Chapter 5
Surgical Algorithm for Recurrent and Peristent Hyperparathyroidism

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Introduction

Persistent and recurrent hyperparathyroidism occurs in approximately 3.2% and 0.7% of patients, respectively. Taken together, these circumstances may be termed recalcitrant hyperparathyroidism. Initial studies of patients with persistent or recurrent elevated calcium levels after an initial parathyroid procedure suggested that the majority of patients in this category had multiglandular disease not appreciated at the initial operation [1–3]. However, these reports originated from institutional series with considerable experience in parathyroid surgery and are not representative of the general population after a failed parathyroid procedure [4]. A missed single abnormal parathyroid adenoma accounts for the majority of patients who fail initial procedures for the treatment of primary hyperparathyroidism [5, 6]. The causes for failed cervical exploration include the presence of multiple abnormal, ectopic, or supernumerary glands, surgeon experience, inadequate exploration of the neck and superior mediastinum, and incomplete resection of hyperplastic glands [4, 7]. Those patients not cured by the first operation pose a significant problem because of the more difficult and technically demanding nature of re-operative parathyroid surgery. As a result of scarring and distortion of normal tissue planes in the neck after a prior cervical exploration, success rates at subsequent surgery for primary hyperparathyroidism are decreased, and operative complications, including recurrent laryngeal nerve injury with vocal cord paralysis and hypoparathyroidism, can be even more problematic.

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Operative Strategy

Following the decision to proceed with re-exploration and having performed a review of the initial operative procedure and localization studies, the surgeon then considers the operative approach. Ideally, the objective is to remove a single gland without extensive dissection, which may result in injury to the surrounding structures, i.e., recurrent laryngeal nerve or devascularization of remaining parathyroid tissue. The likelihood of accomplishing the objective is very dependent upon two factors: the experience of the initial operating surgeon and the demonstration of an enlarged hyperfunctional parathyroid gland on correlative localization studies.

In most cases, reoperation following initial surgery by an experienced surgeon will be difficult and tedious because the initial dissection that will have been comprehensive and the surgical bed will have significant fibrosis. In contradistinction, the extensiveness of initial exploration and resulting degree of fibrosis may be significantly less in patients having had the original surgery performed by a relatively inexperienced surgeon. In both of these circumstances, a localizing study will be of prime importance in targeting the putative hyperfunctional gland and limiting the re-operative dissection.

The best of all scenarios, and the most common, is unequivocal localization to a cervical site, which may also include the anterior superior mediastinum. The previous neck incision is generally used for access, in some cases by excising the old scar completely. The usual superior/inferior flaps are raised and access gained to the side of the neck indicated by the localization studies. A lateral to medial approach to dissection is undertaken, to avoid the dense fibrosis in the region of the tracheoesophageal groove where the recurrent laryngeal nerve resides. In this manner, dissection proceeds medially from the sternocleidomastoid muscle superficial to the great vessels and then directly to the region overlying the cervical spine. This approach exploits the concept of the viscero-vertebral angle (VVA), as described by Tenta [8]. This potential anatomic space is defined as that area bordered laterally by the carotid sheath structures, medially by the trachea and esophagus, anteriorly by the thyroid, and posteriorly by the cervical spine (Fig. 5.1). In accessing this region, the surgeon may take advantage of a tissue plane with relatively little vascularity and fibrosis. This area will allow extension to examine the superior mediastinum inferiorly, the retroesophageal compartment medially, and as far as the hyoid bone superiorly, all within planes of dissection that separate with relative freedom. The recurrent laryngeal nerve may be identified and extensively exposed for protection during this approach. Dense fibrosis is infrequently encountered over the prevertebral space, even following a thorough initial exploration. In the event a gland is suspected in the superior retro-thyroidal area, the nerve should be identified as it may be lateral to a medially displaced superior gland. The majority of missed adenomas, which are accessible through a cervical incision, may be approached using this technique, which also allows for thyroidectomy if necessary. A situation whereby localization studies indicate a mediastinal location usually mandates a thoracic approach, either by median sternotomy or lateral open or video-assisted thoracotomy, depending on the location within the mediastinum. An enlarged gland identified within the anterior mediastinum and not accessible

