Preoperative Identification of Ectopic Retroesophageal Parathyroid Adenoma Using 4D Computed Tomography Scan

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Background	Primary hyperparathyroidism, which is most often caused by a parathyroid adenoma, requires parathyroidectomy for curative treatment. Due to variations in the locations of parathyroid glands, preoperative localization is important to decrease the risk of failed surgery and minimize the rate of complications.
Summary	We report a patient who presented to the endocrine surgery clinic for management of primary hyperparathyroidism discovered after a workup of her osteoporosis. The ultrasound and sestamibi scans were non-localizing. In hopes of enabling a targeted excision, the patient elected to pursue a 4D computed tomography scan of the neck for surgical planning rather than proceeding directly to surgical exploration, understanding that bilateral exploration would be the fallback option if the CT were also negative. CT neck revealed a mass posterior to the upper esophagus consistent with an ectopic adenoma. Intraoperative findings were identical to those predicted by the 4D-CT scan, resulting in an efficient and successful surgery.
Conclusion	In our case, the success of our patient's operation was facilitated by 4D-CT scanning, which correctly predicted a retroesophageal adenoma and allowed for a targeted and focused operation. We support the use of 4D-CT when ultrasound and sestamibi scans are negative for the localization of a potentially ectopic adenoma to yield higher success of index operation, fewer complications, and more cost-effectiveness.
Key Words	primary hyperparathyroidism; ectopic adenoma; 4D-CT scan

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Case Description

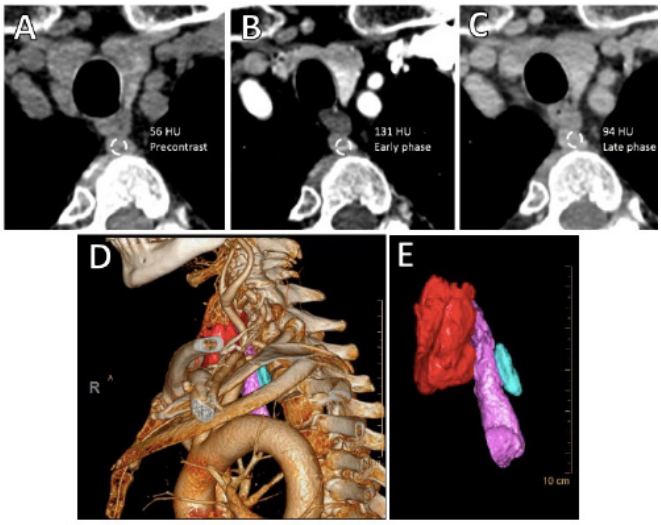
A 71-year-old female was referred to the endocrine surgery clinic for management of asymptomatic primary hyperparathyroidism discovered after a workup of her osteoporosis. Her past medical history was otherwise notable for hypertension, obesity, stress incontinence, diverticulitis, and esophagitis; she did not have a history of fragility fractures or kidney stones. Her past surgical history included right knee replacement, cholecystectomy, appendectomy, and hemicolectomy.

No abnormalities were appreciated on physical examination; her thyroid gland was normal, and there was no appreciable lymphadenopathy. Her serum calcium was 10.8 mg/dL (normal level ≤10.2 mg/dL), and her parathyroid hormone (PTH) level was 150.5 pg/mL (normal ≤65.0 pg/mL). Her 25–OH vitamin D level was 24 ng/mL (normal 30-60 ng/mL). Following ultrasound and sestamibi scintigraphy scan, which were non-localizing even on retrospective review, the patient was offered either surgical exploration or 4D computed tomography (CT) scan of the neck to further evaluate for an occult adenoma and the potential of a targeted operation.

CT neck revealed an 11 × 12 × 21 mm mass posterior to the upper esophagus. This mass measured 56 Hounsfield units (HU) on non-contrast imaging, enhanced to 131 HU on arterial phase, and washed out to 94 HU on delayed imaging, a pattern suspicious for parathyroid adenoma (Figures 1A–1C). Computer-aided 3D-CT reconstructed rendering images clearly demonstrated the enlarged retroesophageal parathyroid adenoma and its precise anatomic location (Figures 1D and 1E). Operative findings were identical to those predicted by the CT scan (Figure 2).

Intraoperative PTH (obtained via direct aspiration from the left internal jugular vein) values were 121 pg/dL at baseline, 54.5 pg/dL at the time that the adenoma was removed, and 33, 29, and 27 pg/dL at 5, 10, and 15 minutes post-excision. Pathological examination demonstrated a 9 × 14 × 31 mm parathyroid adenoma. Prior to discharge, her calcium and PTH levels were 9.9 mg/dL and 16.6 pg/dL, respectively, and have remained normal in 25 months post-operation.

Figure 1. CT Scan of Neck and 3D-CT Reconstructed Rendering. Published with Permission



A) 11 × 12 × 21 mm mass measuring 56HU on non-contrast imaging was noted posterior to the upper esophagus; B) which enhanced to 131 HU on arterial phase; and C) washed out to 94 HU on late phase. D and E) 4D-CT rendering images demonstrated enlarged retroesophageal mass (light blue mass; thyroid gland indicated in red, esophagus in lavender).

Figure 2. Intraoperative Findings. Published with Permission

Operative findings were identical to those predicted by scan.

