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Mediastinal Parathyroid Tumors: A Clinical and Pathological Study of 84 Cases

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FORTY-FOUR years after the first description of hyperparathyroidism, the disease⁸ still poses many difficult problems. One of these stems from the anatomical variation in the distribution of the parathyroid glands. Mediastinal parathyroid tumors in particular have frustrated many surgeons. A typical example is that of the first patient ever treated in this country, Sea Captain Charles Martell.² In January, 1926,

this patient presented with severe skeletal and chemical manifestations of hyperparathyroidism. A normal parathyroid gland was removed at each of the first two of the eventual six neck explorations. The causal adenoma lying deep in the mediastinum was not discovered until the seventh operation 6 years later. Unfortunately, patients having problems similar to Charles Martell are still encountered today. Management of these patients is not always easy. Procrastination and failure are common experiences.

Since 1930, 400 hyperparathyroid patients have been operated upon at the Massachusetts General Hospital. The diseased parathyroid glands were widespread and have been located from as high as the submaxillary triangle down to the pericardium. Eighty-four parathyroid tumors were located in the mediastinum, 67 in the anterior, and 17 in the posterior mediastinum (Table 1).

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TABLE 1. *Mediastinal Parathyroid Tumors—
Massachusetts General Hospital Series
of 84 Cases (1930-1968)*

Anterior Mediastinum		Posterior Mediastinum	
Upper	58	Upper	14
Lower	9	Lower	3
	—		—
Total	67	Total	17

Nineteen tumors, eight in the anterior and eleven in the posterior mediastinum, were removed by mediastinotomy; 62 through neck incision; three identified at autopsy.

The mediastinal position of parathyroid glands is generally predetermined by embryologic development. It may result from subsequent pathologic displacement. Parathyroid glands originate in the third and fourth pharyngeal pouches. The parathyroids III, along with the thymus, arise from the third pouch, whereas the parathyroids IV come from the fourth pouch associated with the lateral thyroid lobes. In the adult, the parathyroids IV become the upper parathyroid glands. They are normally located in an area limited above by the superior edge of the larynx and below by the lower pole of the thyroid gland. As the parathyroid gland increases in size, the tumor mass may descend because of its weight and deglutition and may eventually be sucked into the posterior mediastinum. Such an enlarged parathyroid is often attached to the thyroid by a long and large-sized vascular pedicle. In contrast, parathyroid III, which becomes the lower gland, may normally be found anywhere in the area spreading from the larynx to the pericardium. It may accompany the thymic buds in their descent into the anterior mediastinum. Intrathymic locations have been found in the lower, as well as in the upper part of the thymus. It is possible, but doubtful, that the lower parathyroid glands could descend lower in the mediastinum than the thymus. Although the lower parathyroid glands may be variably located in the anterior medi-

astinum, they normally remain in close association with the thymus, due to their common embryologic origin. As it becomes enlarged, the parathyroid gland may sink into the posterior mediastinum, if it originates in the neck, or posteriorly toward the lung root, if it is already in the mediastinum.

Not all mediastinal parathyroid tumors require sternal split for their removal. Of the 84 mediastinal parathyroid tumors, 62 were successfully excised through a low collar thyroid incision and only 19 by mediastinotomy (Table 2).^{*} Thus, a majority of the parathyroid tumors in the mediastinum can be removed from the neck, particularly those tumors located in close proximity to the thoracic inlet. Some tumors, however, may be too large or located too deep in the mediastinum, making it impossible to approach them through a neck incision. The forceful search through a neck incision is extremely hazardous.

In one patient (MGH #24-54-82, Parathyroid Case #50) during a blunt and blind dissection of the anterior mediastinum through the collar incision, a bilateral partial pneumothorax resulted, and the patient died 2 hours after the operation. Post-mortem examination confirmed the presence of a large parathyroid adenoma poking its nose out of the thymic capsule, lying just in front of the upper portion of the right auricle. It was fully 2 inches from the notch of the manubrium beyond the reach of the fingers. This parathyroid adenoma was in the lowest position of any we have found and lower than any parathyroid gland ever reported in the literature. The experience with this patient demonstrates that parathyroids may be beyond reach from the neck, and the danger of blunt dissection of the chest is obvious. Thus, a second stage mediastinotomy must be resorted to.

