PRIMARY HYPERPARATHYROIDISM PRESENTING AS UNILATERAL EXOPHTHALMOS

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Abstract — Primary or secondary hyperparathyroidism can present with a brown tumor of the mandible. Involvement of other skull and facial bones is extremely rare. Only a few cases with brown tumor of the orbital bones have been reported. An 18 year old girl with primary hyperparathyroidism presented with unilateral exophthalmos caused by brown tumor of the orbital roof. The patient had a 1.5 cm palpable parathyroid adenoma and significant widespread hyperparathyroid bone disease. After parathyroid excision and excision of the brown tumor of the orbit, the patient has remained asymptomatic and normocalcemic during a 16 year follow-up. The bone lesions of hyperparathyroidism have completely healed. This report documents brown tumor of primary hyperparathyroidism as a rare cause of unilateral exophthalmos, prolonged follow-up after excision of the parathyroid adenoma showed healing of associated skeletal lesions, a finding ruling out other conditions in this patient. A Medline search in August 1996 revealed fewer than 12 similar case reports. Although brown tumor of the orbit due to secondary or primary hyperparathyroidism is rare, giant cell tumor of the orbit should be considered in patients with orbital tumors presenting with unilateral proptosis.

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INTRODUCTION

The usual causes of unilateral exophthalmos are thyroid - associated orbitopathy (1), orbital tumor (2), intraorbital inflammatory processes (3), and orbital myositis (4). Among the orbital tumors, giant cell tumor of the orbital bones as a cause of exophthalmos is rare (5). Unilateral exophthalmos caused by brown tumor of the orbit in primary or secondary hyperparathyroidism is also unusual (6-11). In hyperparathyroidism, brown tumors occur commonly in the mandible and rarely in the maxilla or other orbital bones (7,12-15). In 1980, Naiman et al. (8) reported a case of brown tumor of the orbit in primary hyperparathyroidism and collected 7 other cases from the literature: 4 with primary hyperparathyroidism and 3 with secondary hyperparathyroidism. Three of the patients had presented with significant proptosis. In this report, we describe a young patient with normocalcemia and unilateral exophthalmos in whom primary hyperparathyroidism was diagnosed after excision of a brown tumor of the orbit, followed by removal of a parathyroid adenoma. A 16 year follow-up did not show any recurrences.

Case Report

An 18 year old single nulliparous woman was referred to the University Hospital in 1978 with a diagnosis of endocrine exophthalmos. She had noted bulging of the right eye of 2 months in duration. She had a 6 month history of nervousness, low back pain, and a sensation of a foreign body in the right eye. On physical examination, height was 158 cm, weight 52 kg, blood pressure 110/70 mm Hg, and pulse rate 80 beats per minute. There was marked proptosis of the right eye: Hertel exophthalmometer readings were 24 mm on the right and 16 mm on the left. The right eye had a mild degree of chemosis and limitation of upward global motion. Funduscopic examination and visual acuity measurements were normal. The thyroid was estimated to weight approximately 20 g on palpation, and there was a 1.5 cm firm nodule in the area of the right lower pole of the tyroid. Results of physical examination were otherwise unremarkable. Results of thyroid function tests, including serum total thyroxine, triiodothyronine resin uptake, and thyroid stimulating hormone, were within normal limits. A thyroid isotope scan showed a cold nodule inferior to the right lobe. Results of routine laboratory studies, including creatine levels, were within normal limits. Serial serum calcium measurements showed values of 9.8 mg/dL, 9.3 mg/dL, and 10.5 mg/dL (normal, 8.5 to 10.5 mg/dL), and serum phosphorus levels were 3.2 mg/dL, 2.5 mg/dL, and 2.8 mg/dL (normal, 3.0 to 4.7 mg/dL). Serum immunoreactive parathyroid hormone measurement was not available at the time. The serum sodium and potassium values were normal. The alkaline phosphatase value was increased at 11.6 King-Armstrong units (normal, 0.8 to 2.8 units). Skull roentgenograms showed destruction of the roof and superior orbital rim on the right side (Fig. 1). Computed tomography of the orbits showed a superior orbital mass.

The orbital tumor was excised through a right frontolateral craniotomy approach. A soft, brownish tumor measuring 3 by 3 by 2.5 cm involving the frontal bone and the roof of the orbit which was adherent to dura mater was completely excised. Tenon's capsule was intact. Histologic examination demonstrated fibrous and

giant cell proliferation with osteoclastic and osteoblastic activity, bone destruction and hemorrhage, and cystic formation. The findings were compatible with a brown tumor (Fig. 2). Postoperatively, a skeletal bone survey showed multiple cystic lesions of the ribs and clavicle. Roentgenograms of the hands showed small cystic formations with subperiosteal bone resorption of the middle phalanges, compatible with hyperparathyroid bone disease (Fig. 3).

