

Primary Hyperparathyroidism Through an Ectopic Parathyroid Adenoma

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Rezumat

Hyperparatiroidism primar prin adenom paratiroidian ectopic

Introducere: Glandele paratiroide, de obicei patru la număr, sunt localizate la nivelul regiunii cervicale anterioare. Poziția acestora poate varia, dar de obicei sunt situate posterior de glanda tiroidă. Glandele paratiroide participă în reglarea calcemiei prin intermediul parathormonului, produs ca răspuns la hipocalcemie. Hiperparatiroidismul se definește ca excreția excesivă de parathormon.

Material și metodă: Prezentăm cazul unei femei în vârstă de 48 de ani, internată cu dureri osoase intense, dureri de cap și amețeli. Studiile imagistice efectuate au identificat un mic nodul, hiperfixant la scintigrafia efectuată, în mediastinul anterior. Am decis efectuarea intervenției chirurgicale, în urma căreia nodulul a fost extras și identificat ca un adenom paratiroidian ectopic.

Rezultate și discuții: Evoluția postoperatorie a pacientei a fost favorabilă, fără complicații. Având în vedere că nu există o investigație imagistică cu sensibilitate și specificitate 100% ce singură poate evidenția un adenom paratiroidian, recomandăm ca procedurile diagnostic să include: ecografia cervicală, scintigrafia, tomografia computerizată și IRM. Prin utilizarea medicinei nucleare, sensibilitatea identificării imagistice a adenoamelor paratiroidiene ajunge la 90%. Abordul adeno-

melor paratiroidiene mediastinale este încă controversat, dar considerăm că localizarea precisă preoperatorie a acestora este obligatorie.

Concluzii: Hiperparatiroidismul primar este o afecțiune rară, dar cu manifestări clinice severe. Ea este de cele mai multe ori expresia unui adenom paratiroidian hipersecretant. Diagnosticul trebuie să se bazeze pe identificarea imagistică a formațiunii, tratamentul chirurgical este obligatoriu, iar, în cele mai multe cazuri, postoperator se obține remisia complete a simptomelor.

Cuvinte cheie: adenom paratiroidian, hiperparatiroidism, hipercalcemie

Abstract

Introduction: Parathyroid glands, usually four, are localized at the anterior cervical level, in several positions, on the posterior side of the thyroid gland. Parathyroid glands participate to calcium level regulations by producing the parathormone as a response to hypocalcemia. Hyperparathyroidism is defined as the excess secretion of the parathormone.

Material and method: We present the case of 48 year-old women, admitted with intense bone pain, headache and dizziness. Imaging studies performed identified a small nodule localized in the anterior mediastinum. This nodule was positive for high levels of tracer fixation. Surgery was performed and the nodule was identified as a small parathyroid adenoma.

Results and discussions: The outcome of the surgical intervention was favorable, without any postoperative complications. We suggest for the imaging diagnostic procedure to include: ultrasonography, scintigraphy, computed tomography, MRI. Using nuclear medicine, the sensibility for the imagistic

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identification of parathyroid adenomas increased to approximately 90%. The approach for mediastinal ectopic parathyroid glands is controversial, but their preoperative localization is mandatory.

Conclusions: Primary hyperparathyroidism is a rare, important disease, with severe clinical manifestations. The diagnosis must be based on imaging finding, with mandatory surgical treatment, and in most cases, with the remission of the severe clinical manifestation.

Key words: parathyroid adenoma, hyperparathyroidism, hypercalcemia

Introduction

Parathyroid glands, usually four in number, are localized at the anterior cervical level, on the posterior side of the thyroid gland. There is, however, a great variability regarding their localization (1). Usually the parathyroid glands (4 of them in 83% of the general population), are yellow-white, ovoid, encapsulated entities. Up to 20% of the general population may have ectopic parathyroid glands. The most frequent ectopic localizations for the upper parathyroid glands are: the hyoid bone, carotid artery sheath, inside the thyroid gland, the mediastinum, and inside the thymus, while for the lower parathyroid gland the most frequent ectopic localizations are: behind the esophagus, tracheal-esophageal notch, carotid artery sheath, or the postero-superior mediastinum.