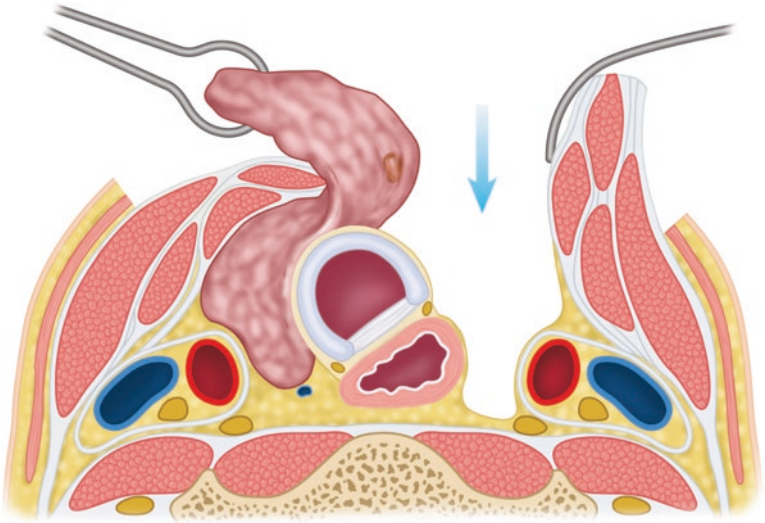

Fig. 5.1 The viscero-vertebral angle approach

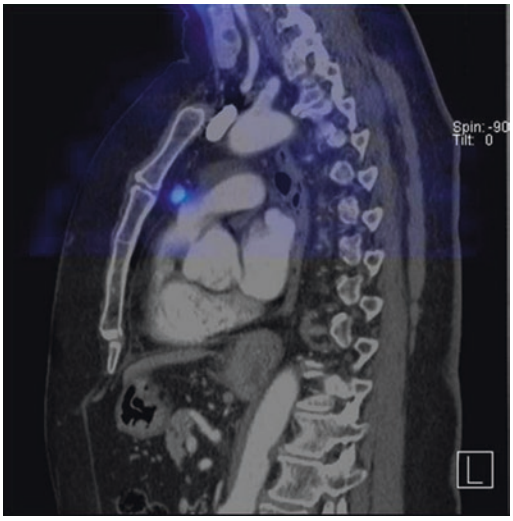

Fig. 5.2 Mediastinal parathyroid adenoma within middle posterior compartment demonstrated in fusion imaging

transcervically is usually associated with the thymus and may be accessed by either median sternotomy or video-assisted mediastinoscopy. These glands are usually found at the level of the innominate vein within thymic tissue but may also be found adjacent to the aortic arch or between the thymus and pleura. Should the localization studies demonstrate a posterior-based mediastinal gland, a lateral or posterolateral approach should be undertaken, either with open or video-assisted (VATS) technique (Figs. 5.2 and 5.3) in order to avoid dissection thru critical structures in the anterior

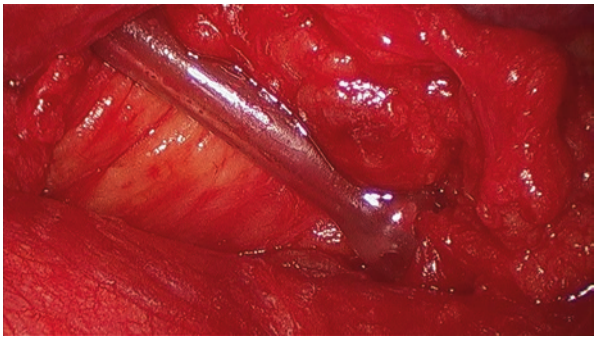

Fig. 5.3 Thoracoscopic approach to mediastinal parathyroid adenoma shown in Fig. 5.2

mediastinum. These posterior-based glands may reside in the aortopulmonary window or the retroesophageal region. One should be aware that the recurrent laryngeal nerve may be injured when approaching the posterior mediastinum through a left lateral thoracotomy. Despite what may be interpreted as compelling localization results, the surgeon should be prepared to perform concurrent cervical exploration in the event that initial intra-operative PTH levels (IOPTH) do not confirm removal of all hyperfunctional parathyroid tissue.

