Reoperative Parathyroidectomy: Overly Descended Superior Adenoma

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Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

Abstract

Objectives. To identify the importance of the ectopic, overly descended superior parathyroid adenoma variant and its prevalence in primary and reoperative parathyroid surgery and the implications for successful initial parathyroidectomy.

Study Design. Case series with planned data collection.


Subjects and Methods. An analysis was undertaken of 561 consecutive patients undergoing parathyroid surgery in a tertiary endocrine surgery practice from March 2004 to April 2013. There were 270 patients who had curative primary or reoperative surgery for single-gland parathyroid adenomas during this time. Clinical records, imaging studies, operative reports, and pathology findings were evaluated, and cases from a subset of patients who had an ectopic, overly descended superior parathyroid adenoma were further analyzed. The prevalence of this entity in primary and revision surgeries was calculated.

Results. Among the 270 patients with single-gland parathyroid adenomas, there were 251 primary operations and 19 reoperative procedures referred from outside institutions. An ectopic, overly descended superior parathyroid adenoma was present in 23 (9.2%) primary cases and 4 (21.1%) reoperative cases.

Conclusion. An overly descended superior parathyroid adenoma is frequently encountered during primary parathyroid surgery. It is more than twice as common in reoperative parathyroidectomy, reflecting the propensity to be missed at the first exploration. Recognition and proper treatment of this entity at the initial operation will reduce the need for revision surgery.

Keywords

parathyroid adenoma, ectopic, parathyroidectomy, parathyroid surgery

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Given these reports, endocrine surgeons are familiar with the phenomenon of an underdescended ectopic inferior gland. Less familiar is the phenomenon of an overly descended superior gland, mimicking an inferior gland adenoma on planar technetium-99m-sestamibi (sestamibi) imaging.

Our experience suggests that an overly descended superior parathyroid adenoma (ODSPA) is more prevalent than what is recognized in the literature and that it is a major cause of the need for reoperative surgery. These glands appear in an “inferior” position on sestamibi imaging (Figure 1). Intraoperatively, they are found low in the neck but dorsal to the plane of the RLN, confirming that they are superior parathyroid glands (Figure 2). Recognizing this variant may assist surgeons during primary and reoperative surgery, decrease the incidence of persistent disease, and prevent the misinformed and clinically unhelpful removal of normal inferior parathyroid glands.

Methods
A quality assurance database of all parathyroid surgeries at a tertiary endocrine surgery practice from March 2004 to April 2013 was interrogated under the auspices of the Georgia Regents Medical Center Institutional Review Board (Pro00000155). Populations excluded from consideration were patients with renal hyperparathyroidism, syndromic patients, and those with multigland disease. All patients undergoing curative surgery for PHPT due to a single-gland adenoma were included. Patient demographics and clinical information were recorded, including preoperative imaging results, whether or not the patient was undergoing primary or reoperative surgery, and the location of the adenoma. All cases of ectopic ODSPA were identified. An ODSPA was defined as an adenoma that appeared to be in an inferior location on a 2-dimensional planar sestamibi scan (below the interpolar horizontal and usually below the inferior pole of the thyroid gland) but was found intraoperatively to be dorsal to the coronal plane of the RLN and usually in the presence of an identified orthotopic normal inferior parathyroid gland. This anatomic relationship confirms that the adenoma is of superior parathyroid origin.

The prevalence of ODSPA in primary and revision surgeries was calculated, and a chi-square test was performed to explore for differences in the prevalence of ODSPA between these 2 surgical cohorts. All statistical analysis was performed with SAS 9.3 (Cary, North Carolina) with an alpha level of 0.05 to assess significance.

Results
There were 561 parathyroid operations accomplished during the study period. After renal hyperparathyroidism and syndromic cases were excluded as well as those with multigland disease, 270 curative procedures for PHPT were included in this analysis. Most patients (n = 213, 78.9%) were female, and the mean patient age was 57.8 ± 14.3 years. The majority of patients (n = 192, 71.1%) were Caucasian or African American (n = 71, 26.3%).

Medical surgery was performed in 251 patients (93%). There were 19 reoperative procedures (7%). All patients undergoing reoperative surgery had their initial operations performed at outside institutions. The location of each adenoma is shown in Table 1. The majority (n = 207, 82.5%) of adenomas in the primary cohort were found in orthotopic locations. In contrast, the majority of the adenomas in the reoperative cohort were ectopic (12 of 19, 63.2%; P = .000002).

Most ectopic glands in the primary surgical setting were in a deep location, such as a retropharyngeal, retro- or paracricopharyngeal, paraspinal, or overly descended position (n = 27, 61.4%). ODSPAs accounted for the majority of the deep adenomas (n = 23, 85.2%) as well as 52.3% of all ectopic adenomas in the primary surgery cohort. The remainder of the ectopic glands in the primary surgical group were found in the thymus or anterior mediastinum (n = 13, 29.5%), undescended in the submandibular region (n = 2, 4.5%), or within the thyroid gland (n = 2, 4.5%; Table 1).
Ectopic glands in the reoperative cohort were also most commonly identified in deep locations (n = 8, 66.7%). ODSPAs accounted for the majority of these deep glands (n = 4, 50%) and were the most common ectopic gland type (33.3%) identified during reoperative surgery. Other ectopic locations in this group included the thymus or anterior mediastinum (n = 2, 16.7%) and the submandibular region (ie, undescended; n = 2, 16.7%).

