Mediastinal Parathyroid Tumors

Experience with 38 Tumors Requiring Mediastinotomy for Removal

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Most hyperfunctioning parathyroid tumors situated in the mediastinum can be removed by means of a cervical approach. However, a few tumors, because of their location deep in the chest, require mediastinotomy for removal. These tumors are probably derived from parathyroid glands that have developed from the third branchial pouch. Between 1942 and 1980, 38 such tumors were removed at the Mayo Clinic, using a sternum-splitting procedure. With one exception, the patients had undergone previous parathyroid exploration. Almost all of the patients had significant complications of primary hyperparathyroidism (HPT). Thirty-seven patients (97%) were cured after removal of their mediastinal parathyroid tumors, but postoperative chest complications were encountered in eight patients (21%), and eight have permanent hypoparathyroidism. Six patients had selective arteriography, two had selective thyroid venous sampling and parathyroid hormone assay, and 13 had mediastinal computed tomography in an attempt to localize tumors before operation. The anatomic locations of the tumors at operation were variable, but the vast majority (68%) were in or near the thymus.

CHURCHILL WAS THE FIRST to recognize that hyperfunctioning parathyroid tumors might be located within the mediastinum.[1] In 1932, he successfully performed a sternum-splitting procedure to remove a mediastinal parathyroid adenoma from a Captain Charles E. Martell. This unfortunate patient had previously undergone six unsuccessful cervical explorations for primary hyperparathyroidism, which was complicated by severe osteitis fibrosa cystica generalisata and nephrolithiasis.

Several authors[2,3] have since reported finding mediastinal parathyroid tumors relatively frequently during the course of routine parathyroid surgery. Most of these tumors have been accessible to removal via the neck incision—thus, of 84 mediastinal parathyroid tumors described in a report from the group at the Massachusetts General Hospital,[2] only 19 required median sternotomy for removal. These 19 patients represented less than 5% of all patients undergoing operation for primary hyperparathyroidism during the period of the study.

Between 1942 and 1980, 2,770 patients underwent operations for primary hyperparathyroidism at the Mayo Clinic. Mediastinal explorations were performed in 59 patients, in 38 of whom hyperfunctioning parathyroid tumors were found. The following report details the pertinent clinical, laboratory, and operative findings in this group of 38 (1.4% of all the patients), 11 of whom were included in an earlier communication from our institution.[4]

Clinical Findings

There were 21 females and 17 males included in the study; their mean age was 51 years. All but one patient had undergone prior cervical exploration for primary hyperparathyroidism—one operation in 26 patients, two operations in ten patients, and three operations in one patient. Two patients also had had unsuccessful mediastinal explorations performed elsewhere, in addition to the previous cervical operations. Of the 37 patients with histories of prior parathyroid surgery, only one had recurrent hyperparathyroidism, as defined by a minimal period of six months of normocalcemia after the initial operation before hypercalcemia recurred; all the rest had persistent hyperparathyroidism after unsuccessful neck surgery.

The one patient who had a primary mediastinal exploration without prior cervical operation was a 63-year-old man, who was being evaluated for hypercal-

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TABLE 1. *Results of Preoperative Selective Arteriography in Six Patients*

Case	Preoperative Report	Tumor Location	Weight (mg)	Dimensions (cm)
1	Positive	Thymus	680	1.2 × 1.1 × 0.8
2	Positive	Thymus	315	1.0 × 0.8 × 0.8
3	Positive	Superior mediastinum	3,800	3.0 × 2.5 × 1.0
4	Negative	Thymus	800	1.5 diameter
5	Positive	Anterior mediastinum	2,600	2.0 × 1.5 × 1.2
6	Positive	R. lateral esophagus	7,900	5.0 × 2.5 × 1.3

cemia when he presented to the emergency room with acute, severe retrosternal pain and dysphagia. A roentgenogram of the chest revealed a superior mediastinal mass suggestive of a dissecting thoracic aortic aneurysm. Aortographic examination demonstrated, however, an intact aorta, and a large (7.9 g) hemorrhagic parathyroid adenoma was found at mediastinotomy. This unusual case has been detailed elsewhere.[5]

In each of nine patients (24%), four cervical parathyroid glands had been identified at the previous operation. In eight of these, identification of the glands had been confirmed by biopsy specimen and histologic examinations.

