinomas are associated with underlying inactivation of germline CDC73 [5]. Skeletal involvement, such as bone pain, osteoporosis, and pathologic fractures, such as long bones or spine, occurs in ≤80% [7]. Initial surgery offers the best prognosis for these patients. The recurrence rate in the first years is high (40-60%). Multiple surgeries are required, which increases postoperative complications [9].

Case Presentation

We report the case of a 21-year-old African American woman, a gymnast who consulted for a general check-up. Unknown family history for being adopted. The analytical study revealed total serum calcium of 15.2 and 16mg/dL (normal ranges (NR) 8.5-10.5), serum PTH 1312 and 1540pg/ml (NR 15-65), calcium 650mg/24h. Normal phosphate and creatinine. She denied symptoms due to hypercalcemia, and reported drinking 3 liters of water linked to exercise. On examination, neck examination revealed a 2-centimeter hard cervical swelling a painless left shoulder tumor was palpated. An X-ray was requested, reporting a pathological fracture of the left humerus (Figure 1A). Magnetic resonance imaging revealed a heterogeneous lytic mass at the proximal end of the same humerus (Figure 1B).
The pathology study reported a 25 x 24 mm parathyroid tumor with perineural invasion, angioinvasion, and invasion of adjacent adipose tissue. Eleven mitoses per 10mm and Ki 67 of 8%. In short: parathyroid carcinoma (Figure 4A-4C).

Discussion

Commonly a functioning neoplasm, with an indolent tendency to local invasion [8]. Therefore, the majority of parathyroid carcinoma have an indolent course and the most frequent clinical manifestations, due to PTH-related hypercalcemia, are similar, but more severe, to benign adenoma. The renal involvement (nephrolithiasis) and bone (diffuse osteopenia, pathologic fractures) involvement is present in up to 80 and 90% of patients, respectively; both present in this patient. The main clinical indicators of malignancy have been reported in many studies and, as stated above, are severe hypercalcemia and high levels of PTH, as well as a large lesion. Although palpation here did not show a large lesion, it was hard and adherent, which aroused suspicion [10,11].

Ultrasonography and MIBI (99mTc-sestamibi scan) are the most commonly used imaging studies to detect enlarged parathyroid due to their higher level of retention in parathyroid masses than healthy parathyroid tissue [12]. Neck ultrasound plays an important role in the preoperative localization of pathological parathyroid glands, but it has low specificity in differentiating carcinoma from adenoma or hyperplasia [13].

It is suggested that some ultrasound characteristics could allow differentiation of carcinoma from adenoma in the preoperative period: large lesions (>3.0 cm) and marginal irregularity with local invasion and heterogeneous echotexture, calcifications and palpability. With these features, the diagnostic performance values of ultrasound for differentiation of carcinoma and adenoma were 100% sensitivity, 96.9% specificity, and 97.4% accuracy [14,15]. Regarding the MIBI, until now it was believed that the MIBI intensity uptake could not differentiate between malignant and benign. However, parathyroid carcinoma was shown to have a higher level of MIBI retention than parathyroid with benign lesions [16]. Complete surgical resection is the only known curative treatment to prevent local recurrence, the lesion must be excised in bloc with clear margins. Although patients with parathyroid carcinoma have a long survival, they often develop local recurrence and/or distant metastases. Most patients do not die directly from tumor burden, but from severe uncontrolled hypercalcemia [11]. Survival rates at 5 and 10 years are less than 50-85%. Adverse prognostic factors are [8].

a) Initial treatment with parathyroidectomy alone
b) Presence of distant/lymph node metastatic disease at the time of presentation
c) Non-functioning parathyroid carcinoma.

Other factors that can aggravate prognosis are: older age [17,18], male gender [19] tumor size [17], higher serum calcium level at diagnosis [18]. A prognostic scoring system has been developed for recurrence-free survival rates in patients with parathyroid carcinoma. It is combined: age >65 years, preoperative calcium levels (> 15 mg/dL), and vascular invasion. These three adverse characteristics can be used to stratify patients and identify those who are at high risk of recurrence and might warrant aggressive surveillance or adjuvant treatment [11].
Conclusions

It has high recurrence rates and considerable mortality from severe hypercalcemia. It should be suspected and treated in a multidisciplinary team to improve its prognosis and complete primary surgical resection’s bloc with microscopically negative margins is the best chance of cure. Although prolonged survival is possible in patients with recurrent disease, the cure is unlikely.

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

References