Case report

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Ectopic intrathyroid parathyroid adenoma: diagnostic and therapeutic challenges due to multiple osteolytic lesions. Case report.

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Abstract:

Intrathyroid parathyroid adenoma is a rare lesion. Its location is usually achieved by cervical ultrasound and scintigraphy. We present the case of a 48-years old woman admitted for malaise, weight loss, generalized bone pain, and important limitation of hip and scapular-humeral joints mobility. Cervical ultrasound identified a 4 cm nodular mass in the right thyroid lobe. Computed tomography revealed multiple osteolytic lesions in the pelvis, femur, ribs, phalanx, and humerus.Imagery and elevated serum levels of calcium and parathormone led to primary hyperparathyroidism, right parathyroid adenoma and bone "brown tumors". Intraoperatively, the adenoma was found in intrathyroid location. Total right lobectomy was performed. Postoperatively, the patient developed "hungry bone" syndrome requiring prolonged calcium and vitamin D treatment.

Key words: intrathyroid parathyroid adenoma, hyperparathyroidism, ultrasonography, scintigraphy, brown tumor

Rezumat:

Adenomul paratiroidian intratiroidian este o leziune rară, diagnosticată clasic prin ecografie cervicală şi scintigrafie paratiroidiană. Prezentăm cazul unei paciente de 48 ani cu stare generală alterată, scădere în greutate, dureri osoase generalizate, limitarea mobilităţii articulaţiei şoldului şi scapulo-humerale şi dificultate la deplasare. Ecografia cervicală a identificat o formaţiune nodulară de 4 cm la nivelul lobului tiroidian drept iar tomografia computerizată a evidenţiat leziuni osteolitice multiple la nivelul bazinului, coastelor şi humerusului, interpretate iniţial ca determinări secundare. Valorile crescute ale calcemiei şi parathormonului au pus diagnosticul de hiperparatiroidism primar prin adenom paratiroidian drept însoţit de prezenţa "tumorilor brune" osoase. Intraoperator s-a identificat localizarea intratiroidiană a adenomului, practicându-se lobectomia totală dreaptă. Post-operator a dezvoltat un sindrome "hungry bone" necesitând tratament îndelungat cu preparate de calciu şi vitamina D.

Cuvinte cheie: adenom paratiroidian intratiroidian, hiperparatiroidism, ecografie cervicală, scintigrafie, tumori brune

Introduction

Parathyroid adenoma (PA) is the most common cause of primary hyperparathyroidism (85%), other rare etiologies being the parathyroid hyperplasia from family syndromes and parathyroid cancer [1].

PA is a benign tumor, unique in about 90% of cases, generally interesting the inferior parathyroid glands (most commonly the left). Rarely, two concomitant PAs or ectopic locations (such as intrathyroid) can be identified. Identification of intrathyroid parathyroid adenoma (ITPA) by imagery is sometimes difficult, being often an intraoperative discovery that requires special surgical strategy [2]. In this case report we present a patient with ITPA with diagnostic and therapeutic challenges due to the ectopic location and association with osteolytic lesions.

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Case report

A 48 year old woman was admitted for malaise, loss of appetite, moderate weight loss (8 kg in the last 4 months), polyuria, polydipsia, generalized bone pain and altered hip and scapular-humeral joints range of motion. There was neither family history of thyroid or

cancer disease, nor personal record of irradiation to the neck. Clinical examination revealed an increased thyroid volume, grade II WHO, with elastic consistency, mobile with swallowing, and no tenderness. A 3 cm mass in the inferior right pole of the thyroid, well defined, without adherence to the skin was detected. No cervical adenopathy was found.

Thyroid ultrasound revealed a slightly increased thyroid volume (18 ml) with isoechoic homogeneous structure. In the right lobe, a hypoechoic macronodule, measuring 4.2/2.75/3.6 cm, well-defined, inhomogeneous, and hypervascularized centrally and peripherally was described (fig 1).

X-ray exam showed osteolytic lesions with moderate perilesional condensation in the ischio-pubic branch, humerus, right scapula, costal bows, skull, proximal femur, right IIIrd proximal phalanx, and incipient resorption of the distal phalanx of fingers (fig 2). *Thoraco-abdomino-pelvic* computed tomography (CT) showed no evidence of tumor or adenopathy and confirmed the presence of multiple osteolytic lesions measuring between 3 mm to 5 cm. The largest were found in the iliac wing, femoral neck and humerus, initially suspicioned to be bone metastases (fig 3). There were no osteolytic lesions in the spine or sternum. Cervical CT confirmed the mass in the right thyroid lobe, hypodense compared to thyroid parenchyma, without latero-cervical adenopathy, raising the suspicion of a thyroid cancer with bone metastases.