Renal lithiasis (either nephrocalcinosis or calculi or both) was present in 28 of the 38 patients (74%). Ten patients (26%) had convincing radiologic evidence of parathyroid bone disease—areas of osteitis cystica in five patients and subperiosteal resorption of the fingers in five patients. Six other patients demonstrated chondrocalcinosis or nonspecific osteoporosis. One patient had hyperparathyroidism as one component of the multiple endocrine neoplasia syndrome, type 1; no patients had familial hyperparathyroidism. The study group of patients had a high frequency of complications of hyperparathyroidism, probably because only those patients with significant disease problems were referred for additional surgery. Serum calcium levels immediately before mediastinal exploration ranged from 10.8 to 17.0 mg/dl, with a mean value of 12.1 mg/dl (normal: 8.9 to 10.1).

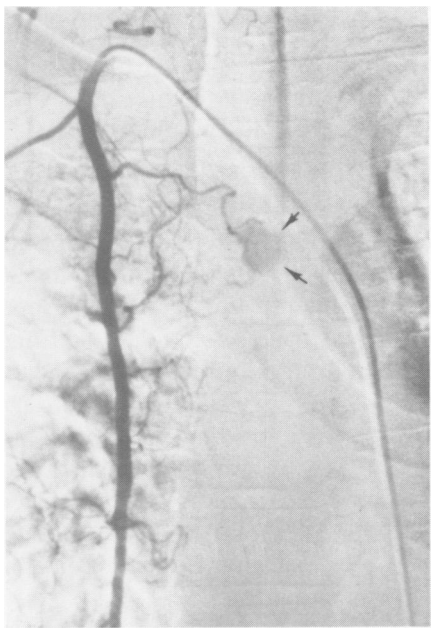

FIG. 1. Parathyroid angiogram. Injection into right internal mammary artery (late arterial phase) with subtraction technique demonstrates 1.0 cm tumor (arrows) in anterior mediastinum.

TABLE 2. *Results of Preoperative Mediastinal Computed Tomography in 13 Patients*

Case	Preoperative Report	Tumor Location	Weight (mg)	Dimensions (cm)
1	Positive	L. common carotid artery	7,450	3.0 × 2.2 × 1.7
2	Positive	Aortic arch	4,500	2.0 × 1.5 × 1.5
3	Negative	Thymus	570	1.7 × 0.7 × 0.4
4	Positive	Thymus	1,955	1.8 × 1.8 × 1.4
5	Negative	Thymus	500	No record
6	Positive	Innominate artery	No record	3.8 × 2.5 × 1.9
7	Negative	L. common carotid artery	3,330	2.6 × 1.9 × 1.3
8	Negative	Thymus	180	No record
9	Negative	Thymus	80	No record
10	Negative	Thymus	1,000	1.0 × 1.0 × 1.2
11	Positive	Aortic arch	1,500	1.2 × 0.8 × 0.2
12	Positive	Aortic arch	2,250	3.0 × 2.0 × 1.5
13	Positive*	Thymus	170	No record

* False-positive (see text for discussion).

Localizing Studies

Preoperative tumor-localizing studies were performed in 20 of the 38 patients. Arteriographic examination was done in six patients and identified the mediastinal tumor in five (83%) (Table 1, Fig. 1). Selective thyroid venous catheterization and sampling with assay of immunoreactive parathyroid hormone concentration was performed in two patients but failed to lateralize the tumor in either. Computed tomography (CT) of the mediastinum was used in 13 patients (Table 2). The tumor was correctly localized before operation in six patients (Fig. 2); in the other seven patients, the scan failed to identify the mediastinal tumor. In one of these patients, a "tumor" was identified on the scan, but it was not at the site of the adenoma that was subsequently found at operation (false-positive).

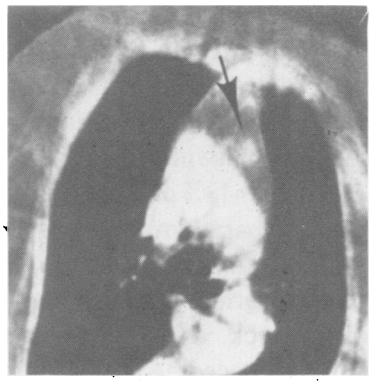

FIG. 2. CT scan of mediastinum after intravenous infusion of contrast material shows 1.2 cm parathyroid adenoma (arrow) adjacent to ascending aorta.

Operative Details

Thirty-eight patients underwent median sternotomy either alone (23 patients) or in conjunction with cervical re-exploration (15 patients). Eighteen (47%) of the 38 parathyroid tumors retrieved from the mediastinum were located within the thymus gland; a further eight tumors (21%) were situated in the anterior mediastinum near the thymus (Fig. 3). Nine tumors (24%) were intimately related to the ascending aorta, aortic arch, and great vessels arising from the arch. Two adenomas (5%) were adherent to the pericardium, while a single gland was located on the right lateral aspect of the esophagus.

