Imaging findings of parathyroid lesions in primary hyperparathyroidism.

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Learning objectives

- To discuss the commonly used techniques for imaging of the parathyroid glands and their role in the preoperative evaluation of patients with primary hyperparathyroidism

- To examine the various presentations of parathyroid diseases that characterize the hyperparathyroidism

Background

HYPERPARATHYROIDISM

Hyperparathyroidism, due to excessive production of parathyroid hormone (PTH), is classified as primary, secondary or tertiary form.

The PHTP, due to autonomous hypersecretion of PTH, may occur in sporadic (90%) or in familial form (10%) within the group of multiple endocrine neoplasia (MEN 1-2). The PHTP is due to the presence of a gland adenoma (85%), or a singular (10-15%) or multiple glandular hyperplasia (4%) and finally, 1% of cases a parathyroid carcinoma.

ROLE OF THE IMAGING

Although the diagnosis of primary hyperparathyroidism is mainly bio-chemical, in recent years the role of preoperative imaging is consolidated, because its use has been associated with increased surgical success and with a significant reduction in operating times and in complications; moreover imaging techniques allow to identify ectopic locations of parathyroid glands.

In fact the purpose of imaging is the identification of one or more pathological parathyroid glands, always associated with an increase in their volume so that makes it recognizable to the imaging techniques.

In PHTP, for preoperative localization of the abnormal parathyroid gland, US and scintigraphy are performed usually as first-step imaging studies due to their lack of invasiveness, limited cost, and good overall diagnostic accuracy. However, an important limitation to the accuracy of sonography and scintigraphic studies can be represented by the coexistence of a thyroid disease which may introduce false-positive observations, which are frequently caused by thyroid nodules.
In the case of the results of US/scintigraphy are both negative or just the scintigraphic has given positive results, or in the case of persistence of PHTP, a second-level technique (CT or MR) is necessary.

- **ANATOMY AND EMBRYOLOGY OF PARATHYROID GLAND**

The parathyroid glands arise from the third and fourth branchial pouches. The inferior parathyroids, together with the thymus, are derived from the third pouch and have a complex pattern of migration before they assume their final position caudad to the derivation of the fourth pouch. Failure of separation of thryd pouch parathyroid from the thymus results in its appearance in the lower neck within the thymic tongue, anterior mediastinum, or, rarely, in the posterior mediastinum. Early separation from the thymus, conversely, may result in its final position cephalad to fourth pouch parathyroid.

The upper or superior parathyroid glands arise from the fourth branchial pouch along with the lateral angles of the thyroid gland. Because the superior parathyroid glands are closely related to the thyroid gland and have minimal descent, their positions are relatively constant along the dorsal aspect of the upper thyroid. Less than 2% of the superior parathyroid glands are ectopic in location.

The most common anatomic location of the upper parathyroid glands is posterior to the middle one third of the thyroid gland (75% of the time). The majority of the remainder of the upper parathyroids are located behind the upper or lower one third of the thyroid, with approximately 7% found below the inferior thyroidal artery.

The superior parathyroids may, on occasion, be present within the carotid sheath or in the retroesophageal or retropharyngeal space.

The inferior parathyroids (from third pouch) exhibit considerably more variation in their anatomy: sixty-one percent are inferior, posterior, or lateral to the lower pole of the thyroid, whereas 17% are present high up on the anterior aspect of the thyroid. Other sites for the inferior glands include the thyrothymic ligament, cervical thymus, lower thymus, and lower mediastinum.

Intrathyroidal parathyroid glands are uncommon, occurring in 2% of cases.

**Imaging findings OR Procedure details**

- **PARATHYROID HYPERPLASIA AND ADENOMA**

Hyperplasia is also a more difficult diagnosis to make sonographically because the single gland size is generally much smaller than an adenoma; however, as with adenomas,
compact cellularity may render hyperplastic glands hypoechoic relative to the overlying thyroid.

Parathyroid adenoma are almost always homogeneously hypoechoic to the overlying thyroid gland and are commonly detected when they are larger than 1cm in diameter. Hypoechogenicity may be a result of the marked, compact cellularity that is characteristic of adenomas. They are usually oval or bean-shaped, but larger adenomas can be multilobulated.