Laboratory tests showed normal levels of thyroid hormones and calcitonin. Elevated total serum calcium of 13.7 mg/dl (normally 8.6-10.2 mg/dl), ionized calcium of 6.12 mg/dl (normally 3.82-4.82 mg/dl) and PTH of 1200 pg/ml (normally < 56 pg/ml) were found. The fine needle aspiration of the cervical mass was performed and no malignant thyroid cells were found. In the cytological specimen *parathyroid cells were not present.*

Technetium-99m sestaMIBI (methoxy-isobutyl-isonitrile) scintigraphy showed intense tracer uptake corresponding to the mass detected by ultrasound and CT (fig 4). DXA evaluation showed the presence of osteoporosis. Iliac crest bone biopsy revealed the presence of a high degree of fibrosis. CD 123 specific immunohistochemical marker for multiple myeloma was negative.

The diagnosis of primary hyperparathyroidism with inferior right parathyroid adenoma was established. Osteolytic lesions corresponded to "brown tumors" caused by fibro-osteoclastic proliferation. Calcitonin 100 IU/day treatment was initiated and surgery was performed. During surgery no extracapsular parathyroid adenoma was identified so total right lobectomy was performed. Histological examination confirmed the presence of the ITPA (fig 5) and no malignant cells were found .

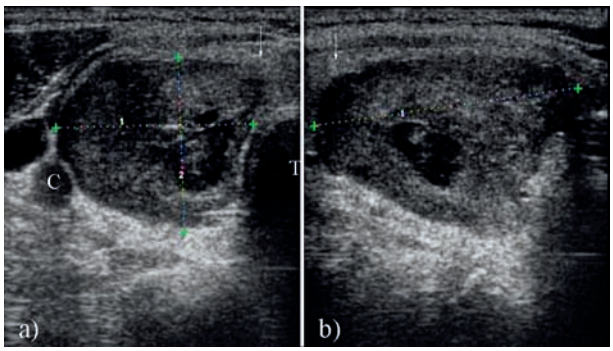


Fig 1. Ultrasound aspect of the intrathyroid parathyroid adenoma in a) transversal view; b) longitudinal view. C-carotid artery, T-tracheea, arrows- compresed thyroid parenchyma.



Fig 2. Hand Rx-ray – osteolytic lesions in the IIIrd proximal phalanx (black arrow), resorption of the distal phalanx of fingers (white arrow).

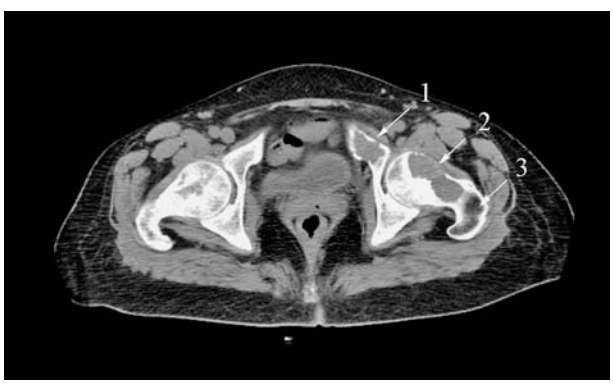


Fig 3. CT scan of the pelvis- osteolytic lesions ("brown tumors") in ischio-pubic branch-1, femoral neck-2, and great trochanter-3.

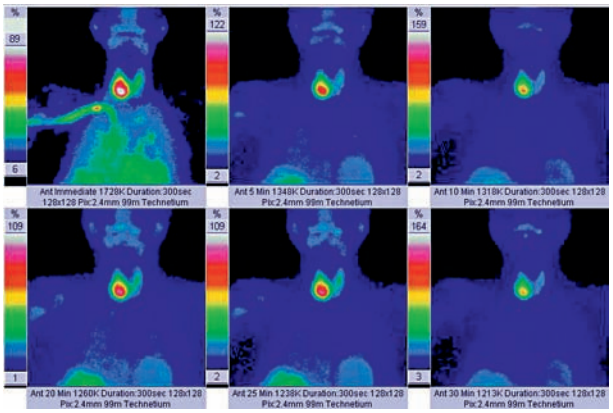


Fig 4. Technetium-99m sestamibi scintigraphy showing intense tracer uptake in the lower right lobe of the thyroid