The most problematic preoperative scenario to confront is that in which localization fails to identify any suspicious putative site suggestive of parathyroid abnormality. It is in this situation where re-operative surgery for hyperparathyroidism is potentially the least successful and the most morbid. Failure to localize usually mandates a bilateral cervical exploration that comprehensively and methodically addresses all potential sites that may harbor a missing gland or glands. A properly constructed initial operative note that accurately documents remaining histologically identified parathyroid glands and regions explored is of utmost importance and potential value for the re-operative surgeon. An orderly systematic approach to re-exploration is necessary in these circumstances to locate the missing gland(s) and limit morbidity. The order in which regions are approached may vary according to the surgeon; however, it is important that all potential areas be accessed to increase the chance of success and avoid a failed re-exploration. The author's preference is to approach each side explored through the VVA via a lateral to medial orientation. Regions are then addressed in the following manner: the anterior superior mediastinum is dissected first, with careful attention to the thyrothymic ligament and tracheoesophageal groove region adjacent to the recurrent nerve. Cervical thymectomy, if not performed at initial surgery, is completed at this time. Dissection then turns to the retropharyngeal, retroesophageal region where blunt dissection within the prevertebral space will allow for digital exploration superiorly above the cricoid cartilage and larynx and inferiorly into the posterior mediastinum. Enlarged glands in this anatomic plane may often be felt by digital palpation before they are seen using these maneuvers. Next, the thyroid lobe is mobilized, possibly truncating the superior vascular pedicle to allow rotation of the thyroid gland anteromedially so that the posterior capsule may be thoroughly examined for a folded, lobulated parathyroid gland under cover of the capsular fascia. Using this technique, the thyroid lobe is

palpated for any nodular densities, which may be suspicious for an intrathyroidal or subcapsular parathyroid gland. The carotid sheath is then opened from the superior mediastinum to the hyoid bone, inspecting and palpating for nodular structures within the sheath. Failing identification on the side explored first, the dissection proceeds contralaterally in the same manner, with orderly inspection of all regions noted above. In the event that a bilateral exploration fails to identify the offending gland, thyroid lobotomy/lobectomy may be performed on the side suspected of harboring the offending gland. It is in this situation where surgeon-performed ultrasound, pre- or intraoperatively, may be of the most benefit to help avoid unnecessary thyroid removal.

In the event that all maneuvers described are unsuccessful in identifying the abnormal missing gland, the procedure is terminated and further measures undertaken to the gland's position by imaging or angioinvasive techniques. Mediastinal dissection is not advisable in the immediate setting, owing to lack of localization and length of time required after a thorough bilateral re-exploration. It should be emphasized that re-exploration should not be undertaken unless there is a reasonable potential for success based on localization studies and/or previous documentation which identifies the putative missing gland.

Intraoperative Assessment of Parathyroid Hormone

Intraoperative assessment of parathyroid hormone (IOPTH) represents a useful adjunct in the performance of parathyroid reoperation, both for single and multiple gland disease entities. The usefulness of biochemically confirming the removal of hyperfunctional parathyroid tissue by applying IOPTH becomes apparent when one considers the previous operative procedure(s) performed by the initial surgeon with respect to what was identified/removed and whether normal glands were identified and histopathologically confirmed. The utilization of IOPTH allows the surgeon to determine the physiologic effect of removal of the putative abnormal gland, indicating removal of all hyperfunctional parathyroid tissue provided the appropriate criteria (>50% decline in PTH) is achieved intraoperatively. Should this decrement not be achieved, further exploration proceeds until IOPTH confirms removal of all hyperfunctional tissue.

