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MODESTUM

Case Report **OPEN ACCESS**

Multiple endocrine neoplasia type 1 with brown tumors as first manifestation in a patient with pituitary adenoma: A case report

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ABSTRACT

Introduction: Multiple endocrine neoplasia type 1 (MEN 1) is an infrequent autosomal dominant hereditary syndrome. Common manifestations are related to hypercalcemia, which is caused by primary hyperparathyroidism (PHPT). Brown tumors are infrequent as initial presentation of PHPT associated with MEN 1. It occurs in less than 2% of MEN 1 population.

Results: A 36-year-old woman started the disease 25 years ago in an insidious and progressive manner. She presented a soft tumor in the left malar region that progressively increased in volume. We treated recurrent multiple brown tumors in a patient with PHPT and pituitary adenoma.

Conclusion: The follow-up was demanding and multidisciplinary. The long-term prognosis is uncertain; therefore, close monitoring of the patient should be carried out through clinical, laboratory and imaging evaluation.

Keywords: multiple endocrine neoplasia type 1, osteitis fibrosa cystica, recklinghausen's disease of bone, pituitary neoplasms, case reports

INTRODUCTION

Multiple endocrine neoplasia type 1 (MEN 1) is an infrequent autosomal dominant hereditary syndrome with a prevalence of 1 in 30,000 people, and it is characterized by tumors in pituitary gland, parathyroid gland (90%) and pancreas [1,2]. Among main manifestations, hypercalcemia is due to primary hyperparathyroidism (PHPT), causing depression, vomiting, fractures and brown tumors, the latter is a rare sign of initial presentation of PHPT associated with MEN 1, it occurs in less than 2% of MEN 1 population [3]**.** We present a case of MEN 1 in an adult female with facial brown tumors as initial manifestation. We followed the CARE recommendations to write this case report. We obtained the informed consent of the patient.

CASE REPORT

A 36-year-old woman who started the disease 25 years ago in an insidious and progressive manner presented a soft tumor in the left malar region that progressively increased in volume. She went to a hospital where the tumor was removed without further studies. Six years later, she presented another soft tumor in the left submandibular region, consequently, she underwent a surgical resection in Argentina, and it was diagnosed as a brown tumor. Four years later, she presented a mild trauma to the right upper limb, causing a humerus fracture, and multiple lytic lesions were observed on the radiograph.

Subsequently, she sustained a fall, which caused a right femur fracture, and due to this she was asked for serum parathormone (PTH) value 1,100 Ug/ml (20-30). She underwent a cervical scintigraphy (sestamibi-Tc99), finding an area of uptake removed below the lower pole of the left thyroid lobe, suggestive of parathyroid adenoma. In the whole-body scintigraphy, areas of hyperuptake were found in lower right maxilla, proximal third of both humerus, both iliac bones and proximal third of the right femur, which corresponded to brown tumors, thereupon the resection was performed. Neither calcium nor PTH were measured after this first resection. Anatomical pathology confirmed the diagnosis of adenoma.

Three years later she presented galactorrhea, additionally a first measurement of serum prolactin levels evidenced high values, and a magnetic resonance imaging showed a pituitary microadenoma, so she started receiving cabergoline 0.5 mg weekly to the present day. Subsequently, she presented headache, dizziness, asthenia and another tumor in upper right maxilla (**Figure 1**), cataloged as a recurrent brown tumor. After this, several serum parameters were taken: PTH 98.10 Ug/dL and serum prolactin 77 ng/mL were elevated. She underwent