^{*} Three instances of mediastinal tumors were found at autopsy.

TABLE 2. *Nineteen Cases of Mediastinal Tumors Uncovered by Mediastinotomy*

MGH Unit No.	Parathyroid Case No.	Pathological Type	Position of Tumor
31-72-99	66	adenoma	Intrathymic, at right 3rd interspace
150-46-24	386	adenoma	Intrathymic, in front of right lung root
82-61-01	150	adenoma	Posterior to right thymic tongue
142-69-74	361	adenoma	Intrathymic, in front of right innominate vein
99-18-87	223	adenoma	Behind esophagus, posterior mediastinum
114-10-29	253	adenoma	In front of left pulmonary artery
26-45-41	53	adenoma	In front of ascending aorta
116-21-21	263	adenoma	In front of main pulmonary artery
27-58-90	6	adenoma	Intrathymic, superior anterior mediastinum
110-66-57	239	carcinoma	In front of the right and left innominate veins and the left common carotid artery
37-48-40	72	adenoma	In front of right lung root
27-78-54	54	adenoma	In front of and above left innominate vein
29-20-18	56	adenoma	Behind the aortic arch
14-43-13	18	adenoma	Anterior to right innominate vein
101-94-78	209	adenoma	Anterior to left common carotid, anterior superior mediastinum
18-24-37	40	adenoma	In front of left innominate vein
142-88-74	362	adenoma	In front of aortic arch and innominate vein
62-08-61	92	adenoma	In front of ascending aorta
82-42-09	170	hyperplasia	Behind right innominate vein

Caution, however, must prevail. Mediastinotomy should not be undertaken lightly except for valid reasons, as given above. Many patients have undergone unnecessary mediastinal exploration without having had a thorough and adequate search in the neck. Thus, one may overlook an obvious parathyroid tumor in the neck or in the upper mediastinum that could be safely approached with ease.

Our experience with one patient (MGH #79-96-87, Parathyroid Case #143) illustrates the futility of such a mediastinal exploration. A 48-year-old woman, six years prior to entry to the MGH on January 19, 1953, had repeated episodes of renal calculi. In May, 1949, a right renal stone was removed. In December of the same year two large calculi were found in the right upper ureter with marked hydronephrosis and numerous calculi of the right kidney. A right nephrectomy was carried out. In June, 1952, she had a serum calcium of 13.4 mg./100 ml. and phosphorus of 1.8 mg./100 ml. The diagnosis of hyperparathyroidism was made. She underwent negative neck exploration in another hos-

pital. A part of the left parathyroid was removed but was subsequently found to be normal. One month later, at mediastinal exploration no parathyroid tumor was found. The patient subsequently developed a blocked ureter with anuria necessitating a uretero-pyelolithotomy. She was referred to Dr. Albright for further evaluation. Re-exploration was performed by Dr. O. Cope, and a large parathyroid adenoma in the posterior mediastinum was successfully removed through a neck incision.

As mentioned previously, the lower parathyroid glands are closely associated with the thymus. Thus, Weller has called these glands the "parathymic" glands.¹⁰ This embryological association has significant surgical implications.

First, the lower parathyroid glands are commonly located within the tongue of the thymus, which extends from the lower thyroid poles to the anterior mediastinum. Lower parathyroid tumors are, therefore, frequently found in association with the thymus in these locations, although they may, of course, be displaced into the posterior mediastinum.