Postoperative Complications

There were no operative deaths, but significant postoperative complications occurred (Table 3). Eight patients (21%) had chest complications, such as pleural effusion (four patients), requiring thoracocentesis, and pneumothorax (one patient), necessitating chest tube drainage. Pre-existing congestive cardiac failure was believed to have been a contributing factor in two of the patients with pleural effusions. Wound complications developed in three patients (8%): hematoma in one patient, sternal dehiscence in another, and severe anterior mediastinitis requiring surgical drainage in the third patient.

Of the 20 patients whose postoperative vocal cord function was documented, two experienced transient unilateral paresis, recovering completely within three months. In a third patient, the left vocal cord has remained fixed in the midline five months after operation, with the right vocal cord compensating fully to produce a normal speaking voice.

Both patients in whom atrial fibrillation developed after mediastinal exploration underwent conversion to sinus rhythm with the use of digitalis.

Results of Operation

Of the 38 patients, 37 were cured of their hyperparathyroidism. After operation, serum calcium levels for these patients ranged from 6.8 to 9.9 mg/dl (mean: 8.3 mg/dl). Four patients experienced temporary postoperative symptomatic hypocalcemia requiring the administration of oral calcium supplements; another eight patients have permanent hypoparathyroidism and are still on replacement therapy 1–11 years after operation. One patient, a 55-year-old man with multiple endocrine neoplasia syndrome, type 1, remained hypercalcemic after removal of a 2,300 mg parathyroid tumor from the mediastinum. Previously, he had had three "adenomatous" parathyroid glands removed from his neck. Presumably, he had a hyperplastic supernumerary parathyroid gland situated somewhere in the neck or mediastinum. He died in 1973, 12 years after mediastinal

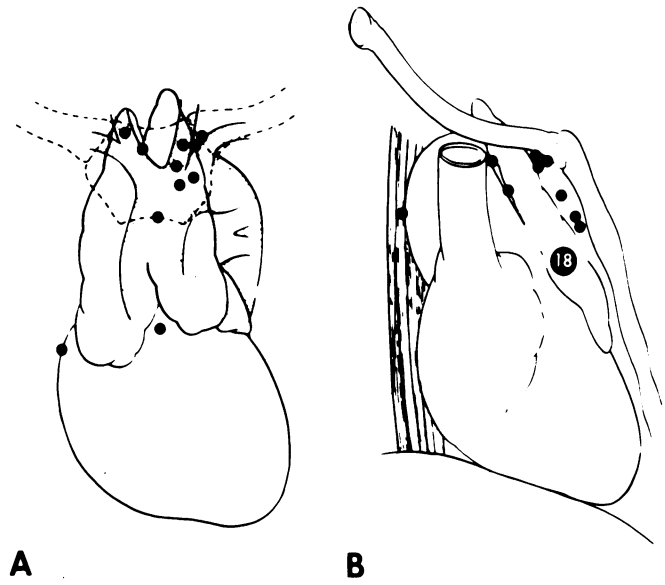

FIG. 3. Distribution of 38 mediastinal parathyroid tumors requiring median sternotomy for removal. (A) Locations of 11 tumors related to pericardium and great vessels. (B) Locations of 27 tumors related to thymus gland and esophagus.

TABLE 3. *Postoperative Complications after Median Sternotomy in 38 Patients*

Complication	No. of Patients
Chest	
pleural effusion	4
pneumothorax	1
atelectasis-pneumonitis	3
Wound	
hematoma	1
sternal dehiscence	1
anterior mediastinitis	1
Unilateral vocal cord paralysis*	
temporary	2
permanent	1
Atrial fibrillation	2
Deep vein thrombosis	1

* Postoperative indirect laryngoscopy was performed in 20 patients.

exploration. An autopsy examination was not performed.

Discussion

Mediastinal parathyroid tumors are of two types.[6,7] The first type probably derives from parathyroid glands originally situated in the neck, which subsequently descend into the chest after enlargement, presumably under the influence of their weight and perhaps, in addition, due to the effect of swallowing and negative intrathoracic pressure.[6] These tumors usually involve the superior parathyroid gland, and they retain a vascular pedicle from the neck, which may serve as a guide to their location.[7] The vast majority of these tumors are accessible to removal from the neck.