Thus, the application of IOPTH in re-exploration potentially limits the extent to which surgical dissection is required in the previously operated neck, thereby limiting the possibility of injury to the recurrent laryngeal nerve and iatrogenic hypoparathyroidism due to manipulation/biopsy of normal glands. Another capability of IOPTH is through intraoperative sampling of blood from the internal jugular veins simultaneously in order to determine a gradient difference in PTH levels, thereby indicating on which neck side a hyperfunctional gland resides (Fig. 5.4). This technique may also be employed to potentially identify an ectopically located undescended inferior parathyroid adenoma, or so-called parathymus, which was not identified at the time of initial exploration (Fig. 5.5). Ultimately, the use of IOPTH in all parathyroid explora-

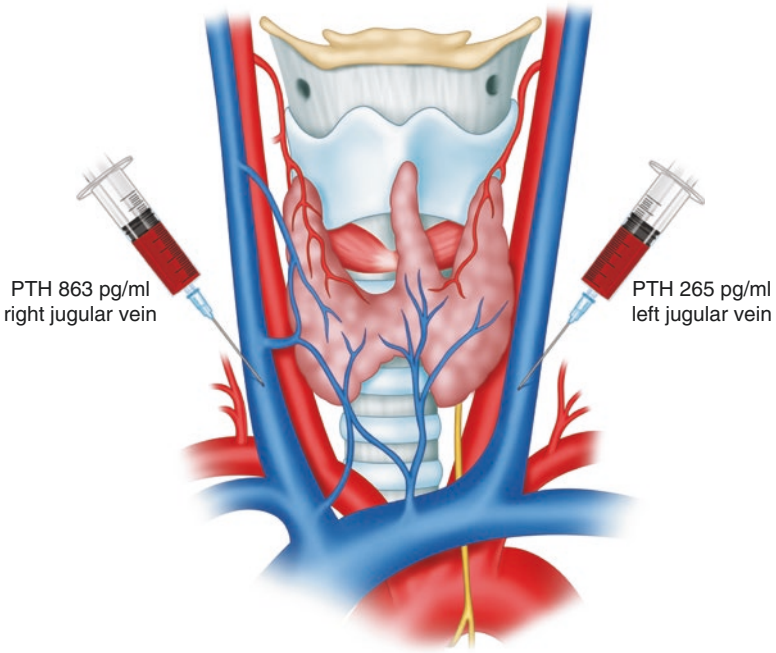

Fig. 5.4 Simultaneous IJV sampling for intraoperative PTH assessment

tions provides a measure of biochemical confidence that will serve to limit the extent of surgical dissection and reduce the potential for morbidity.

Mediastinal Exploration

Re-exploration for parathyroid disease may require exploration of the mediastinum. Ectopic parathyroid glands located within the mediastinum and below the level of the thymus account for a small percentage (0.2%) of all abnormally located glands [9]. These inferior parathyroid glands are associated in almost all circumstances with the thymus with which they descend during the embryonic development, having arisen with this structure as a third pharyngeal pouch derivative (Fig. 5.6).

Several approaches to the mediastinum are possible for re-exploration. The choice of approach utilized is dependent on the location of the putative adenoma. Definitive localization is required prior to considering mediastinal surgery. Fusion imaging, combining the anatomic and physiologic capabilities of computed tomography and sestamibi nuclear scintigraphy, provides for simultaneous correlative imaging for hyperfunctional parathyroid glands (Fig. 5.7). The techniques available for approaching the mediastinum include transcervical substernal with cervical