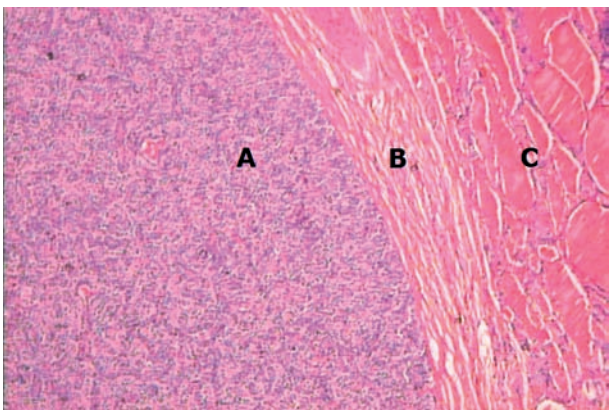


Fig 5. Histological aspect 4XHE: parathyroid adenoma principal cells-A, fibrous capsule-B, thyroid follicles-C.

Postoperatively the patient developed a "hungry bone" syndrome with crisis of manifest tetany requiring prolonged calcium and vitamin D treatment. Bisphosphonates were subsequently introduced. Ionized calcium and PTH levels decreased (45 pg/ml and 4.2 mg/dl respectively) and remained normal within the observation period, one year after surgery the patient being symptoms free.

Discussion

Since the advent of laboratory screening and imaging techniques, hyperparathyroidism is detected with increasing frequency. Primary hyperparathyroidism is more common in women, with a prevalence of 4/1000 women over 60 years. It is estimated that over 85% of diagnosed cases are asymptomatic or oligosymptomatic. Classical clinical picture include osteo-articular signs (bone pains, bone deformities, spontaneous fractures with slow or vicious consolidation, arthralgia), renal and urinary signs, and general signs induced by hypercalcemia.

Our patient had a complex clinical picture suggesting a neoplastic impregnation syndrome, especially in the presence of multiple osteolytic lesions. Differential diagnosis was made with thyroid carcinoma with bone metastases, parathyroid carcinoma, tumors with different localization and secretion of PTH related peptide or intact PTH, other diseases with osteolytic lesions such as multiple myeloma. The osteolytic lesions have turned out to be brown tumors, bone lesions that can occur in both primary and secondary hyperparathyroidism, in fibrocystic osteitis or Recklinghausen's disease of bone. The name of tumor is misfit because the lesion does not have malignant potential (although is sometimes invasive) and must be differentiated from giant cells primary bone tumors. The reported prevalence of brown tumors is 0.1% and has been reported to occur in 4.5% of patients with primary hyperparathyroidism [3]. The most common sites are the hip bones, long bones, clavicle, ribs and jaw. It is more common over 50 years of age and is three times more frequent in women than in men. Brown tumors appear as a mass with partly cystic and partly solid areas. Microscopically, they are characterized by intensely vascular fibroblastic stroma serving as a background for numerous osteoclast-like multinucleated giant cells. Cysts develop as a result of intraosseous bleeding and tissue degeneration [3].

PA is the most common cause of primary hyperparathyroidism. Ectopic locations are rare and include: intrathyroid location, latero-cervical (adenomas were described near the jugular vein, carotid sheath - more frequently at carotid bifurcation), in paraaortic position (aortic arch), on the anterior side of the sternocleidomastoid muscle, inside the hypoglossal nerve [4], paraesophagian, retropharyngeal, anterior mediastinum, aorto-pulmonary window [5] or in the pericardium [6]. Generally, parathyroid tissues are associated with structures related to the third or fourth pharyngeal pouches that traveled to regions where the ectopic lesions ultimately developed. Rarely PA develops from parathyroid tissue that migrates due to an anomalous pathway of parathyroid travel [5].

ITPA are very rare, their incidence is variable depending on the series of evaluated patients. In a retrospective study on 10,000 patients subjected to surgery for primary hyperparathyroidism, PA was identified in intrathyroid position in 0.7% of cases. A total of 1163 reinterventions for persistent primary hyperparathyroidism were examined and the adenoma was subsequently found on the lobectomy side in 64% and on the opposite side in 36% *[7]*. Bahar et al found 6 out of 426 patients (1.4%) who underwent parathyroidectomy for hyperparathyroidism

to have intrathyroid parathyroid glands [8]. In another series of 112 patients operated for ectopic parathyroid adenomas, intrathyroid location was found in 27 patients representing 22.68% of cases [9].

