

Parathyroid adenoma versus primary hyperparathyroidism

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ABSTRACT

This is a narrative review of literature. We focus on the issue of identifying a parathyroid adenoma without anomalies of function (non-functioning parathyroid adenoma) which is incidentally detected or not, via routine neck ultrasound or through advanced imaging techniques which are mostly performed for other conditions (like assessment of a non-parathyroid oncological condition or emergencies – related neck exploration).

The traditional diagnostic of primary hyperparathyroidism is exclusively a biological one based on high calcium and parathormone (PTH), and only a second step of assessment actually involves the localization procedures. However, the detection of a parathyroid tumor does not necessarily mean that it is associated with an over-secretion of PTH. Ultrasound is usually followed by Tc Sestamibi scintigram and/or computed tomography in order to refer the patient to parathyroidectomy in cases with biological confirmation of primary or renal hyperparathyroidism; yet, in cases with non-functioning profile, there is no clear indication of further imaging exploration.

In conclusion, the identification of a parathyroid adenoma is rarely associated with a normal parathyroid function and this entity, which most probably is an incidentaloma, is not a subject of particular guidelines yet. Whether it is necessary to continue with other imaging techniques as typically seen in primary hyperparathyroidism is still an open issue, and so is the panel of indications to perform its surgical removal instead of serial follow-up.

Keywords: parathyroid, hyperparathyroidism, functioning parathyroid adenoma, non-functioning parathyroid adenoma, adenoma, tumor, neoplasia, primary hyperparathyroidism, ultrasound

INTRODUCTION

A parathyroid adenoma may be incidentally detected or not; however, the traditional diagnostic of primary hyperparathyroidism is exclusively a biological one based on high calcium and parathormone (PTH), and only a second step of assessment means actually finding the underlying tumor like a parathyroid adenoma (orthotopic or ectopic) (1,2). Thus, the detection of a parathyroid tumor or tumor-like gland does not necessarily mean that it is associated with an over-secretion of PTH (3,4).

Finding a parathyroid mass or a gland enlarge-

ment (for instance, through neck ultrasound, *etc.*) is part of the primary hyperparathyroidism management (in order to locate it and remove it to provide the cure), but a parathyroid adenoma might be actually be a clearly non-secretor mass (5,6) (Figure 1).

AIM

We focus on this specific matter, the issue of identifying a parathyroid adenoma without anomalies of function (non-functioning parathyroid adenoma) which is incidentally detected or not *via* routine neck ultrasound or through advanced imaging tech-

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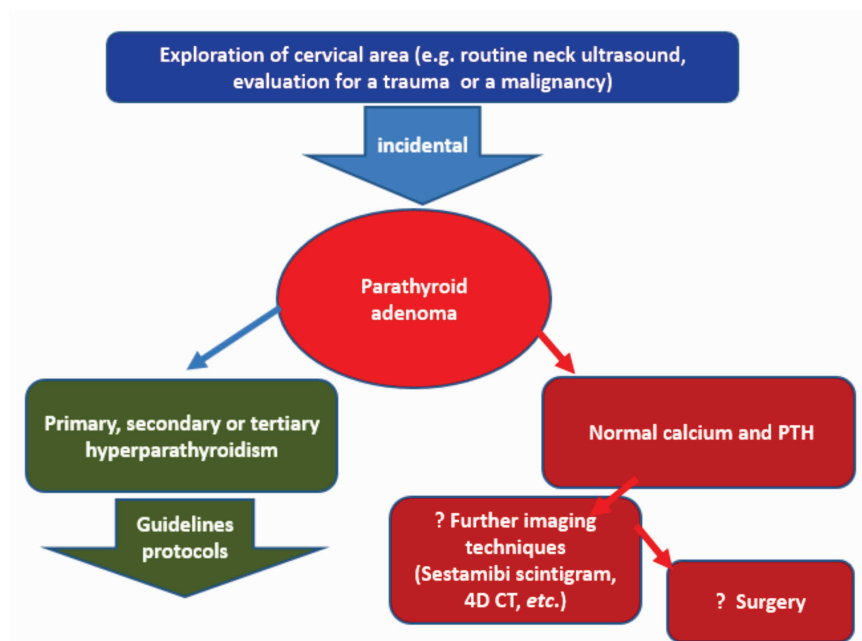


FIGURE 1. Approach of parathyroid adenoma in relationship with primary hyperparathyroidism (1-18). PTH = parathormone, CT = computed tomography

niques which are mostly performed for other conditions (like assessment of a non-parathyroid oncological condition or an emergency neck exploration for trauma).

METHOD

This is a narrative review of literature. Inclusion criteria: PubMed database – indexed journals, search is based on the following terms: “parathyroid adenoma”, “primary hyperparathyroidism”, “non-functioning parathyroid adenoma”, “parathyroid ultrasound”, and “incidental parathyroid adenoma”. 57 references are cited.