Color Doppler US was proved to be useful for characterizing parathyroid lesions. Color and power Doppler imaging show a characteristic extrathyroidal feeding vessels (typically a branch off the inferior thyroidal artery), which enters at one of the poles.

Internal vascularity is also commonly seen in a peripheral distribution. The artery feeding the adenoma tends to branch around the periphery of the gland before penetrating deeper, resulting in a characteristic arc or rim of vascularity. Instead, the lymph nodes, found in patients with thyroiditis, the "parenchymal" flow, when present, has a central and linear distribution. Lymph nodes detected in patients with Hashimoto's thyroiditis, on the contrary, showed lack of flow in all cases.

The CT axial thin-collimation images, with useful of contrast media, show a intense enhancement in the typical locations for parathyroid tissue in the setting adenoma, and has the additional advantage of detecting most ectopic gland.

Unlike MRI, the multi-slice CT allows an exploration of the entire cervical region and upper mediastinum quickly; in fact CT allows to make multiplanar reconstructions through post-processing of images obtained in a single acquisition. The CT also allows a distinction of parathyroid lesions from other cervical masses, especially lymph node.

Parathyroid lesions will show a significantly densitometric increase in the arterial phase and a slow wash-out in the later stages, behavior that can be compared, in terms of differential diagnosis, with other swellings, such as less vascularized lymph nodes, especially in cases of mediastinal location.

The Magnetic Resonance Imaging is less commonly used for preoperative localization.

More commonly, MRI is used in patients with persistent or recurrent hyperparathyroidism, in whom a locating remaining abnormal parathyroid tissue has been shown. In T1 and T2 weighted sequences, the typical MR imaging of abnormal parathyroid tissue is variable. The most common MR appearance of parathyroid tissue is an intermediate to low-intensity T1 signal and high-intensity T2 signal. Less commonly, fibrosis or old hemorrhage can cause low signal intensity on T1- and T2-weighted images. Subacute
hemorrhage into adenomas can cause high signal intensity on both T1- and T2-weighted images. The acquisition of gadolinium-enhanced T1-weighted images with fat suppression has not been shown to significantly increase detection of adenomas. Abnormal parathyroid tissue cannot be diagnosed on MRI by signal characteristics because cervical lymph nodes have similar signal characteristics. Therefore, accurate MR diagnosis depends both on knowledge of the typical morphology and location of the parathyroid glands both on common sites of ectopic glands.

- **INTRATHYROIDAL PARATHYROID ADENOMA**

In the case of ectopic gland, especially intrathyroidal parathyroid adenoma, an abnormal gland may be considered as one of the nodules in the thyroid gland.

At US the intrathyroidal parathyroid adenoma is presented as a regular shape, smooth border, hypoechoic level of internal echo, solid content and with polar vessels feeding. A hyperechoic line on the ventral surface, between the parathyroid and thyroid gland represents the very thin capsules of both and it is produced by the strong reflection of ultrasound in the layer where the parathyroid is histologically separated from the thyroid tissue. Except for calcification, the peripheral rim of a thyroid nodule is not represented by a hyperechoic line, but for a hypoechoic halo.

- **PARATHYROID CYSTIC ADENOMA**

Parathyroid cysts are a rare lesions and they represent 0,6% of all thyroid and parathyroid lesions.

Parathyroid cysts are divided in two categories:

- **Functional cyst**, associated with clinical hyperparathyroidism
- **Nonfunctional cyst**, with normal PTH levels; they may be asymptomatic or present with symptoms determined by compression of adjacent structures (dysfagia, dysphonia and dyspnea)

They are histological differences between functional and non functional cysts: nonfunctional cysts are simple cysts lined by a flattened-cubic to low-columnar epithelium, with sever types of parathyroid cells in their wall. The presence of smooth muscle in the wall suggests that these may arise from branchial pouch remnants.
The functional cysts lack of an identifiable lining and may contain foci of hemorrhage or necrosis and it is believed that these may arise from degenerating adenomas.

The nonfunctional parathyroid cysts are solitary and unilocal, located near the lower poles of the thyroid gland; the functional cysts, are multilocular and complex, with thin wall, and are found in association with adenoma or an hyperplastic gland.

Cystic degeneration of parathyroid adenoma is seen in 4% of abnormal parathyroid glands and 1-2% of patients with primary hyperparathyroidism.

