ORIGINAL RESEARCH PAPER
Volume - 10 | Issue - 10 | October - 2021 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

ONCOCYTIC INTRATHYROID PARATHYROID ADENOMA MASQUERADING AS HURTHLE CELL NEOPLASM: FINE NEEDLE ASPIRATION CYTOLOGY OF TWO CASES

Pathology

Mega Lahori* Mount Sinai St. Luke's-Roosevelt hospital, Department of Pathology, New York, NY, USA. *Corresponding Author

Hua Chen Mount Sinai Downtown Union Square, FNA clinic, Department of Pathology, New York, NY, USA.

ABSTRACT

Ectopic parathyroid adenomas in thyroid tissue are uncommon (0.7 - 6%), and their oncocytic variants are exceedingly rare. We report two cases of intrathyroid parathyroid adenoma which were diagnosed as Hurthle cell adenoma on cytology. Case 1 is a 49-year-old female with a 2.4 cm hypoechoic nodule in the left lateral neck. Electrochemiluminescent immunoassay of the aspirate revealed PTH level of 422 pg/ml, confirming the presence of hyperfunctional parathyroid tissue. Subsequent resection of the left thyroid lobe revealed an enlarged intrathyroidal parathyroid. Case 2 is a 58-year-old female with a 2.1 cm hypoechoic nodule in the posterior-mid left thyroid lobe. Strong overexpression of parathyroid hormone and Chromogranin A genes and low expression of thyrocyte-related genes suggested parathyroid origin of the cells sampled. MEN1 mutation and multiple copy number alterations indicated the neoplastic nature of the nodule.

Parathyroid oxyphil cells and oncocytic thyrocytes share cytomorphological findings and distinguishing them by cytology alone is challenging, especially when the targeted lesion is intrathyroidal. Distinguishing intrathyroid oncocytic parathyroid adenoma from oncocytic thyroid follicular lesions has significant clinical implications as Bethesda-IV category lesions have 20%–30% risk of malignancy. While stippled chromatin or intracytoplasmic fat vacuoles may be suggestive of parathyroid origin, these are not specific. Classifying the origin of a nodule as parathyroid vs thyroid rests upon the detection of PTH in aspirate material by ECL, immunocytochemistry or next-generation sequencing. In parathyroid aspirates, PTH level ≥ 100 pg/mL is suggestive of the presence of PTH-secreting tissue at the site biopsied or along the needle track.

KEYWORDS

Parathyroid, Oncocytic, Intrathyroid, Hurthle cell, Bethesda.

INTRODUCTION

Parathyroid adenomas are benign neoplasms composed of parathyroid epithelial cells. Three different types of parathyroid epithelial cells may be seen: Chief cells (resembling follicular cells of the thyroid), oxyphil cells (resembling Hurthle cells of the thyroid), and water clear cells (have clear cytoplasm) (1). The overlapping cytologic features of chief cells and oxyphil cells with follicular and Hurthle cells, respectively, may make it difficult to distinguish parathyroid from thyroid on both cytologic and sometimes histologic specimens. FNAs from thyroid follicular lesions show cells arranged in a microfollicular pattern (6–12 crowded cells in a ring- or rosette-like configuration), a pattern that may also be observed in FNAs of parathyroid tissue. Hurthle cell lesions of the thyroid pose a similar diagnostic dilemma (2).

Ectopic parathyroid adenomas have been noted in thyroid, mediastinum, within thymus, submandibular region, soft palate, pyriform sinus, etc. Intrathyroidal parathyroid adenomas are uncommon, with prevalence varying between 0.7 % to 6% (3,4). Generally, it is impossible to discern between parathyroid adenomas and parathyroid hyperplasias by histology alone (5). Ideally, histologic findings should be correlated with the PTH serology (2).

Parathyroid adenomas represent clonal proliferations and approximately 20% to 40% of sporadic adenomas have overexpression of cyclin D1 (CCND1/PRAD1) oncogene on 11q13 resulting from pericentric inversion of chromosome 11p, with placement of the CCND1 gene under the control of tissue-specific enhancer elements of the PTH gene promoter sequences. Loss of one MEN1 allele (MEN 1 gene on chromosome 11q13) has been observed in up to 40% of sporadic parathyroid adenomas, with an inactivating mutation of the second allele occurring in 50% of these tumors (6).

Oncocytic cells have been reported to occur normally (from puberty and increase with age) in parathyroid glands and as metaplastic and/or neoplastic components in parathyroid, thyroid, salivary gland, nasopharynx, larynx, hard palate, tongue, bronchus, trachea, pituitary, adrenal, cortex, kidney, pancreas, gallbladder, liver, fallopian tube, lacrimal gland, and caruncle of eyelid.

