CLINICAL VIGNETTE

FNA of Intrathyroidal Parathyroid

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Case Report

A 77-year-old woman with a history of polycythemia vera and a low vitamin D level was referred for evaluation of persistent hypercalcemia of 5 years duration. Her past medical history included a remote episode of kidney stones of uncertain composition. Physical exam was notable for a left lower pole thyroid nodule. Her recent laboratory data included: Sodium 133 mg/dl, Potassium 5.4 mg/dl, Chloride 101 mmol/L, CO2 26 mmol/L, BUN 12 mg/dL, Creatinine 0.5 mg/dL, eGFR > 89, albumin 4.8 g/dL, Calcium 11.1, 11.2 mg/dL, Phosphorous 2.4 mg/dL, 25-hydroxy Vitamin D 16 ng/dL, Intact PTH 251 pg/mL, timed urine collection 411 mg/24 hours.

Because of the elevated calcium and PTH, and the physical exam finding compatible with a left thyroid nodule, imaging was obtained. A sestamibi scan showed inferior extension of the left thyroid lobe but was otherwise negative for a parathyroid adenoma. An ultrasound of the thyroid revealed an 11 x 8 x 11 mm left lower pole hypoechoic nodule, and 14-15 mm ovoid isoechoic nodule in the left mid gland as well as a complex cyst on the right but no extrathyroidal nodules compatible with a parathyroid adenoma. An FNA of the thyroid nodule was performed and the sample was sent for cytology and PTH.

Results from the FNA were as follows:

Microscopic: Mildly cellular smears containing sheets and clusters of overlapping epithelioid cells, perfectly round nuclei, fine salt-and-pepper chromatin, small nucleoli, moderate amount of granular cytoplasm and no background colloid.

Antibody probe: Parathyroid hormone – positive

TTF1 - Negative

PTH in aspirate >3000 pg/mL

Based on the FNA, it was felt that the left lower lobe nodule corresponded to a parathyroid adenoma despite the negative sestamibi scan. The patient underwent an uneventful left hemithyroidectomy. Pathology found hypercellular intrathyroidal parathyroid tissue, two intrathyroidal lymph nodes and a benign multinodular goiter.

One month postoperatively, her calcium was 9.0 mg/dL, her ionized corrected calcium was 1.11 (1.09-1.29) mmol/L and her intact PTH was much improved but remained minimally elevated at 67 (11-51) pg/mL. Her previously identified vitamin D deficiency and her calcium intake will be re-evaluated as potential sources of a minimally high PTH in face of a low normal calcium level.

This patient's clinical course provides an opportunity to review the value of parathyroid FNA in the evaluation and management of primary hyperparathyroidism.

Approximately 80-85% of primary hyperparathyroidism is caused by a single adenoma. The traditional surgical approach has been bilateral neck exploration with or without preoperative localization and in experienced hands; this approach was capable of successfully treating 90-95% of hyperparathyroidism. However, with the advent of minimally invasive surgical techniques, it has become important to localize adenomas preoperatively.

Sestamibi scanning has been the most frequently used technique for this purpose but has difficulty identifying ectopic parathyroid tissue. In retrospect, our patient may have had a negative Sestamibi scan based on the ectopic intrathyroidal location of her parathyroid adenoma.

With increasing sensitivity, sophisticated ultra-sonography has been useful in the preoperative localization of parathyroid adenomas. In addition, the identification of various and sometimes incidentally discovered neck lesions during thyroid ultrasound has created the need for more specific diagnostic studies. As with the Sestamibi scan, ultrasound has difficulty diagnosing ectopic parathyroid adenomas. Our patient ultimately proved to have an ectopic intrathyroidal parathyroid adenoma which may explain why sestimibi scan was negative and the thyroid nodules were considered non-diagnostic.

In a study of ultrasonographic characteristics of intrathyroidal thyroid nodules[1], the detection of a hyperechoic line anterior to an intrathyroidal lesion was the only characteristic that reliably diagnosed parathyroid adenomas. The more commonly described characteristics of intrathyroidal nodules such as shape, smooth versus jagged borders, echogenicity, and internal flow on Doppler were not helpful. However, it should be noted that all the parathyroid adenomas were hypoechoic (as were many of the true thyroid lesions) and the presence of a feeding vessel was much more likely in lesions of parathyroid origin. In our patient, although the lesion was hypoechoic on ultrasound, no mention was made about an anterior hyperechoic line or a feeding vessel.

FNA of suspected parathyroid nodules has been used to improve preoperative diagnosis, but unfortunately the histology of parathyroid lesions is non-specific and there is overlap with various thyroid lesions including papillary, follicular and medullary cancers[2]. Immunohistochemical stains have also been used to distinguish parathyroid from thyroid lesions but the success of this approach is often limited due to an inadequate sample. Our patient did have immunohistochemical staining which was positive. In addition, the TTF1 which is a marker for thyroid tissue was negative, increasing the likelihood that the lesion in question was a parathyroid adenoma which was responsible for the hyperparathyroidism.

Several studies have looked at the usefulness of measuring PTH by washout of the needles from FNA aspiration. Erbil et al[3] looked at 27 consecutive patients with primary hyperparathyroidism who were sent to surgery based on a positive Sestamibi scan and/or ultrasound. The negative mean PTH was 48 +/- 7 pg/mL (range 5-57 pg/mL) and the positive PTH aspirates averaged 4,677 +/- 123 pg/mL (range, 3600-5000 pg/mL). In this series, the PTH washout was 100% sensitive. There were no false positives or false negatives. By contrast the sensitivity of ultrasound was 88% and that of sestamibi scan only 77%. The same authors[4] performed another prospective study examining parathyroid FNA and parathyroid hormone assay in patients with primary hyperparathyroidism and thyroid nodules. They compared the accuracy of ultrasound alone with sestamibi alone, combined ultrasound and sestamibi, and FNA/ PTH assay. The positive PTH levels averaged 4,511 pg/mL (range, 3,700-5,000 pg/mL) and the negative PTH assays averaged 11.5 pg/mL (range, 4-20 pg/mL). Again, the sensitivity and positive predictive values of the FNA washout for PTH assay were both 100%.

A third study performed at the Mayo Clinic[5] retrospectively looked at all parathyroid FNA's performed over a period of 8 years. These represented a tiny sample of the total FNA's for hyperarathyroidisn performed at the Mayo Clinic over the same time period and included the 3% of parathyroid patients with recurrent or persistent hypercalcemia, prior neck surgery, discordant sestabmibi and ultrasound results, or multinodular goiter which complicated the imaging. For those samples in which the washout PTH was detectable, the median PTH was 3,963 pg/mL (range 45-5,000,000 pg/mL). Overall the sensitivity was 94%, specificity 100%, positive predictive value 100% and accuracy 84%.

Our patient's PTH on the FNA washout was well within the range above and close to the median of 3,963 pg/mL in the above study. It certainly met the commonly held criterion of being higher than the serum PTH level and also met other less commonly used but more stringent criteria of being at least 3 times the level of the serum PTH or greater than 1,000 pg/mL. Indeed, our patient underwent a successful hemithyroidectomy and was found to have an intrathryoidal parathyroid adenoma. One month after surgery, her PTH is dramatically improved but remains slightly elevated. This slight elevation could possibly be explained by her previously identified vitamin D deficiency or inadequate intake of calcium and will be addressed in future visits.

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