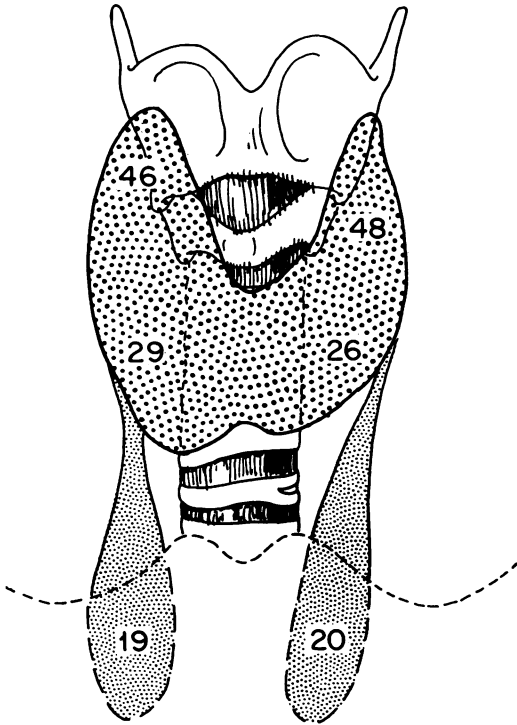


FIG. 1. Location of parathyroid glands in 47 post-mortem subjects (Figure indicates the number identified).

Second, since the lower parathyroid glands may accompany the thymus in its descent, the mediastinum is naturally a rich hunting ground for the lower parathyroids. Twenty-six of the 84 mediastinal parathyroid tumors in the MGH series were found either within the capsule of the thymus or closely associated with it. By their anatomical relationship, they were evidently the lower parathyroid tumors. This unique feature of the lower parathyroid glands is further borne out by the post-mortem studies of 47 subjects.⁹ Of the 94 normal parathyroid glands identified in the right side of the neck, 19, or 20 per cent, were located within the thymic capsule in the lower neck or in the substance of the thymus in the anterior mediastinum. Similarly, of the 94 normal parathyroid glands uncovered in the left side, 20, or 21 per cent, were found inside the thymic capsule in the neck or the mediastinum (Fig. 1).

Since half of the 94 glands found on either side were upper glands, and half lower, it may be inferred that over 40 per cent of lower glands are likely to be found within the thymic capsule in the lower neck or in close proximity to the thymus in the anterior mediastinum.

A detailed discussion on the technic of mediastinal exploration has been presented.⁴ A brief summary follows:

First Stage—Neck Exploration. As a general rule neck exploration is first undertaken once the diagnosis of hyperparathyroidism is made. If the offending gland is not disclosed in the neck after meticulous and bloodless search, it is unwise to extend the exploration into the mediastinum through the neck incision. Persisting in blunt dissection with the fingers from the neck into the mediastinum not only subjects the patient to undue risk but also jeopardizes the chances of success with subsequent mediastinal exploration. However, before terminating the search in the neck, it is absolutely imperative that the entire region of the neck, posterior and anterior, as well as within the thyroid,* have been adequately explored. Such a search should enable the surgeon to identify at least one, or more, normal glands. Failure to uncover and prove by biopsy one parathyroid gland in the neck implies that the exploration has not been completely or expertly carried out.

Second Stage—Exploration of the Mediastinum. It is the practice at the Massachusetts General Hospital that in most instances the mediastinal exploration will take place 2 to 3 weeks after the neck operation. During the immediate post-operative period, reactions of the neck wound will subside, and the patient usually sufficiently recovers from the effects of the previous operation.

The neck wound is re-opened; the ante-

* Intrathyroidal parathyroid adenoma has been encountered in 2 per cent of the MGH series.

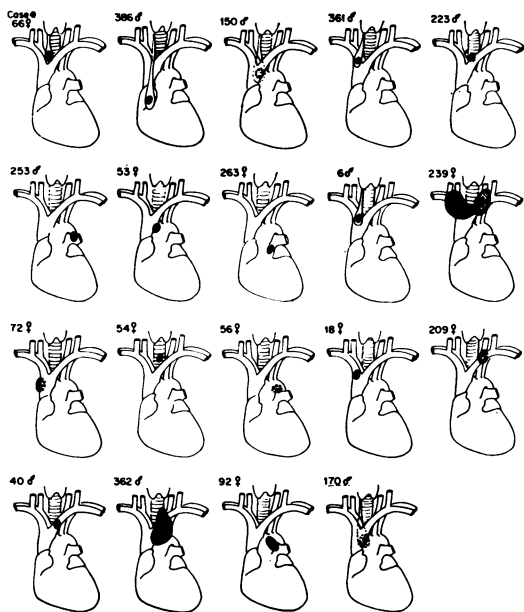


FIG. 2. The schematic representation of the position of 19 mediastinal parathyroid tumors uncovered by mediastinotomy.

rior mediastinum is exposed through the third interspace immediately adjacent to the sternum. Care is taken that the internal mammary vessels and the pleura are displaced laterally. A space behind the sternum is created connecting the manubrium with the third interspace. The sternum is then split by a sternal knife in a hockey stick incision from the third interspace to the manubrial notch. Excellent exposure of the anterior mediastinum is obtained. Exploration begins with the search for the thymus, which often leads to the discovery of the parathyroid.