Hyperparathyroidism is defined as the excess secretion of the parathyroid hormone – parathormone. This hypersecretion of parathormone is causing hypercalcemia and hypophosphatemia. Taifeller (2), in 1992, established that primary hyperparathyroidism is generated by a parathyroid adenoma in up to 80% -

85% of cases, by parathyroid hyperplasia in 10% - 15% of cases, by multiple parathyroid adenomas in 2% - 3% of cases, and with the same incidence of 2% - 3%, by a parathyroid carcinoma.

Parathyroid glands participate to calcium level regulations by producing the parathormone (PTH) as a response to hypocalcemia. Parathormone stimulates the release of calcium from bones, which may lead to osteoporosis. In case of PTH excess, hypercalcemia appears, leading to clinical manifestations.

Primary hyperparathyroidism has an incidence in general population of 1:1000 (3). Primary hyperparathyroidism prevalence is estimated at about 3:1000 in general population and may reach 21:1000 in post-menopause women (4). Primary hyperparathyroidism is three times more frequent in women than men.

Most patients with primary hyperparathyroidism are asymptomatic. Clinical manifestations arise following the calcium resorption in bones and high levels of calcemia: nephrolithiasis, bone pain, muscle cramps, pancreatitis, depression, anxiety, and fatigue.

Case report

We present the case of 48 year-old women, known with arterial hypertension and osteoporosis of uncertain etiology. The patient was admitted with intense bone pain, headache and dizziness. Clinical examination identified a small, unpainful cervical goiter, without any regional adenopathy. Blood pressure on admission was measured at 170/110 mmHg, with a ventricular rate of 80 bpm. From the blood sample, we retain the following values: serum calcium of 9.38 mg/dl (normal values: 8 – 10 mg/dl), urinary calcium over 24 hours of 326.8 mg (normal values: 100 – 300 mg), alkaline phosphatase of 98 U/L (normal values under 105 U/L), and a PTH level of 320 ng/ml (normal values under 67 ng/ml). All other biological constants were within normal limits.

Bone X-rays were performed (Fig. 1), and they reveal a

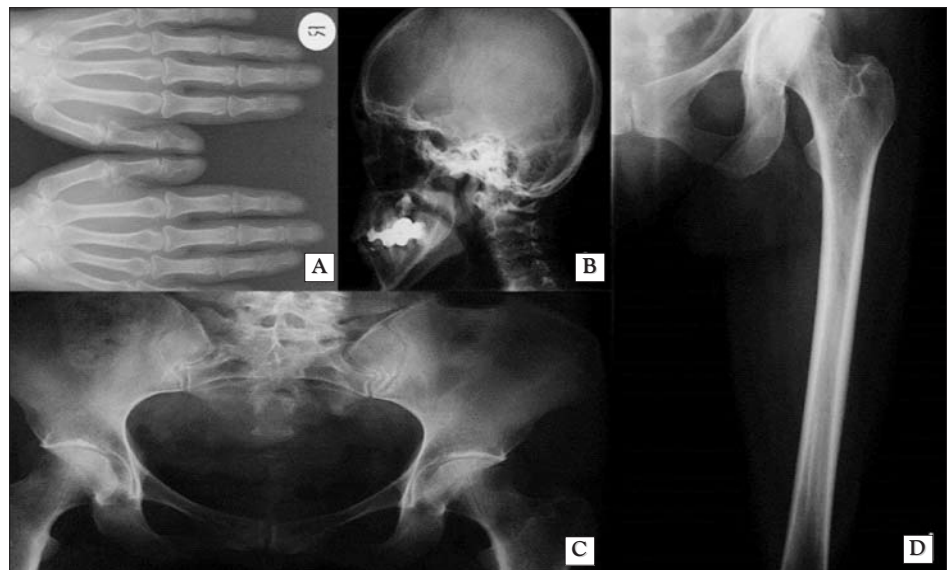


Figure 1. X-rays showing bone demineralization in A) hand bones, B) cranium, C) pelvic bones, and D) thigh-bone

high level of demineralization, aspect strengthen by the results of DEXA osteodensitometry: -3.2 standard deviations.