Cytology smears containing cells with oncocytic changes may correspond to lesions of various types and with different clinical behavior, such as non-neoplastic lesions (multinodular goiter, nodular hyperplasia, lymphocytic thyroiditis, and long standing Graves' disease), in patients who have received radiotherapy or chemotherapy, and in all types of benign or malignant neoplasms (including follicular adenoma, follicular carcinoma, follicular variant of papillary thyroid carcinoma and Hurthle cell carcinoma), parathyroid (normal, hyperplastic or neoplastic), paraganglioma, neoplasms of salivary gland, liver, kidney, adrenal, pancreas, gallbladder, etc. (7). It is important to combine clinical, radiological, and cytological and laboratory features, in order to prevent misdiagnosis in these cases (8).

MATERIAL AND METHODS:

We report two cases of intrathyroid parathyroid adenoma which were diagnosed as Hurthle cell neoplasm on cytology.

Case 1 is a 49 year old African female (originally from Congo) who presented with a history of frequent palpitations (3-4 times/week), and was subsequently found to have hypercalcemia and elevated PTH levels. Ultrasonogram revealed a 2.39 x 2.18 cm hypoechoic nodule in the left lateral neck. FNA of the nodule was suggestive of Hurthle cell neoplasm (Bethesda category IV) - **Fig A**. Electrochemiluminescent immunoassay (Roche) of the aspirate material revealed PTH level of 422 pg/ml, thus confirming the presence of hyperfunctional parathyroid tissue, with oncocytic metaplasia. Subsequently, en-bloc resection of left thyroid lobe and parathyroid adenoma was done, and histopathological analysis of formalin fixed paraffin embedded sections revealed the tissue to be an enlarged intrathyroid parathyroid, 1.9 cm **(Fig B and C)**.

Case 2 is a 58 year old female with hypercalcemia detected in routine labs. Further testing elevated PTH levels, and a 2.1 cm hypoechoic nodule close to the posterior mid left thyroid lobe. FNA of the nodule was suggestive of Hurthle cell neoplasm (Bethesda category IV). Strong overexpression of parathyroid Hormone (PTH) and Chromogranin A {CHGA) genes and low expression of thyroid cell-related genes was found, strongly suggesting that the sampled nodule was composed of parathyroid cells.

In addition the MEN1 mutation and multiple copy number alterations were identified in this sample. The presence of clonal copy number alteration indicated that the nodule was a neoplasm, i.e. parathyroid adenoma or carcinoma, and not hyperplasia.

The parathyroid FNAs were moderately cellular with cells arranged predominantly as clusters of enlarged cells and few single intact cells in the background. A moderate amount of thick, colloid-like material was observed in both cases. The cells had abundant eosinophilic cytoplasm (with occasional foamy change), mild anisonucleosis, regular rounded nuclei with stippled chromatin and occasional, small nucleoli. On average, the cell nuclei were about 2-3 times the size of a red blood cell (RBC).

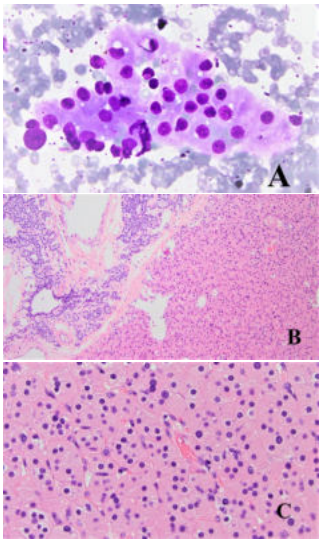

IMAGE CAPTIONS

Fig. A: FNAC smears revealed clusters of monomorphic polygonal cells with abundant granular cytoplasm- diagnosed as Hurthle cell neoplasm on cytology (MGG stain, 400X).

Fig. B: Intrathyroid mass with acinar arrangement of two distinct cell populations- chief cells on the upper left aspect and oncocytic (oxyphil) cells on the lower right aspect. Note the sharp demarcation between the two cell types. (H&E stain, 200X).

Fig. C: Sheets of oncocytic (oxyphil) cells with abundant granular eosinophilic cytoplasm, distinct cell membranes, rounded nuclei with stippled chromatin and perinuclear halo. (H&E stain, 400X).

DISCUSSION

Intrathyroid oncocytic parathyroid adenoma is a diagnostic pitfall in case of unsuspected thyroid nodule FNAs (particularly if the patient's history of hyperparathyroidism is unknown), and distinguishing it from oncocytic thyroid follicular lesions has significant clinical implications as Bethesda-IV category lesions carry a 20%–30% risk of malignancy. Ultrasound imaging may aid in clinical suspicion, but there are no specific image findings to distinguish parathyroid, thyroid, and lymph nodes (9). Serum PTH level or hypercalcemia is useful only for functional adenomas.