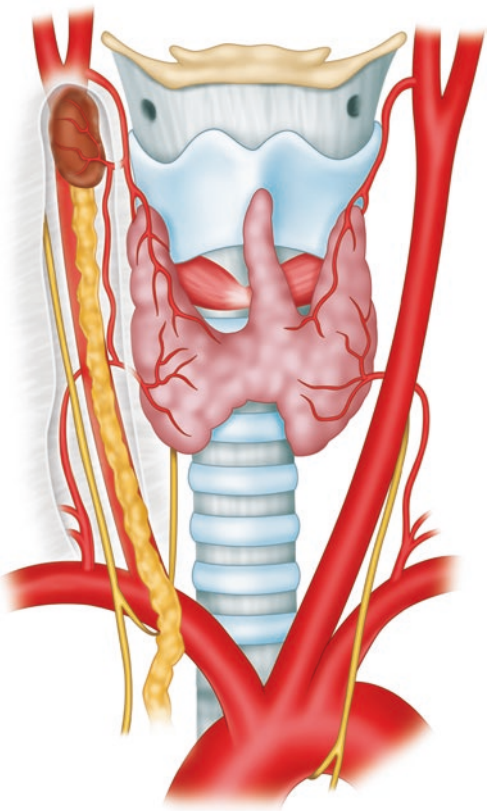

Fig. 5.5 The undescended inferior parathyroid gland, so-called parathymus

thymectomy using sternal retraction (with or without video assistance) for superior mediastinal glands, median sternotomy with direct approach to the anterior middle and caudal compartments, posterolateral thoracotomy for posteriorly based glands in the lower mediastinal compartment, and video-assisted endoscopic minimally invasive dissection for selectively focused exploration.

Secondary/Tertiary Hyperparathyroidism and MEN

Recalcitrant hyperparathyroidism following total or subtotal parathyroidectomy in patients with renal-induced disease represents a unique challenge to the surgeon. Problems with persistent disease usually result from inadequate resection following subtotal parathyroidectomy in which three or fewer glands are removed initially or when supernumerary gland(s) are not recognized during four-gland parathyroidectomy. Recurrent hyperparathyroidism usually results from delayed hyperplasia developing in cervical parathyroid remnants or within autotransplanted tissue placed during initial surgery.

