



Median Sternotomy in Reoperations for Primary Hyperparathyroidism

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Thirty-three patients underwent median sternotomy at reoperation for persistent or recurrent hyperparathyroidism. Radiographic studies correctly localized abnormal tissue to the mediastinum in 21 patients and surgery was successful in 19 of them. In the 12 patients without preoperative localization, surgery was successful in 9. Twenty-six of 29 patients with a diagnosis of parathyroid adenoma had successful surgery, while only 2 of 4 patients with hyperplasia had successful procedures. In 10 patients the median sternotomy proved unnecessary since the parathyroid abnormality was located at a site reachable through the cervical incision. Abnormal parathyroid glands were found in the thymus (21), posterior to the thymus along the arch (6), within the thyroid (4), and at other ectopic locations. Abnormal parathyroid glands found within the thymus were often smaller than 1 cm in diameter and were detected by the pathologist after dissecting the entire thymus, indicating the need for total thymectomy. The complication rate was 12%, and the mortality rate was 6%.

Initial operations for primary and secondary hyperparathyroidism are successful in 95-98% of cases [1]. In most patients undergoing reexploration for persistent or recurrent hyperparathyroidism, the hyperfunctioning parathyroid gland will be found in the neck [2]. In 21 (60%) of 35 patients reported by Beazley and associates [3] and 25 (49%) of 51 patients reported by van Vroonhoven et al. [4] undergoing reoperation for hyperparathyroidism, the abnormal parathyroid glands were located in a normal position. Even when ectopic parathyroid

glands are located in the mediastinum, the majority can be removed through a cervical incision [2].

In an anatomic study of 315 dissections, Wang found 6 (2%) subjects who had glands within the mediastinal thymus [5]. In a more recent autopsy study of 503 cases, Ackerstrom et al. demonstrated that in 64 cases (13%) there were supernumary glands [6]. Most of the supernumary glands were a fifth gland located in the thymus. Parathyroid glands do exist in the mediastinum usually within or near the thymus.

Median sternotomies and deep mediastinal explorations for primary hyperparathyroidism are rare. In reoperative series, this procedure varies from 3 to 22% [3, 7-9]. We have previously reported 24 patients receiving sternotomy at reoperation [9]. Since August, 1975, we have performed reoperations on 175 patients for persistent and recurrent hyperparathyroidism. Our total experience has been reviewed and recently reported [10]. In this analysis, we would like to consider only the 33 patients (19%) who underwent median sternotomy for primary hyperparathyroidism. We have reviewed aspects important to successful surgery: radiographic localization, size and location of abnormal tissue, complications, and outcome. We describe this experience to develop a rational surgical approach to abnormal deep mediastinal parathyroid tissue.

Methods

Between August, 1975, and April, 1984, reoperation was performed on 175 patients for hyperparathyroidism at the Clinical Center of the National Institutes of Health and Memorial Sloan-Kettering Cancer Center. Forty-five (26%) patients were found to have abnormal tissue in the mediastinum

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Table 1. Patient characteristics.

Group	No.	Age	Sex M:F	Symptoms	Prior surgery
Persistent	31	45 ± 17	14:17	16 Nephrolithiasis 13 Bone disease 2 Muscle weakness	45 Cervical 1 Mediastinal
Recurrent	2	33	0:2	2 Nephrolithiasis	5 Cervical

[10], but some were able to have this tissue removed through a cervical incision. These patients will not be considered in this report. The 33 patients who required median sternotomy and deep mediastinal exploration will be considered here. We included only patients with primary hyperparathyroidism caused by adenoma or hyperplasia. Patients with parathyroid carcinoma or familial hypocalciuric hypercalcemia (FHH) are excluded.

All patients had primary hyperparathyroidism documented by serial elevated serum calcium levels, abnormal serum parathyroid hormone levels, and/or elevated urinary cyclic adenosine monophosphate (UcAMP) levels [11]. The majority of the patients underwent radiographic localization procedures including selective arteriography with inferior thyroid artery and internal mammary injections [12], selective venous catheterization (including thymic veins) for parathyroid hormone levels, and computed tomography (CT) and/or nuclear magnetic resonance (NMR) imaging.

Patients were either explored through a cervical incision plus median sternotomy or through a median sternotomy. The initial cervical approach was used for 2 reasons: the abnormal parathyroid gland was not localized radiographically, or an attempt was made to remove mediastinal tissue through a cervical incision. The size, exact location, and pathologic diagnosis of abnormal parathyroid tissue were recorded. Surgical complications, deaths, and final outcome were noted.

For analysis, patients were divided into 2 groups: those with persistent disease and those with recurrent disease. Persistent disease meant that the patient never achieved hypo- or normocalcemia following an initial surgical procedure. Recurrent disease meant that the patient was hypo- or normocalcemic for at least 6 months following the initial surgical procedure, and that he or she subsequently developed recurrent hypercalcemia. Data are presented as mean ± standard deviation unless otherwise specified.

Results

Of the 33 patients who required median sternotomy for excision of abnormal parathyroid tissue, 31 had

persistent disease and only 2 had recurrent disease. Most of the patients had significant symptoms of either documented nephrolithiasis or parathyroid bone disease with bone radiograph changes and elevated serum levels of bone alkaline phosphatase (Table 1).