Previous studies have demonstrated significant overlap between cytological features of benign thyroid and parathyroid adenomas. While stippled chromatin or intracytoplasmic fat vacuoles (if present) maybe suggestive of parathyroid origin, no single feature is specific for distinguishing these two entities (2,9,10,11). The sensitivity of FNA in the diagnosis of parathyroid tissue has been reported to be between 40% and 86% (11). FNA from both cases, in this study, showed clusters of cells with abundant eosinophilic cytoplasm (with occasional foamy change), mild anisonucleosis, regular rounded nuclei with stippled chromatin and occasional, small nucleoli. FNA diagnosis of Hürthle cell neoplasm was given in both cases, due to the presence of abundant oncocytic cells (enlarged cells with abundant granular eosinophilic cytoplasm). Oncocytic metaplasia is a phenomenon that occurs in situations that result in cellular stress (e.g. inflammation, neoplasia, etc.) - proliferation of oncocytes gives rise to hyperplastic and neoplastic nodules. Oxyphil cells of parathyroid gland have similar appearance as oncocytes (abundant eosinophilic cytoplasm rich in mitochondria). Oxyphil adenomas were earlier thought to have reduced functional capacity for PTH production compared to chief cells), but this has not been substantiated by later studies, and immunohistochemical studies show that these lesions express PTH. In general, however, oncocytic parathyroid tumors tend to be larger than non-oncocytic tumors with similar concentrations of circulating PTH (12).

PTH assay and/or immunocytochemical studies performed on FNA specimens are highly specific for classifying the origin of a nodule as parathyroid vs thyroid (2,13). In parathyroid aspirates, PTH level ≥ 100 pg/mL are suggestive of the presence of PTH-secreting tissue at the site biopsied or along the needle track (Mayo Clinical Lab reference). However, it is not a usual clinical practice to perform PTH analysis on thyroid FNAs unless intrathyroidal parathyroid tissue is clinically suspected (2).

CONCLUSIONS

Parathyroid oxyphil cells and oncocytic thyrocytes share cytomorphological findings and distinguishing them by cytology alone can be very challenging, especially when the targeted lesion is intrathyroidal. Presence of stipple nuclear chromatin and intracytoplasmic vacuolization may be suggestive of parathyroid origin, but ultimate diagnosis rests upon along with detection of PTH in aspirate material (by electrochemiluminescent immunoassay, immunocytochemistry or next-generation sequencing.

REFERENCES:

1. Mills SE. Histology for Pathologists. 3rd ed. Philadelphia: Lippincott Williams and Wilkins; 2007.
2. Sung S, Saqi A, Margolskee EM, Crapanzano JP. Cytomorphologic features distinguishing Bethesda category IV thyroid lesions from parathyroid. *Cytojournal*. 2017;14:10. Published 2017 Apr 28. doi:10.4103/1742-6413.205313
3. McIntyre RC Jr., Eisenach JH, Pearlman NW, et al. Intrathyroidal parathyroid glands can be a cause of failed cervical exploration for hyperparathyroidism. Am J Surg 1997;174:750–3. doi:10.1016/S0002-9610(97)00190-6
4. 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(6):867-871.
5. Taxy, J.; Husain, A; Montag, A. (2009). Biopsy Interpretation: The Frozen Section (1st ed.). Lippincott Williams & Wilkins. pp. 191. ISBN 978-0781767798.
6. Arnold A, Shattuck TM, Mallya SM, et al. Molecular pathogenesis of primary hyperparathyroidism. J Bone Miner Res 2002;17:N30–N36.
7. Calderaro J, Andreiuolo F, et al. Fine needle aspiration cytology of oxyphilic parathyroid hyperplasia. Cytopathology. 2010 Apr; 21(2):135-6.
8. Onur, I & Yilmazer, D et al. (2010). Intrathyroidal Oncocytic Parathyroid Adenoma: A Diagnostic Pitfall on Fine-Needle Aspiration. Diagnostic cytopathology. 38. 833-6. 10.1002/dc.21338.
9. Solbiati L, Osti V, Cova L, Tonolini M. Ultrasound of thyroid, parathyroid glands and neck lymph nodes. Eur Radiol. 2001;11:2411–24.
10. Kumari N, Mishra D, Pradhan R, Agarwal A, Krishnani N. Utility of fine-needle aspiration cytology in the identification of parathyroid lesions. *J Cytol*. 2016;33(1):17-21. doi:10.4103/0970-9371.175490.
11. Odronic SI, Reynolds JP, Chute DJ. Cytologic features of parathyroid fine-needle aspiration on ThinPrep preparations. Cancer Cytopathol. 2014;122:678–84. [PubMed: 24943645].
12. Asa SL. My approach to oncocytic tumours of the thyroid. *J Clin Pathol*. 2004;57(3):225-232. doi:10.1136/jcp.2003.008474
13. Owens CL, Rekhtman N, Sokoll L, Ali SZ. Parathyroid hormone assay in fine-needle aspirate is useful in differentiating inadvertently sampled parathyroid tissue from thyroid lesions. Diagn Cytopathol. 2008;36:227–31. [PubMed: 18335560]