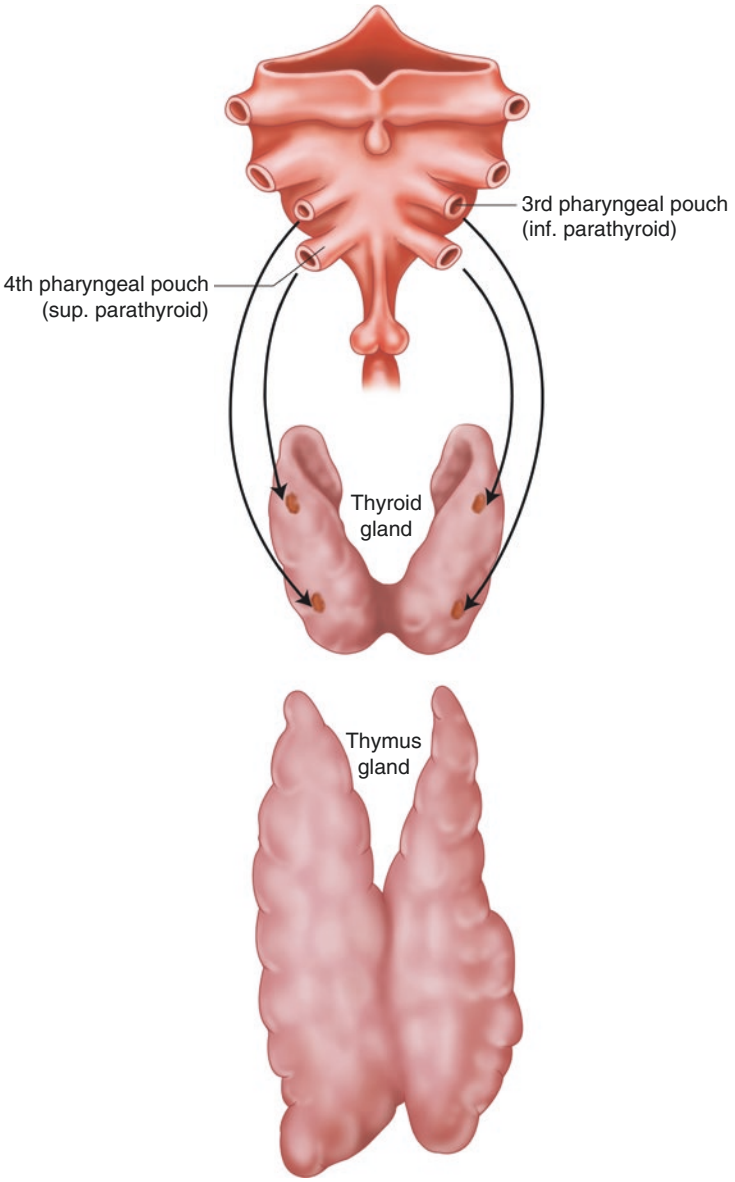

Fig. 5.6 Embryonic derivation of the parathyroid glands

The surgical evaluation for patients recommended for re-exploration includes sestamibi imaging and the determination of the serum PTH gradient in the graft-bearing arm as compared with the contralateral arm in patients who also received autotransplantation initially. Candidate patients in this cohort include those with renal-induced hyperparathyroidism and those with the Multiple endocrine neoplasia type 1 (MEN 1) syndrome in whom total parathyroidectomy was indicated. Patients with the MEN 1 syndrome undergoing re-exploration pose a unique sur-

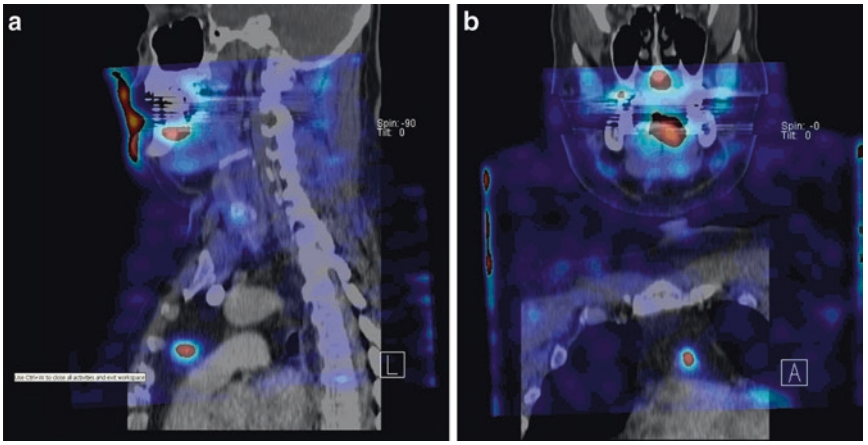

Fig. 5.7 (**a**) Sagittal projection from "fusion" image depicting mediastinal parathyroid adenoma; (**b**) coronal projection of "fusion" image depicting parathyroid adenoma

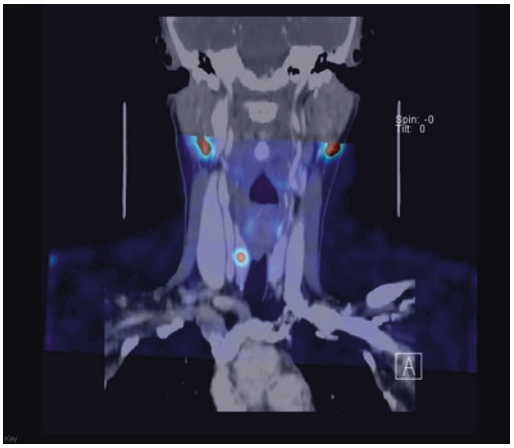

Fig. 5.8 Coronal projection of "fusion" image depicting intrathyroidal parathyroid gland in recurrent MEN 1

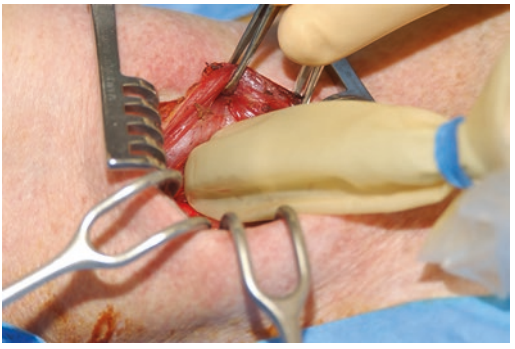

Fig. 5.9 Intraoperative photograph depicting the use of the gamma detection device in localizing intrathyroidal parathyroid gland in pt. with recurrent MEN 1