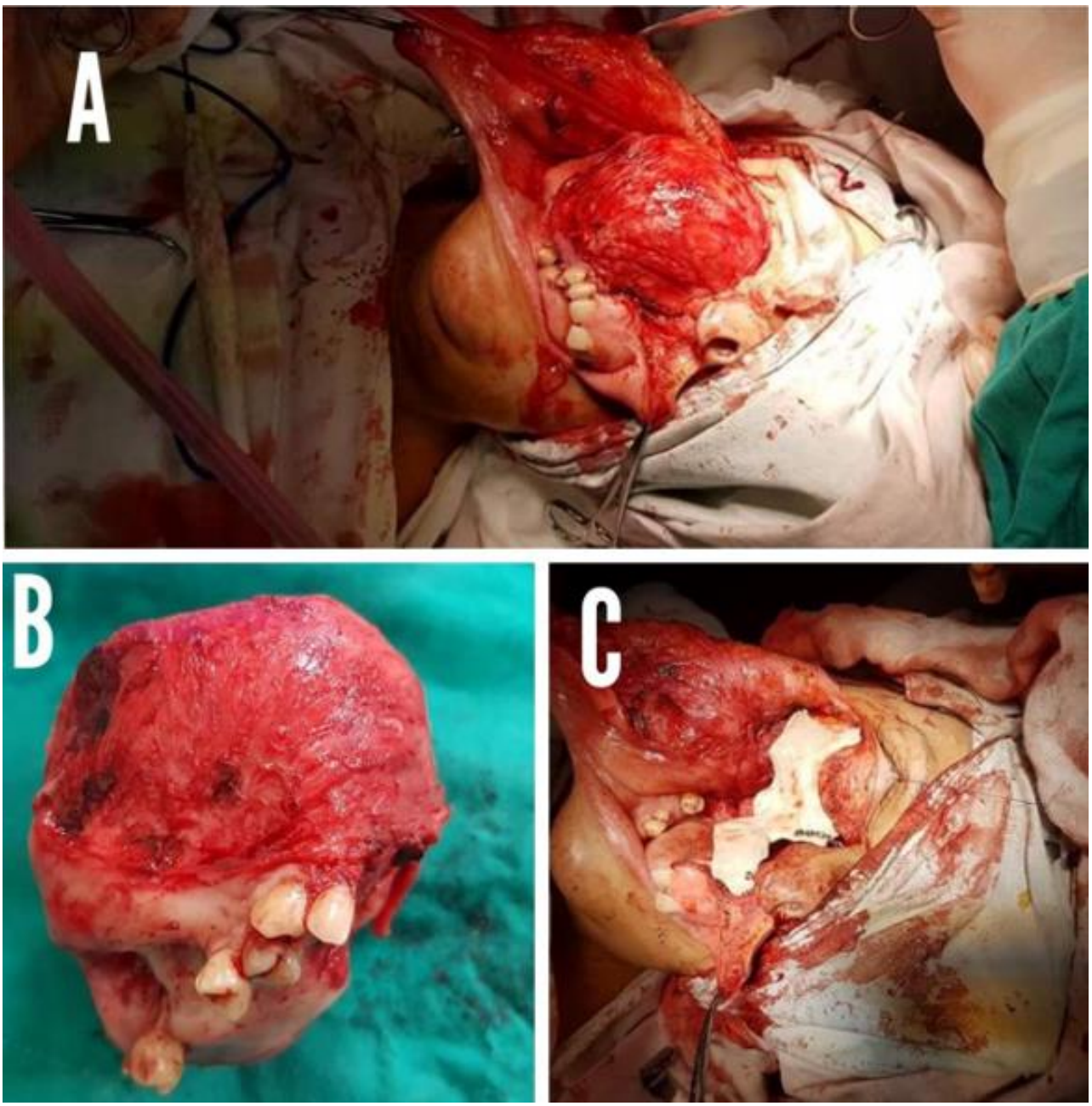

Figure 1. Tumor in upper right maxilla, cataloged as a recurrent brown tumor. (**A**). The brown tumor occupied more than 60% of the right side of the face. (**B**). Surgical resection of brown tumor, dental pieces, gum and a part of palate. Tumor dimensions were 6×5×5 cm. (**C**). Brown tumor removed from the upper right maxilla

another facial surgery successfully and a titanium plate was implanted.