Abdominal ultrasound was performed and it revealed no specific abnormalities. Cervical ultrasound revealed, however, a diffuse right thyroid lobe with a small hypodense nodule of 6.5 mm localized under the thyroid capsule, and a posterior 6.9 mm hypodense nodule localized at the left thyroid lobe level. ^{99m}Tc -MIBI single tracer thyroid scintigraphy was then performed, and it revealed a normal fixation of the tracer at thyroid level, but it also showed a hyperfixation area at the anterior mediastinum level (early and late planar imaging, sagittal and coronal imaging) (Fig. 2).

The computed tomography examination showed a normal thyroid, but in the thymic lodge, in the anterior mediastinum, next to the aorta, a small (0.9 – 1 cm) nodule was identified (Fig. 3).

Surgical intervention, results

Surgical approach of the tumor was through a median, complete sternotomy. We have opted for this approach and not a video-assisted, minimally invasive procedure because we consider that only through this approachone is able to palpate any other masses that could lie inside the mediastinal fat (the patient's symptomatology was so intense we couldn't afford a therapeutic failure). After dissecting the pericardial and mediastinal fat (Fig. 4A), inferior thymic horns were identified and dissected (Fig. 4B).

Following these first steps, the thymic vein was identified, ligated and sectioned (Fig. 4C); phrenic nerves were identified and salvaged on both sides. Superior thymic horns were then dissected and removed from the fat tissue surrounding the thymus, highlighting a small parathyroid adenoma located posterior on the left superior thymic horn (Fig. 4D). Complete thymectomy has been performed, also removing the mediastinal mass.

The resected parathyroid adenoma, located inside the

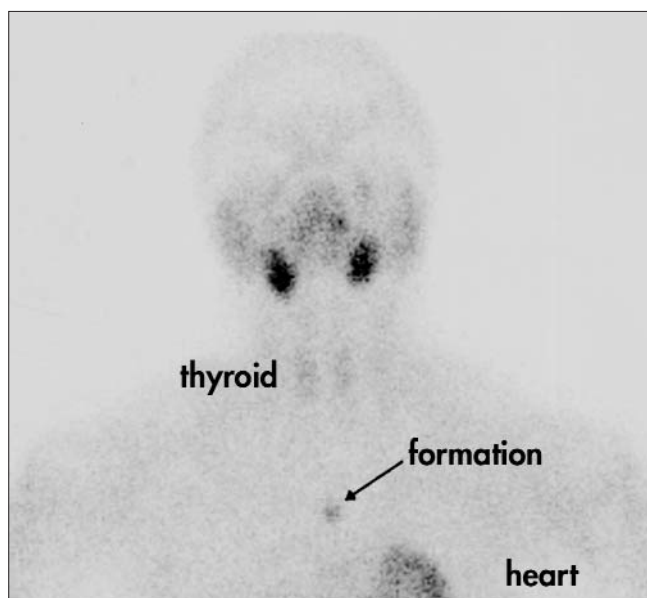


Figure 2. ^{99m}Tc -MIBI scintigraphy revealing higher levels of tracer fixation at the mediastinal level

thymus, along with the thymus, are presented in Fig. 4E.

Histopathology of the resected mass describes thymic tissue with a tumor proliferation of uniform cells, with clear cytoplasm, hyperchromatic nucleus, disposed in islands with sinusoidal blood vessels – aspect compatible with parathyroid adenoma (Fig. 5).

Immediately postoperative the patient was transferred to the intensive care unit, with favorable postoperative outcome. Medical treatment included the administration of 2 grams of ionic calcium and 400 IU of vitamin D, daily for six months, followed by another six months of 1 gram of ionic calcium and 400 IU of vitamin D per day, until the serum parathormone level is normalized.