Although the patient was normocalcemic, neck exploration was performed with preoperative diagnosis of hyperparathyroidism, and the 1.5 cm nodule in the right lower lobe of the thyroid was excised and proved to be a parathyroid adenoma (Fig. 4). The other parathyroid glands were explored and biopsy was performed; These glands were normal. Postoperatively, bone hunger syndrome with transient hypocalcemia developed, and the patient was treated with intravenous calcium. She remained normocalcemic without therapy on follow-up.

The patient was reevaluated in 1994 at the age of 33 (16 years after the initial operation). There was no evidence of exophthalmos. Results of routine laboratory tests, including thyroid function tests and determination of the alkaline phosphatase value, were within normal limits. The serum calcium value was 9.1 mg/dL, and the serum phosphorus value was 3.8 mg/dL. The serum parathyroid hormone level was also within normal limits. Roentgenograms of the hands were normal, and there was no evidence of subperiosteal bone resorption or cystic formation (Fig. 5).

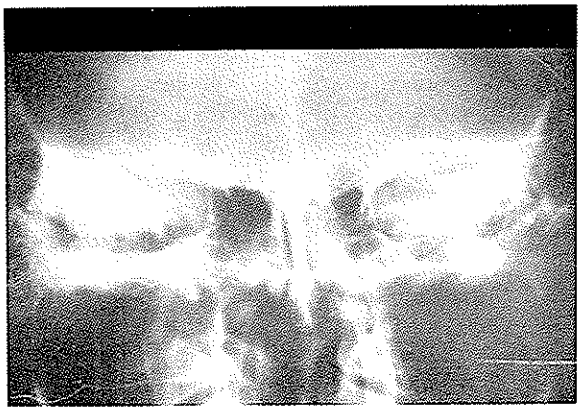

Fig. 1. Skull roentgenogram, showing erosion of the superior portion of orbital rim. Sclerotic lesion of superior external aspect of orbit with thickening of frontozygomatic region is present.

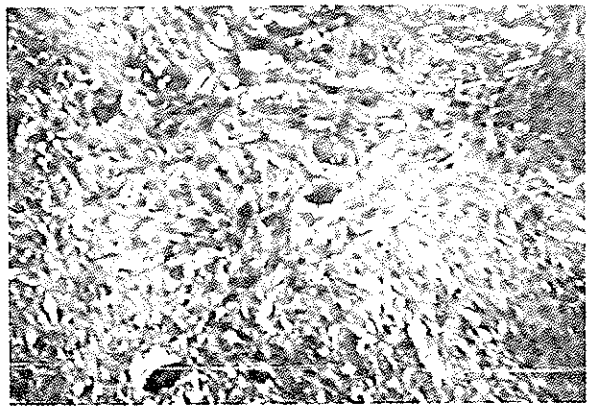

Fig. 2. Brown tumor of hyperparathyroidism removed from orbit, showing spindle cell proliferation and scattered benign giant cells. The lesion is too fibrogenic for a true giant cell tumor. (Hematoxylin - eosin; × 25).

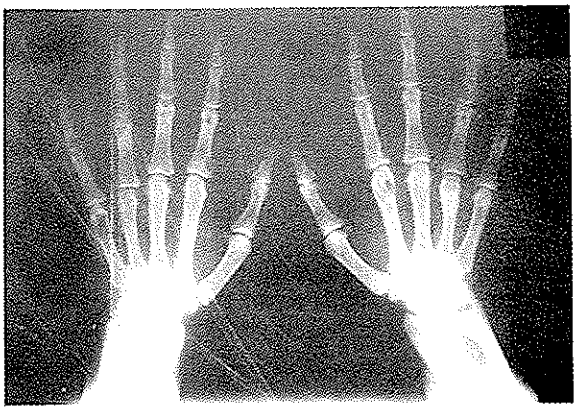

Fig. 3. Roentgenograms of hands, showing multiple cystic lesions in the phalanges. Subperiosteal bone resorption of the phalanges is also present.