PARATHYROID ADENOMA

Primary hyperparathyroidism is the most frequent condition of parathyroid glands; the variants are with normal calcium or even with intermittently normal PTH; sporadic or syndromic (7). Typically the lesions underlying larger parathyroid glands are either adenomas, either hyperplasia (parathyroid cancer accounts less than 1% and intermediate atypical parathyroid adenoma is found up to 1.3% of all cases), 0.1-0.3% of general population having a parathyroid tumor (8,9,10).

PRIMARY HYPERPARATHYROIDISM

Imaging techniques to locate the source of primary hyperparathyroidism – related PTH excess varies from typical Tc ⁹⁹/Sestamibi scintigram to more complex methods like PET (positron emission

tomography), contrast enhanced computed tomography based on different radiolabeled tracers which are more or less used during daily practice (11,12). Pre-operative methods may be associated with intra-operative localization assays (in addition to surgeon’s good skills) (13,14,15). Accuracy of location increases the rate of successful parathyroidectomy (16). It also helps the preservation of a healthy gland which should not be a matter of surgical procedure (17,18).

PARATHYROID INCIDENTALOMA

Incidentally revealed lesions are either benign or malign, either solid, cystic or mixt; either found in adult or pediatric population; they do not necessarily are referred to be removed; endocrine concept around incidentaloma typically associates one more hint: a negative hormonal profile (19-28).

Accidental finding of parathyroid mass may start from an emergency neck imaging exploration, for instance, after a recent trauma (29). A study from 2021 on 336 subjects who were admitted for trauma requiring computed tomography at the level of neck and cervical vertebrae identified 5% of them with at least one parathyroid gland visible and 3% of them with minimum one gland enlargement; these incidental anomalies required supplementary assessments of calcium and PTH levels because there is no linear relationship between imaging features and hormonal profile (29).

The surgical removal (which is still a subject of great variety of approaches) of a parathyroid adenoma that is incidentally detected is required on a

selected number of cases: if there is newly diagnosed over-secreter profile (primary hyperparathyroidism), if there are associated compressive local aspects (mass effect) or a suspected malignancy (meaning a parathyroid carcinoma) is highlighted (30). Even exceptionally rare, the parathyroid carcinoma represents a clinical entity which is typically associated with a heterogeneous area of clues, high calcium levels causing digestive complications including, acute pancreatitis, as well as a PTH-induced severe bone metabolic disorder (including brown tumors) in association with a rapidly progressive, large neck and the incidentaloma scenario of identification is less likely under these circumstances (31-34).

PARATHYROID ULTRASOUND

85% of people have the 4 parathyroid glands located at infra-hyoid level of the neck thus ultrasound evaluation represents a routinely used tool (15% of individuals had an at least one accessory gland, usually following the map of embryological development) (35,36). The underlying histological report of a parathyroid enlargement or mass which was detected based on ultrasound varies from a parathyroid adenoma to hyperplasia or parathyroid cyst (37,38). The hyperplasia is either the effect of a genetic pressor causing a syndromic condition or is a response to vitamin D deficiency as seen in secondary hyperparathyroidism or even tertiary type that accompanies chronic kidney disease in 90% of cases (and some practitioners are using as well the term “secondary hyperparathyroidism” for chronic renal failure) (39,40,41).

Ultrasound is usually followed by Tc Sestamibi scintigram and/or computed tomography in order to refer the patient to parathyroidectomy in cases with biological confirmation of primary or renal hyperparathyroidism; however, in cases with non-functioning profile, there is no clear indication of further imaging exploration (42,43,44). 4DCT (4

dimensional computed tomography) is a common technique performed for enlarged parathyroid glands (42,44).

A review published in 2021 on papers from 2020 included 51 articles concerning 4DCT: the authors identified 56 protocols of scanning (most of them with non-contrast enhancing and a supplementary arterial phase) (44). The results from modern 4DCT technique correlate with other imaging methods (45,46). One alternative is 4D MRI (Magnetic Resonance Imaging) (47,48). Very little is known so far with respect to 4D exploration in individuals with normal parathyroid function and associated anatomical anomalies as a non-functioning parathyroid adenoma (49,50).

PARATHYROID INVOLVEMENT IN GENETIC SYNDROMES

The detection of a parathyroid enlargement or a tumor-like/tumor aspect of any of the parathyroid glands (which does not imply a hyper-function of parathyroid glands but this is mostly expected) is also required in individuals diagnosed with a hereditary syndrome (51-57). Multiple endocrine neoplasia (MEN) syndrome requires a surveillance of parathyroid glands in patients who are most probably already known with a pituitary tumor (MEN 1), an adrenal tumor or thyroid cancer (MEN 2A), different skin anomalies and neuroendocrine tumors (neurofibromatosis type 1) (51-57).

CONCLUSIONS

The identification of a parathyroid adenoma is rarely associated with a normal parathyroid function and this entity, which most probably is an incidentaloma, is not a subject of particular guidelines yet. Whether it is necessary to continue with other imaging techniques as typically seen in primary hyperparathyroidism is still an open issue. So is the panel of indications to perform its surgical removal instead of serial follow-up.

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