Not all the diseased parathyroid glands are found in the anterior mediastinum, for they may be displaced posteriorly. Thus, a negative exploration of the anterior mediastinum must be followed by a search in the posterior mediastinum. Parathyroid tumors are so widely distributed that they have been found even at the root of the lung (Fig. 2).

The following patient (MGH #150-46-24, Parathyroid Case #386) illustrates the error in diagnosis of the pathological

type of parathyroid tumor and the successful removal of adenoma by mediastinal exploration.

A 59-year-old man had enjoyed relatively good health until ten years ago when he underwent a subtotal gastrectomy for duodenal ulcer. During the last 2 years he noted fatigue and lassitude, polyuria and polydipsia, pins and needles in the left hand and leg. On the basis of these symptoms and the blood findings, hyperparathyroidism was diagnosed. He underwent parathyroid exploration in Europe.

When the neck was explored, three parathyroid glands were found and believed to be enlarged. Hyperplasia was diagnosed, and all three glands were resected. Postoperatively the blood serum calcium remained elevated 12–13 mg./100 ml. and the phosphorus depressed 2.0 to 2.5 mg./100 ml. The hyperparathyroidism continued, and the patient was referred to the Massachusetts General Hospital.

Review of the microscopic sections of the glands by pathologists in New York and at the Massachusetts General Hospital indicated that the resected glands were normal parathyroids.

First Stage—Neck Incision. Re-exploration of the neck was undertaken, and the right side of the neck was exposed. The right side was chosen because two of the glands removed at the previous operation came from the left, and only one from the right. A right thyroid adenoma and lymph node were excised. The exploration was



FIG. 3. (MGH No. 150-46-24, Parathyroid Case No. 386) showing the adenoma in the anterior mediastinum (pointed by forceps).

carried down as far as could be reached in the anterior superior mediastinum, but no normal or pathological parathyroid tissue was encountered. It was felt wise at this juncture to abandon further search in the neck.

Second Stage—Mediastinal Exploration. The anterior mediastinum was exposed. The right thymic tongue was identified and was followed downward toward the lung root. Just above and in front of the lung root in the thymus there was a dark cystic mass containing fluid which was like crank-case oil. Below it, still in the thymus, was an enlarged parathyroid measuring 4×1.2 cm. (Fig. 3). Both the thymic tongue and the parathyroid tumor lay in the anterior mediastinum laterally and in front of the lung root on the right side at the level of the fourth rib against the pleura. Both thymus and parathyroid adenoma were removed. The cystic mass was identified as disintegrated chronic lymph node. The enlarged parathyroid was diagnosed as adenoma. Because previously three normal glands were removed, five little pieces of the adenomatous tissue were inserted as grafts into the subcutaneous pockets along the right side of the sternum. Each graft was marked with a dural clip for later identification. Following the operation, the serum calcium came down promptly to a subnormal and tetanic level. The patient had to be given heavy doses of calcium and vitamin D medication. The calcium level was eventually stabilized. He was discharged for further convalescence. Ten months later the patient reported that the serum calcium was normal; he no longer required supplementary calcium and vitamin D medication.

Summary

Parathyroid glands have a wide anatomic distribution. They might be found as high as 3 to 4 cm. above the superior pole of the thyroid, or as low as the pericardium. Among the ectopic locations of the gland,

the mediastinum is by far the most frequent. Eighty-four or 21 per cent of the 400 hyperparathyroid patients in the MGH series presented with the tumor located in the mediastinum. Sixty-two of these tumors were successfully removed through a neck incision; only 19 required mediastinotomy. Thus, the incidence of mediastinal tumors requiring mediastinotomy for removal is about 5 per cent.

Acknowledgment

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