During follow-up, she presented another brown tumor located in the chin. A cervical scintigraphy (sestamibi-Tc99) was requested, it revealed an intrathyroid parathyroid adenoma, consequently right hemiparathyroidectomy and hemithyroidectomy were performed, where a yellowish-colored parathyroid adenoma with dimensions of 2×1 cm and a soft right lower pole was found. During post-operative period, a clear decrease in PTH 1.39 Ug/ml and ionic calcium was evident. At present, the patient is receiving cabergoline, calcium citrate with vitamin D and levothyroxine.

DISCUSSION

Brown tumors are caused by excessive activation of osteoclasts by the action of PTH, replacing osteocytes with fibrous tissue and giant cells that results in bone expansion. The diagnosis of MEN 1 is performed in the presence of two of three tumors in parathyroid gland, pituitary gland or pancreas, clinical suspicion is based on the rise of hormones of the affected organs, a genetic sequence analysis or a genetic deletion/duplication analysis can be performed to detect MEN 1 gene.

There have been few case reports of facial brown tumors due to PHPT [4], and few of them have been associated with MEN 1 in long term. The diagnosis in our patient was made by the presence of endocrine tumors: A prolactin-secreting pituitary microadenoma and multiple brown tumors

secondary to PHPT. At the beginning, patients are asymptomatic, however MEN 1 affects more than two parathyroid glands in 90% of patients [2], so if it is not identified in time it could cause serious complications, such as nephrolithiasis, osteoporosis, bone fractures, severe hypercalcemia and osteitis fibrosa cystica (OFC).

Brown tumors are a localized form of OFC, which histologically is difficult to distinguish from giant cell granulomas, and should be considered as a differential diagnosis to malignant tumors, cherubism, aneurysmal bone cysts, osteochondromas, metastatic carcinoma and fibrous dysplasia [5]. Clinical suspicion of brown tumors as an initial manifestation of the disease is infrequent due the lack of serum calcium routine tests, which can detect hypercalcemia in time in asymptomatic or mild symptomatic stages, in such a way that it does not progress to developing brown tumors. Nevertheless, it has been reported development of brown tumors with serum calcium in normal range [6], which makes PHPT diagnosis much more complicated, therefore a delayed MEN 1 diagnosis is made. Only 0.8% of patients with PHPT develops brown tumors [7]. The frequent locations are clavicle, ribs, tibia, femur and the pelvic girdle, and the less frequent locations are head and neck, but when it occurs, the most affected place is the jaw [8], as in this case.

Occasionally OFC causes pathological fractures as a result of osteoclasts excessive activity. In our patient, brown tumors appeared in the submandibular region, upper jaw and in malar bone, the latter being very infrequent, additionally, the tumor occupied more than 60% of the right side face, and presented multiple osteolytic lesions in the femur and humerus that led her to present pathological fractures. The treatment for these tumors is the surgical removal of the parathyroid, then brown tumors spelling disappears in time [9]. In this case, brown tumors disappeared after correction of hyperparathyroidism, in fact, their tissues calcified, and resection was necessary owing to the large size of the brown tumor.

There are few cases reported in the literature about initial presentation of facial brown tumors and PHPT in patients with MEN 1, so it could go unnoticed. Finally, we must take into account the reappearance of these tumors after years in this pathology, and calcium levels should be monitored in all patients with bone lytic lesions, especially in those pathologically confirmed as a growing giant cell tumor, as is in this case.

CONCLUSION

The follow-up of the patient has been complex, demanding and multidisciplinary, due to the fact that she underwent multiple laboratory tests, imaging and surgical interventions for MEN 1 complications. The long-term prognosis is uncertain and life expectancy is lower compared to other individuals, for this reason close monitoring of the patient should be carried out through clinical, laboratory and imaging evaluation. Finally, calcium levels should be monitored in all patients with bone lytic lesions.

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