Ectopic glands are nearly 4 times more common in the reoperative setting (17.5% vs 63.2%; P = .1). Importantly, the majority of the ectopic glands in the reoperative setting were deep (dorsal) in the cervical neck (8 of 12, 66.7%).

### Discussion

PHPT is most commonly caused by a single adenoma in an orthotopic location.\(^{14}\) However, the complex migration of the parathyroid glands during embryologic development or the presence of supernumerary glands may result in the presence of hyperfunctional parathyroid tissue in ectopic locations. These ectopic foci may be missed at the initial surgery, leading to persistent disease and occasionally the inadvertent removal of normal parathyroid tissue. While it has been suggested that most cases of surgical failure are due to missed adenomas in orthotopic locations,\(^{7}\) in our series ectopic adenomas accounted for the majority (63.2%) of referrals to our center for persistent PHPT. This may be reflective of a new phenotype of parathyroid patient, in whom advanced imaging techniques usually identify the hyperfunctional adenoma, leading to a successful outcome in the hands of most surgeons, except for the occasional patient with an ectopic gland.

The tertiary nature of our endocrine surgery practice and a wide referral base result in our management of a disproportionate number of reoperative surgical patients, patients with nonlocalizing imaging at outside facilities, and patients with renal and syndromic hyperparathyroidism. This broad experience with initial and reoperative parathyroid surgery led us to speculate that an excessive number of parathyroid adenomas, particularly in the reoperative setting, were ectopically located superior parathyroid glands that had descended inferiorly, mimicking inferior parathyroid glands on 2-dimensional planar sestamibi imaging. In these cases, intraoperative inspection of the inferior parathyroid glands reveals normal parathyroid tissue, while dissection deep to the RLN (and oftentimes in the paraeosophageal or retroesophageal space) reveals the adenomas, confirming that these are superior glands. Because of their embryologic origin, inferior parathyroid glands are always ventral to the coronal plane of the RLN, and superior parathyroid glands are always dorsal to this plane.\(^{15}\) This relationship is maintained regardless of the vertical position of the glands in the neck.

An ODSPA may represent a developmental anomaly of parathyroid migration or the result of an enlarged superior parathyroid adenoma drifting inferiorly under the influence of gravity and the forces of deglutition. Regardless of the mechanism, this condition is both a common finding during initial parathyroid surgery and a common cause of operative failures, accounting for almost 10% of all adenomas at the primary surgery and $>20\%$ of the initial surgical failures in this series. If this condition is not recognized, well-meaning surgeons (guided by planar sestamibi scans that suggest an “inferior” adenoma) may remove an otherwise normal inferior parathyroid gland while failing to cure the patient.

The presence of an ODSPA may be suggested by several preoperative and intraoperative findings. Preoperatively, an inferior gland that appears “deep” or posterior on oblique sestamibi projections should be noted. Three-dimensional imaging modalities, such as single-photon emission computed tomography in isolation or combined with a computed tomography scan, may also reveal a particularly posterior location of a suspected inferior adenoma.\(^{16,17}\) The fused computed tomography component of the examination provides additional anatomic information that is helpful in guiding the exploration. Another recently described technique, 4-dimensional computed tomography, may reveal the posterior location of these glands.\(^{18}\) Ultrasound can be useful in predicting an ODSPA, especially when correlated with sestamibi findings and performed by the surgeon.\(^{19}\) These glands may appear low in the neck but deeper than the typical location for inferior adenomas, or they may not be seen at all. While this latter finding can be encountered in patients with multigland disease, it may also indicate an ODSPA that is either too deep to be viewed on ultrasound or hidden behind an overlying structure, such as the esophagus or clavicle, especially when combined with a sestamibi
scan that reveals no mediastinal or submandibular hyperfunctional tissue.

Parathyroid surgeons must be able to visually distinguish normal from abnormal glands. If exploration in the area predicted by preoperative imaging to harbor the abnormal gland reveals normal inferior parathyroid tissue, surgeons should refrain from resecting this tissue and instead direct their dissection deeper. The operative exposure should continue dorsal to the RLN until the esophageal fibers or prevertebral tissues are encountered. Only then can the surgeon be sure that the dissection is sufficiently deep to identify an ODSPA. Intraoperative assessment of parathyroid hormone levels is also useful for ensuring that all hyperfunctional parathyroid tissue has been removed, and it is particularly valuable in the reoperative setting.20

Typical locations for ectopic parathyroid adenomas have been extensively described and are well known to experienced endocrine surgeons.9 However, the ODSPA that mimics an inferior adenoma on preoperative sestamibi has been largely overlooked. A nomenclature system to classify parathyroid locations has been proposed21 but does not specifically include this entity. Mariette et al mentioned finding “overdescended” ectopic glands in 2.5% of patients undergoing reoperative surgery, but they did not distinguish if these glands were superior or inferior.11 Kim et al specifically reported on descended ectopic superior adenomas that mimic inferior glands on single-photon emission computed tomography but did not address their impact on surgical failure and reoperative surgery.17 Given the relatively frequent occurrence of this condition in primary surgery and its even more significant contribution to persistent disease and reoperative surgery, surgeons should be aware of this entity, personally review the preoperative imaging studies, and be prepared to explore deep in the neck when indicated to provide their patients the best chance of surgical success.

Author Contributions

William S. Duke, study design, data acquisition and analysis, drafting, final approval, accountability for the work; Hampton M. Vernon, data acquisition and analysis, drafting, final approval, accountability for the work; David J. Terris, study design, data acquisition and analysis, drafting, final approval, accountability for the work.

Disclosures


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