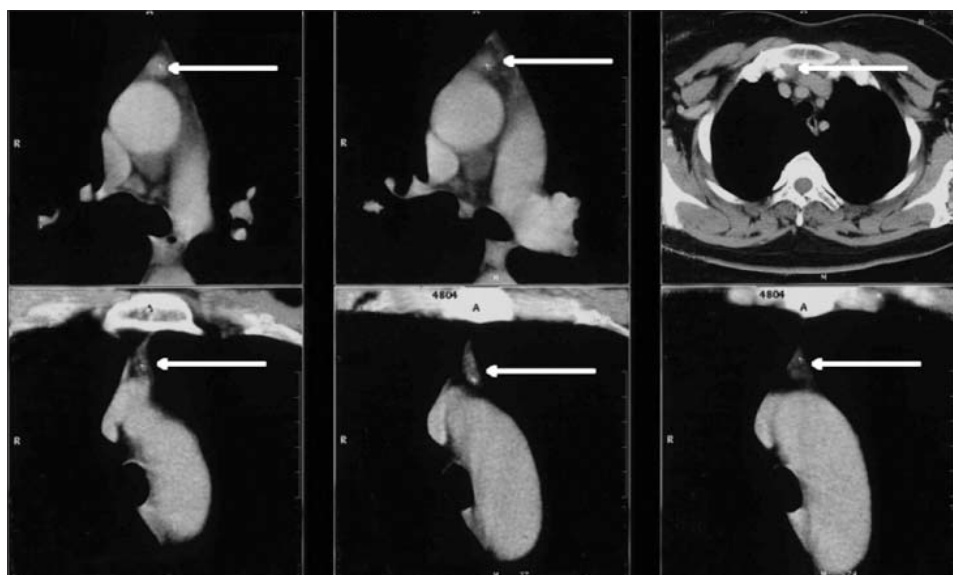


Figure 3. CT examination: a small nodule in the anterior mediastinum is observed (indicated by the arrows)

Figure 4. Intraoperative aspects: A) pericardial and mediastinal fat dissection, B) dissection of the inferior thymic horns, C) ligation and section of the thymic vein, D) identification of the mediastinal tumor – parathyroid adenoma, E) the thymus, containing the ectopic adenoma, completely removed

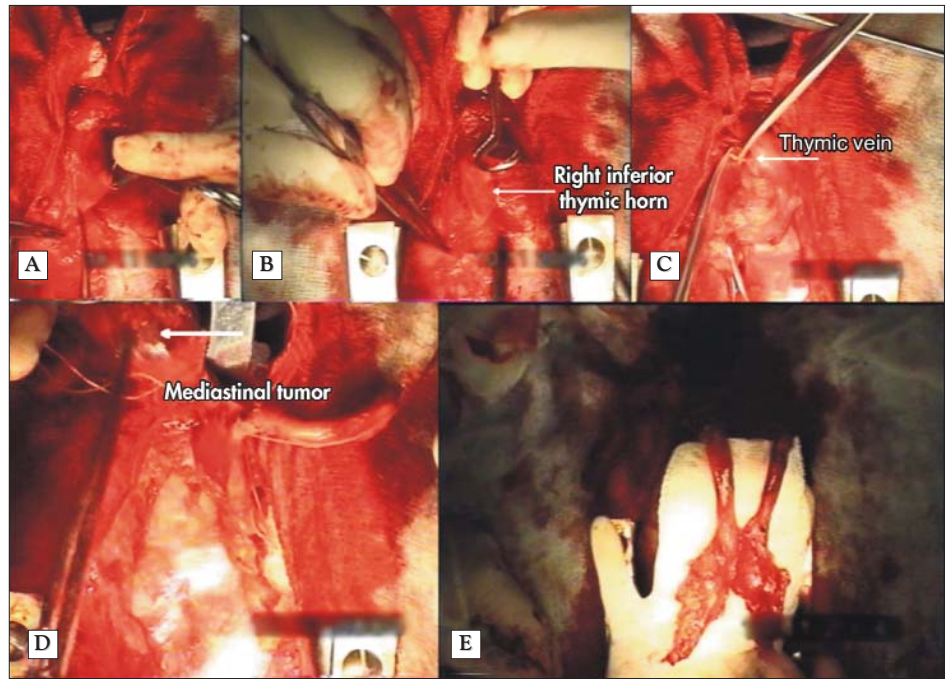
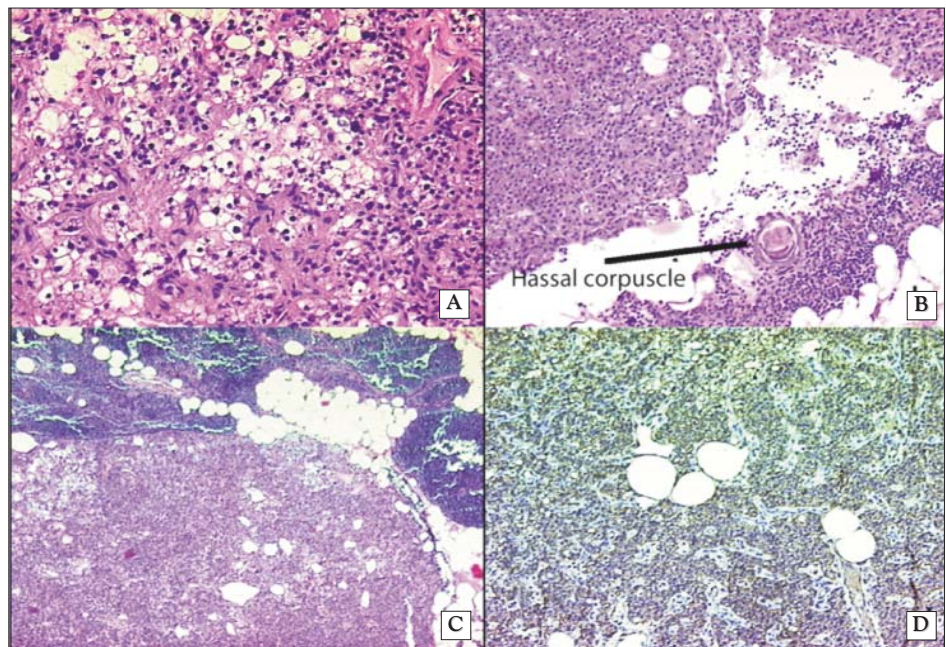