Cystic adenomas have several sonographic features in common with their solid counterparts: the echogenic tissue plane separating the parathyroid gland from the adjacent thyroid and the presence of a polar feeding vessels; these are two features that aid in differentiating cystic adenomas from cystic thyroid nodules.

Less common entities to be considered in the differential diagnosis of cystic neck lesions found in the typical locations of the parathyroids glands: nodal metastases (e.g. lymphoma, papillary thyroid cancer) and cervical thymic cysts. The typical locations of other cystic neck masses, such as second branchial cleft cysts and thyroglossal duct cysts can suggest the diagnosis, but a definitive differentiation on the basis of sonographic appearance and location may not be possible. FNA is useful for diagnosis and therapeutic purposes: in both cases (functional and nonfunctional cysts) high levels of PTH are detected in the cystic fluid.

Management of parathyroid cyst depends on the nature of cyst: for functional cyst surgery is indicated, while for nonfunctional cyst, surgery can be avoided by using fine needle aspiration.

- PARATHYROID CARCINOMA

Parathyroid carcinoma is a rare neoplasm, accounting for less than 1% of patients with primary hyperparathyroidism.

Parathyroid carcinoma is often associated with several clinical factors and hereditary disorders including a prior history of neck irradiation, end-stage renal disease, multiple endocrine neoplasia syndromes, hyperparathyroidism-jaw tumor syndrome and ossifying fibromas of the maxilla and mandible.

The ultrasound appearance of PCA is a hypoechoic soft tissue mass (size is a critical feature) with irregular, poorly defined border, sign of invasion of adjacent structures, and presence of intralesional vessels. Rarely calcification has been present. The structural heterogeneity of lesions is the most frequent finding: however cysts are also found in benign lesions.
CT density measurements and MRI can assist in differentiating abnormal parathyroid tissue from lymph nodes and normal thyroid tissue.

However, the only feature that may permit the preoperative diagnosis of parathyroid cancer is clear evidence of invasion into adjacent tissue.

The use of fine-needle aspiration cytology in a suspected case of parathyroid carcinoma is not recommended for two reasons. First, the diagnosis of parathyroid carcinoma can be extremely difficult histologically and sampling error may lead to false negatives, thus misleading the surgeon preoperatively. Second, by violating the capsule of the tumor there is a risk of seeding parathyroid cells.

Images for this section:

Fig. 1. Typical appearance of superior parathyroid adenoma.
References: dott. Mazzeo, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa

Fig. 1
Fig. 2. Superior parathyroid adenoma

References: dott. Mazzuca, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa
Fig. 3. Typical appearance of inferior parathyroid adenoma

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Fig. 4. Typical inferior parathyroid adenoma

References dott. Mazzeo, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa
Fig. 5. Atypical presentation parathyroid adenoma. a) inhomogeneous and lobulated inferior parathyroid gland. b and c) parathyroid adenoma with cystic areas

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Fig. 6. Inhomogeneous parathyroid adenoma in patient with MEN 1 syndrome

References: Dott. Mazzeo, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa
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References dott. Mazzeo, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa
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References dott. Mazzeo, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa
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References: dott. Mazzocchi, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa
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\textit{References} dott. Mazzeo, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa
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References dott. Mazzeo, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa
Fig. 22. MRI parathyroid adenoma features: a) unenhanced axial T1-weighted image shows a hypointense adenoma just posterior to the inferior pole of the left thyroid lobe. b) axial T2-weighted image shows marked hyperintensity of the adenoma. c) Enhanced axial fat- suppressed T1-weighted image shows homogeneous enhancement of the lesion.

References dott. Mazzeo, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa
Fig. 23. Intrathyroidal parathyroid gland

References: dott. Mazzeo, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa
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References: dott. Mazzeo, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa
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References dott. Mazzeo, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa
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References dott. Mazzeo, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa
Fig. 27. US and CT scan of inhomogeneous parathyroid mass with fluid component: parathyroid carcinoma

References dott. Mazzo, Department of Oncology, Transplants and Advanced Technologies in Medicine, University of Pisa
Conclusion

Imaging can help to know different causes of PTHP (parathyroid adenoma, carcinoma, hyperplasia or intrathyroid mass) with their different presentations (typical and atypical) and to localize parathyroid mass in their normal place (superior or inferior) or in ectopic sites. Moreover preoperative imaging increase surgical success.

Personal Information

References