gical challenge in that, even after initial four-gland removal, the possibility of hyperfunctional supernumerary parathyroid tissue exists together with autograft hyperfunction. Unlike sporadic four-gland hyperplasia in patients with primary hyperparathyroidism, those patients with recalcitrant renal- or MEN 1-induced disease will often localize accurately with nuclear scanning (Fig. 5.8). In these instances, the gamma detection device may be utilized to facilitate the dissection in order to limit disturbance to critical surrounding structures and limit morbidity (Fig. 5.9).

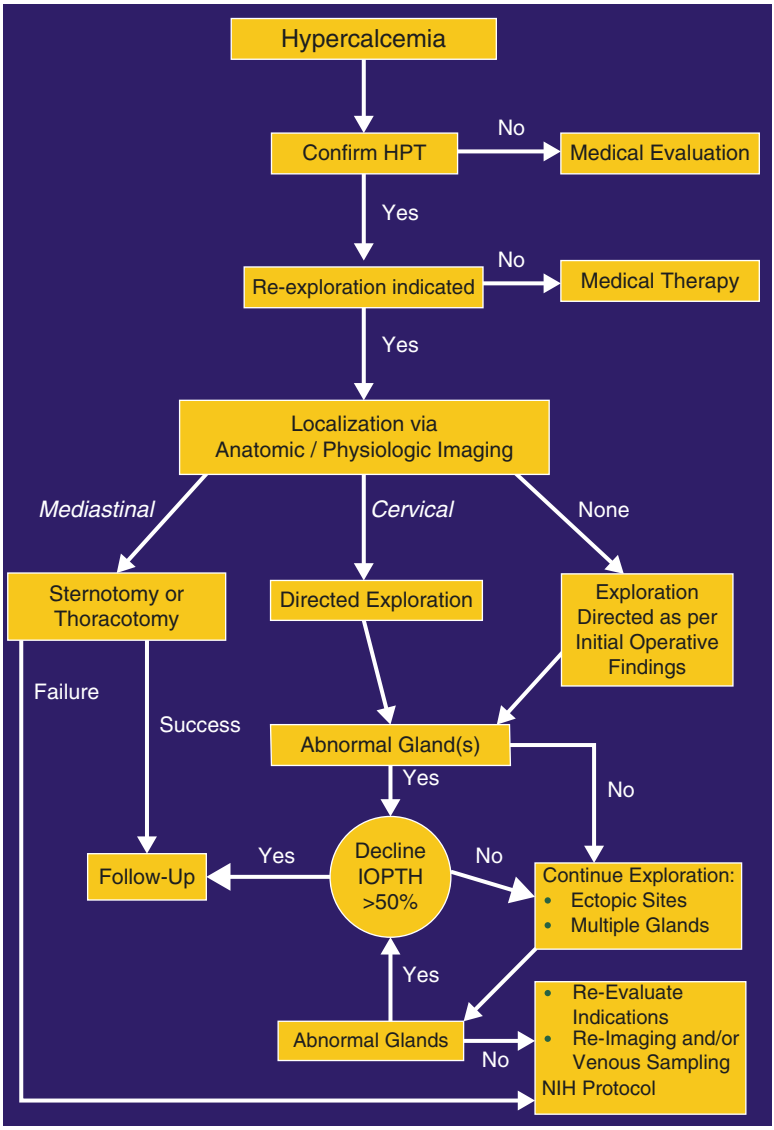

Fig. 5.10 Treatment algorithm for recalcitrant hyperparathyroidism

Summary

Management of recalcitrant hyperparathyroidism represents a unique therapeutic challenge. Opportunity for success and potential morbidity incurred as a result of reoperation differ significantly when compared with initial surgery. The utilization of surgical adjuncts such as invasive/noninvasive localization studies, IOPTH, and gamma probe offers benefit in the management of patients with recurrent hyperparathyroidism. A management protocol is summarized in the treatment algorithm illustrated in Fig. 5.10.

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