Figure 5. Histopathology: A) principal cells disposed in strands, secreting parathormone, along with adipocytes (HE x 250); B) mature parathyroid tissue included in thymic tissue (HE x 160); C) ectopic parathyroid adenoma included in thymic tissue (HE x 50); D) immunohistochemistry stain positive for calcitonin – positive in this parathyroid adenoma (anti-calcitonin antibodies x 125)



Discussion

Considering there is not available an imaging investigation with 100% sensibility and specificity for identifying an ectopic parathyroid adenoma, we suggest for the imaging diagnostic procedure to include a combination of one functional and one structural investigation of the following: cervical ultrasound, scintigraphy, computed tomography, and MRI (5). By using nuclear medicine, sensibility for the imagistic identification of parathyroid adenomas was increased to approximately 90%. False positive result for scintigraphy are sometimes caused by the tracer's blockage inside a great vessel. For this reason, the

diagnosis must be confirmed by at least two imaging methods: scintigraphy and CT, scintigraphy and MRI – thus combining morphological with functional data.

Arterial hypertension may be secondary to hyperparathyroidism, as some authors have observed (6). Other authors do not agree with this statement, and they argue that parathyroidectomy does not always lead to normalization of the blood pressure (7).

Up to 25% of primary hyperparathyroidism is caused by mediastinal ectopic parathyroid glands. Only 2% (1% – 3%) are not accessible through lower anterior cervicotomy. VATS (video-assisted thoracic surgery) and thoracoscopy have lowered the rate

of sternotomies for the removal of mediastinal ectopic parathyroid glands. Thoracoscopic approach is somewhat disputed because of an inadequate visualization of mediastinal parathyroid.

As other authors have observed (8, 9, 10), primary hyperparathyroidism has an increased incidence in post-menopausal women when compared to general population. Our patient makes no exception, as she became symptomatic at 48 year-old, almost two years after the onset of the menopause.

Mediastinal parathyroid adenoma represents a distinct subset of primary hyperparathyroidism and requires a specific, still controversial, surgical approach (11), but their localization pre-operative is mandatory. Options for the surgical approach for mediastinal parathyroid glands are: lower anterior cervicotomy, cervicotomy with partial upper sternotomy, partial sternotomy, total sternotomy, antero-lateral thoracotomy (when the patient already had a sternotomy), thoracoscopy (parathyroid adenoma located in visceral mediastinum or near to the diaphragm), VATS (11). There is universal agreement that surgical treatment should be offered to all patients with symptomatic disease as a major step for these patients' treatment (12).

Conclusions

Primary hyperparathyroidism is a rare, important disease, with severe clinical manifestations. The diagnosis must be based on imaging finding, with mandatory surgical treatment, and in most cases, with the remission of the severe clinical manifestation.

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