Discussion

Primary hyperparathyroidism is the most common cause of hypercalcemia. Due to recent advancements in diagnostic techniques, the prevalence of diagnosed primary hyperparathyroidism has increased to an estimated 1-7 cases in every 1000 adults.[1] The most common cause of primary hyperparathyroidism is parathyroid adenoma, occurring in 85% of cases. Meanwhile, the remaining causes of primary hyperparathyroidism include hyperplasia, double adenoma, or, rarely, carcinoma.[2] Parathyroidectomy is the only curative treatment with a success rate of >97% in experienced hands. Normalization of calcium and parathyroid hormone levels leads to improvement in bone mineral density, reduction in kidney stones, decreased fracture risk, and overall improvement in quality of life.[3]

Parathyroid adenomas can arise from either the superior or inferior glands but can also be found in ectopic locations following patterns predicted by the embryologic migration of the glands, such as the mediastinum, thyroid gland, and retroesophageal plane.[4] Because of this anatomic variability, understanding the embryologic development of parathyroid glands is important for the surgical approach and success of parathyroid surgery.

The parathyroid glands are derived from endodermal epithelial cells. The superior glands arise from the fourth branchial pouch, while the inferior glands are derived from the third branchial pouch. Notably, glands that arise from the third pouch ("inferior glands") typically lie in a plane anterior to the recurrent laryngeal nerve. In contrast, glands arising from the fourth pouch ("upper glands") are usually found in a plane posterior to the nerve and, occasionally, descend below the level of the "lower" parathyroid.[3] The ectopic locations are related to variances in gland migration: either failure of the gland to fully descend, excessive descent, or co-localization with other tissue of similar embryologic derivatives such as the thyroid or thymus glands.

The variation in the locations of parathyroid glands is an important cause of failed parathyroid surgery. In one series, 54 of 102 patients who underwent revision surgery following incomplete parathyroid resection were found to have an adenoma in an ectopic position.[5] Patients who undergo reoperation for incomplete resection are subject to an increased rate of complications as a result of greater technical challenges from distorted tissue planes and adhesions. While the likelihood of vocal cord paralysis or hypocalcemia is roughly 1% for primary surgery, the incidence of these complications, respectively, is reported to be as high as 8% and 6% following reoperative parathyroid surgery.[5] Clearly, improvements in preoperative localization can potentially reduce the number of failed parathyroid operations.

While minimally invasive unilateral parathyroidectomy has become increasingly popular due to the decreased operative time and comparable outcomes, bilateral parathyroid exploration has always been considered the gold standard for patients undergoing surgery for primary hyperparathyroidism.[6] Patients predicted to have a solitary adenoma based upon imaging studies (most commonly, ultrasonography, sestamibi scintigraphy, and sestamibi-single photon emission computed tomography (SPECT)) may be candidates for unilateral parathyroidectomy. Other less frequently used imaging modalities include magnetic resonance imaging and 4D-CT scanning.[7] Accuracy between the imaging studies and their use varies depending on institutional practices and/or regional availability.

Four-dimensional parathyroid CT scans characterize parathyroid tissue based on its rapid contrast uptake and washout, differentiating it from lymphoid or thyroid tissue. Thus, a single scan can combine functional data with precise sectional anatomic detail, which may be reformatted into three-dimensional images using computer software (Figure 1B and C; the 4th dimension in "4D" refers to the timing of contrast uptake and excretion). While 4D-CT scans require slightly higher radiation exposure than conventional parathyroid imaging, their utility in localizing otherwise radiographically occult parathyroid adenomas is unquestioned. A study of 90 patients undergoing reoperative parathyroidectomy confirmed a high rate of concordance between 4D-CT imaging and surgical findings and correlated the 4D-CT group with a shorter operative time.[8] In patients undergoing an initial operation for primary hyperparathyroidism but had non-localizing ultrasonography and sestamibi scans, studies have also shown that preoperative 4D-CT scan improves localization.[9] A retrospective study by Hinson et al. demonstrated that 4D-CT localized parathyroid adenomas to the correct side with 84% sensitivity and 82% specificity in cases with non-localizing preoperative ultrasound and SPECT-CT scans.[10]

Touting its superior accuracy and ability to image the thyroid gland simultaneously, some groups have begun using 4D-CT as the preferred initial localizing test for patients with primary hyperparathyroidism.[7] A recent cost analysis study found ultrasound followed by 4D-CT (if US was indeterminate) to be the most cost-effective localizing strategy when comparing different parathyroid localization techniques.[11]

In our case, the success of our patient's operation was facilitated by 4D-CT scanning, which correctly predicted a retroesophageal adenoma and allowed for a targeted, focused operation that took only a few minutes to identify and remove the gland. While extensive literature describes the value of 4D-CT in parathyroid reoperations, we have increasingly used it to assist with preoperative localization of patients with negative conventional localization studies.

Conclusion

We support the use of 4D-CT when ultrasound and sestamibi scans are negative for the localization of a potentially ectopic adenoma to yield higher success of index operation, fewer complications, and more cost-effectiveness.

Lessons Learned

Ectopic parathyroid adenoma increases the risk of a failed parathyroidectomy surgery and operative complications. Preoperative localization studies can clue the surgeon to the location of a parathyroid adenoma that will better prepare the surgeon for a successful outcome. When ultrasound and sestamibi scans are non-localizing, a 4D-CT scan can help localize ectopic parathyroid adenomas, as seen in our patient.

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