In our patient the imagistic investigation has begun with ultrasound examination of the thyroid. The thyroid nodular mass has raised suspicion of a thyroid carcinoma. Cervical ultrasound is considered to be an accurate imagistic method in identifying PAs which appear as round, oval or polycyclic, with hypoechoic structure compared to thyroid parenchyma, surrounded by a thin hyperechoic border and located outside the thyroid capsule and have to be differentiated from the lymph nodes (oval shape with hyperechoic center, and sit freely around the jugulo carotid axis). The differential diagnosis is more difficult with thyroid nodules, especially when goiter coexists. Ultrasound has the best spatial resolution, the lower cost and greater availability [10].

Rare mediastinal intrathoracic, retro-pharyngeal or para-esophageal ectopic parathyroid glands can not be identified by ultrasound examination due to the lack of acoustic windows.

In a recent study, the cervical ultrasonography has identified the abnormal parathyroid glands in 163 patients with a positive predictive value of 100%. Six patients (3.4%) were found to have ITPA with a positive predictive value of 80% [11].

Ultrasound evaluation should be completed by scintigraphy especially in cases where an ectopic parathyroid is suspicioned. Technetium 99-sestamibi scintigraphy is a sensitive method for PA identification [12]. Single photon emission computed tomography/computed tomography (SPECT/CT) offers the advantage of combining function and anatomy for precise localization of ectopic parathyroid adenomas. Combined SPECT/CT scanners permit more reliable localization of ectopic adenomas [13].

Although the intrathyroid location of a PA is rare, in patients with hyperparathyroidism it should be considered when intraoperative exhaustive exploring of the anterior cervical operative field does not allow the identification of a parathyroid adenoma.

Total lobectomy can be performed. Some authors support the idea that this approach is not efficient because of a high percentage of parathyroid adenoma found in the contralateral lobe [7]. Ideally, intra-operative parathormone measurement in venous blood should be achieved after total lobectomy in order to indirectly confirm the ectopic location. In this case-report, right total lobectomy resulted in removal of parathyroid adenoma with subsequent favorable evolution. More than 1 year after surgery, the patient is symptom free.

References

1. Fang SH, Lal G. Parathyroid cancer. Endocr Pract 2011; 17 Suppl 1: 36-43.
2. Cheng W, MacLennan GT, Lavertu P, Wasman JK. Giant intrathyroid parathyroid adenoma: a preoperative and intraoperative diagnostic challenge. Ear Nose Throat J 2009; 88: E1-3.
3. Soundarya N, Sharada P, Prakash N, Pradeep G. Bilateral maxillary brown tumors in a patient with primary hyperparathyroidism: Report of a rare entity and review of literature. J Oral Maxillofac Pathol 2011; 15: 56-59.
4. Karvounaris DC, Symeonidis N, Triantafyllou A, Flaris N, Sakadamis A. Ectopic parathyroid adenoma located inside the hypoglossal nerve. Head Neck 2010; 32: 1273-1276.
5. Arnault V, Beaulieu A, Lifante JC, et al. Multicenter study of 19 aortopulmonary window parathyroid tumors: the challenge of embryologic origin. World J Surg 2010; 34: 2211-2216.
6. Yadav R, Mohammed TL, Neumann DR, Mihaljevic T, Hoschar A. Case of the season: ectopic parathyroid adenoma in the pericardium: a report of robotically assisted minimally invasive parathyroidectomy. Semin Roentgenol 2010; 45: 53-56.
7. Goodman A, Politz D, Lopez J, Norman J. Intrathyroid parathyroid adenoma: incidence and location--the case against thyroid lobectomy. Otolaryngol Head Neck Surg 2011; 144: 867-871.
8. Bahar G, Feinmesser R, Joshua BZ, et al. Hyperfunctioning intrathyroid parathyroid gland: a potential cause of failure in parathyroidectomy. Surgery 2006; 139: 821-826.
9. Romanchishen AF, Matveeva ZS. Intrathyroid parathyroid adenomas. Vestn Khir Im I I Grek 2007; 166: 40-42.
10. André V, André M, Le Dreff P, Granier H, Forlodou P, Garcia JF. Intrathyroid parathyroid adenoma. J Radiol 1999; 80: 591-592.
11. Abboud B, Sleilaty G, Ayoub S, et al. Intrathyroid parathyroid adenoma in primary hyperparathyroidism: can it be predicted preoperatively? World J Surg 2007; 31: 817-823.
12. Henry JF, Sebag F, Tamagnini P, Forman C, Silaghi H. Endoscopic parathyroid surgery: results of 365 consecutive procedures. World J Surg 2004; 28:1219-1223.
13. Akram K, Parker JA, Donohoe K, Kolodny G. Role of single photon emission computed tomography/computed tomography in localization of ectopic parathyroid adenoma: a pictorial case series and review of the current literature. Clin Nucl Med 2009; 34: 500-502.