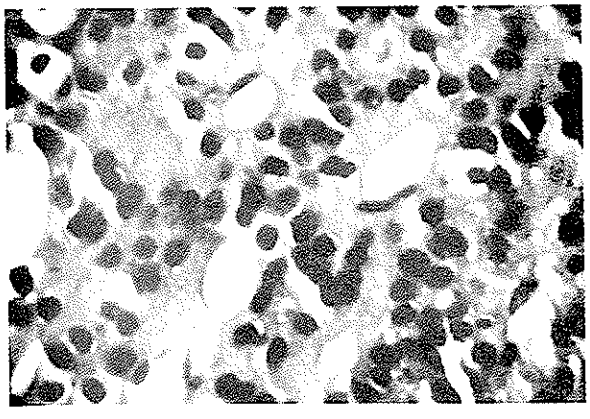

Fig. 4. parathyroid adenoma showing uniform round cells with formation of acinar spaces. (Hematoxylin -eosin; × 1600).

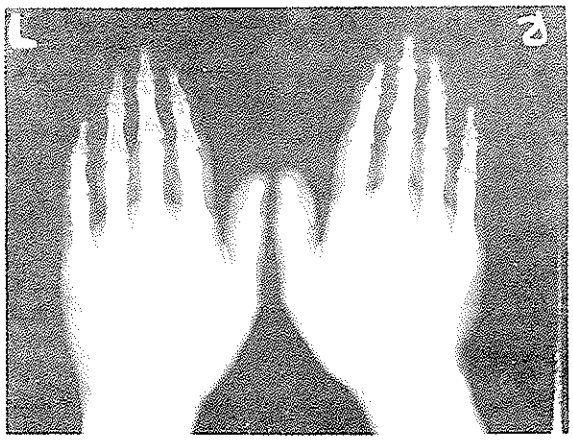

Fig. 5. Roentgenograms of hands 16 years after excision of parathyroid adenoma. Subperiosteal bone resorption of the phalanges has resolved, and lytic lesions are no longer present.

DISCUSSION

Giant cell-containing tumors of orbital bones include true giant cell tumor, giant cell reparative granuloma, aneurysmal bone cyst, and brown tumor of primary or secondary hyperparathyroidism (7). Roentgenographic study alone cannot differentiate among these giant cell lesions (5,8). Histologic features are also similar (5). For a definitive diagnosis, a complete history, evaluation for detection of coexistent systemic bony lesions, evaluation of parathyroid function to determine the presence of primary hyperparathyroidism, and evaluation of renal function to search for secondary hyperparathyroidism are usually necessary. True giant cell tumors are primary neoplasms that occur in a single focus, usually in the ends of the long bones; involvement of the skull and facial bones has been reported, but this is uncommon (5,8). The tumors are usually benign, but they can be locally aggressive and rarely can metastasize to the lung. Reparative giant cell tumor occur in young people and is a reactive process that follows traumatic or infectious injury (8,16-19). These reparative granulomas are more common in the skull bones than are true giant cell tumors, and surgical excision is the treatment of choice (some of these granulomas have involved the orbit). Aneurysmal bone cyst is also a giant cell-containing lesion of unknown orign which usually affects the vertebrae and ends of the long bones (8). A rare case of this giant cell tumor involving the orbital roof also has been reported (20).

Brown tumors associated with primary and secondary hyperparathyroidism are usually multiple. Involvement of the mandible is common (7,8). However, involvement of the maxillary sinus and orbit is rare (7,8,13). In 1980, Naiman et al. (8) reported a brown tumor of the superior orbital rim associated with primary hyperparathyroidism. On review of the literature, they found involvement of the orbit in four cases or primary hyperparathyroidism and in three case of secondary hyperparathyrodism. Three of these patients had exophthalmos. Their ages ranged from 17 to 70 years. There are other isolated reports of brown tumor of the orbit in hyperparathyroidism (6,9,10,12). The involved bones have included maxillary, ethmoid, and frontal bones. Brown tumor of the orbit seems to be extremely rare. Large reviews of giant cell tumors of the skull and facial bones do not include any reference to brown tumor of hyperparathyroidism (5).

We believe that our case has several unusual manifestations. The very young age of the patient, the large palpable parathyroid adenoma, and the widespread osteitis fibrosa cystica generalisata despite the absence of significant hypercalcemia are of interest. Absence of a family history excludes the syndrome of hereditary hyperparathyroidism-jaw tumors (21). Normocalcemia, the lack of evidence of recurrence after 16 years of follow-up, and healing of the bony lesions of the hands exclude parathyroid carcinoma.

In conclusion, althought brown tumor of the orbit due to secondary or primary hyperparathyroidism is a rare condition, giant cell tumor of the orbit should be considered in the differential diagnosis of orbital tumors presenting with unilateral proptosis. Before consideration of therapeutic measures, a systemic evaluation of calcium metabolism is necessary. A histologic differential diagnosis of giant cells tumors of the orbit includes true giant cell tumors, reparative giant tumors, aneurysmal bone cyst, and brown tumors of primary or secondary hyperparathyroidism.

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