The second type of mediastinal parathyroid tumor constitutes the predominant type requiring mediastinotomy for removal. It is believed to occur in a parathyroid gland that originally developed in the chest, usually within the thymus or in relation to the great vessels. These glands either are inferior parathyroid glands that overshoot the neck during developmental descent or are supernumerary parathyroid glands, presumably also derived from the third branchial pouch. They develop in the mediastinum itself, so that their blood supply comes from mediastinal vessels. A significant proportion of these intrathymic tumors can be removed by delivering the upper thymus into the neck, using gentle, steady upward traction on the cervical tongue of thymus. However, some are situated deep in the mediastinum and are inaccessible to retrieval from the neck. These tumors require median sternotomy for their removal.

The data obtained in this study are consonant with the foregoing description. Thus, we find that true mediastinal parathyroid tumors, requiring mediastinotomy for removal, are rare—only 38 such tumors were encountered among 2,770 patients (1.4%) undergoing operation for primary hyperparathyroidism at the Mayo Clinic between 1942 and 1980. Also, the vast majority of these tumors (almost 70%) were located within or intimately related to the intrathoracic thymus. Probably all except one were ectopic inferior or supernumerary glands, which had descended during embryologic development into the chest. The single tumor found alongside the esophagus in the posterior mediastinum most likely was a tumor of a superior parathyroid gland which had originally developed in the neck and had subsequently descended along the tracheoesophageal groove after enlargement. In this context, it is worth noting that, among the 21 mediastinal parathyroid tumors requiring median sternotomy for removal which were reported by Wang,[8] the vast majority (67%) also were located in the thymus.

Interestingly, 21% of the mediastinal parathyroid tumors reported in this study arose in supernumerary (fifth) glands. This should not be altogether unexpected if one considers the various factors involved in selecting these patients for operation and the probability that as many as 13% of the general population may have five or more parathyroid glands.[9,10]

Mediastinal exploration should not be performed without prior thorough and systematic exploration of the neck. Usually one should wait several months before proceeding with the mediastinal operation, taking this time to reconfirm the diagnosis of hyperparathyroidism and to perform appropriate tumor-localizing studies. In the present study, median sternotomy with mediastinal exploration for persistent hyperparathyroidism was associated with significant postoperative morbidity. Thus, the operation should not be undertaken unless the patient's disease is serious enough to warrant exposure to the anticipated risks.

Of the tumor-localizing studies currently available, selective parathyroid arteriography was the most accurate (83% accuracy) in our experience (Fig. 1). A positive arteriogram provided a specific diagnosis and allowed the surgeon to proceed directly with mediastinotomy, thereby obviating the tedium and risk of a cervical reoperation. However, it is well known that this study carries inherent risks of serious neurologic complications.[11–13] Because of this, we are reluctant to perform parathyroid arteriography routinely before reoperative parathyroid surgery.

CT localized six of 13 mediastinal parathyroid tumors in this study: the smallest gland was 1.2 cm (1.5 g) (Fig. 2). We encountered one false-positive scan. Thus, CT failed to detect seven of the 13 tumors before operation. In five of the seven cases, the tumor was small (570, 500, 180, 80, 170 mg) and located in the thymus. In a sixth patient, the tumor was visible on the CT scan in retrospect, but the examination had been done without the use of intravenous contrast material because of a previously documented allergy to iodine. In the seventh case with a false-negative result, the tumor was large (3,330 mg) and was not visible even in retrospect. Again, intravenous contrast material had not been used during the examination because of the patient's poor renal function.

It is evident from these results that mediastinal CT has several limitations as a tumor-localizing tool in this situation. It is, however, essentially risk-free and of relatively low cost. We, therefore, intend to continue using this technique in the routine evaluation of patients undergoing reoperative parathyroid surgery.

After operation, 12 of the 38 patients (32%) developed symptomatic hypocalcemia requiring treatment; eight of these patients have permanent hypo-

parathyroidism. In order to circumvent this distressing problem, we have recently been performing immediate autotransplantation of a portion of the removed parathyroid tumor into the musculature of the forearm[14] whenever we have certain knowledge that three or four parathyroid glands have already been removed. Five of the patients included in the present study had such transplants, and there is evidence that at least three of the grafts are now functioning—by virtue of a higher iPTH concentration in the venous blood draining the grafted arm compared with that in the nongrafted arm, or a significantly decreased requirement for replacement treatment. Our current policy regarding parathyroid autotransplantation in reoperative parathyroid surgery is to perform immediate grafting of a portion of the resected gland if we have unequivocal evidence that three or four parathyroid glands have already been removed.[15] If, however, uncertainty exists regarding the number of parathyroid glands left *in situ*, the resected tissue is cryopreserved[16] for autotransplantation at a later date, should protracted hypoparathyroidism develop.

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