In all 33 patients, there were 24 abnormal parathyroid glands removed from the mediastinum. Ten patients did not have an abnormal mediastinal gland despite having a median sternotomy, and 1 patient with hyperplasia had 2 abnormal mediastinal glands.

The selective arteriogram was the single best localization test, correctly identifying 14 (42%) of 33 abnormal glands. There were no false-positives, and the arteriogram accurately imaged the size and shape of the abnormal tissue. Two patients who required median sternotomy had failed ablation by transcatheter staining [13]. The second best localization test was selective venous sampling for parathyroid hormone level in the thymic vein. A thymic vein step-up was present in 12 of 33 patients. One patient had a false-positive step-up and underwent an immediate median sternotomy only to find the abnormal tissue in the right lobe of the thyroid. All the other patients with a thymic vein step-up had deep mediastinal abnormal parathyroid glands for a true positive rate of 33%. Six patients had abnormal mediastinal glands localized by CT or NMR (12%), but there were 2 false-positives (Thymic cyst and a lymph node). If we include all localization procedures in all patients, 11 did not have any abnormal parathyroid glands localized.

Of the 31 patients with persistent hyperparathyroidism, 10 underwent only median sternotomy, and 21 underwent both cervical exploration and median sternotomy. One patient with recurrent disease underwent both incisions; the other underwent only median sternotomy. All abnormal parathyroid tissue was resected in 27 of 31 patients with persistent disease, and in 1 of 2 of the patients with recurrent disease. A total of 30 abnormal parathyroid glands were resected. nineteen (63%) were present within thymus, 5 (17%) were posterior to the thymus along the aortic arch, 4 (13%) were within the thyroid, 1 was in an undescended parathymus, and 1 was in the tracheoesophageal

Table 2. Surgical exploration.

Group	No.	Incision	Location of abnormal parathyroid tissue	
Persistent	31	21 Both 10 Median sternotomy	Undescended parathyms	1
			Within thymus	16
			Around aortic arch	5
			Within thyroid	4
			Tracheoesophageal groove	1
Recurrent	2	1 Both 1 Median sternotomy	Within thymus	3

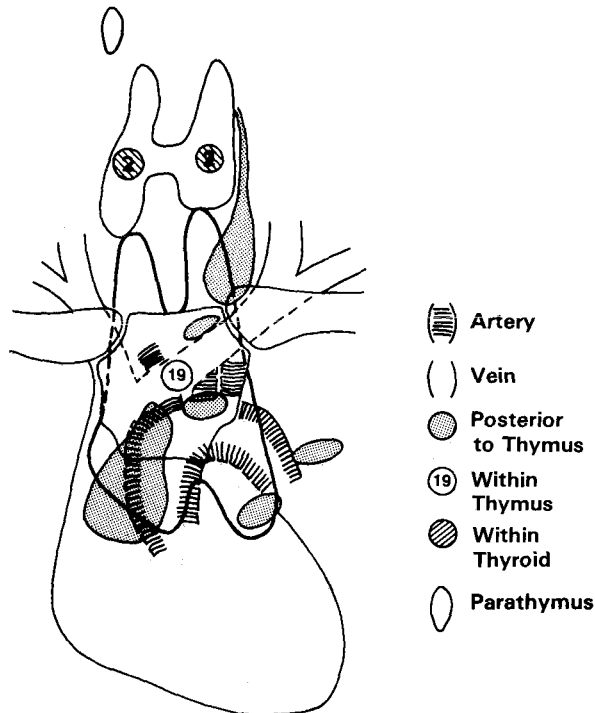


Fig. 1. Drawing of the location of abnormal parathyroid tissue in the 33 patients who underwent median sternotomy at reoperation for primary hyperparathyroidism. Nineteen glands were within the mediastinal thymus; 5 were posterior to the thymus along the aortic arch; 4 were within the thyroid gland. One was within an undescended parathyms, and 1 was in the tracheoesophageal groove.

groove. Most abnormal mediastinal parathyroid tissue was within the thymus (Table 2, Fig. 1).

The size of abnormal parathyroid glands resected were smaller than expected. Eleven (37%) abnormal glands removed were smaller than 1×1 cm in diameter, and 8 of these were found only by the pathologist in the resected thymus or thyroid (Table 3).

Eighty-eight percent (29/33) of patients who required a median sternotomy for primary hyperparathyroidism had the final diagnosis of parathyroid adenoma. All of these patients presented with persistent hyperparathyroidism. Two of 4 patients with hyperplasia presented with recurrent disease, and 2 presented with persistent disease. This differed from patients who only needed cervical reexplora-

tion for hyperparathyroidism. Fifty-eight percent of those patients had parathyroid adenomas, while 39% had hyperplasia [9]. It appears that patients with deep mediastinal disease are more likely to have ectopic adenomas as the etiology of primary hyperparathyroidism.

Surgical outcome was successful in 28 of 33 patients for an 85% success rate. Of the 5 patients with postoperative hypercalcemia, 2 had hyperplasia. Four patients (12%) suffered surgical complications, and 2 patients (6%) died postoperatively. One patient who died was moribund preoperatively with a serum calcium level of 17 mg/100 ml. She died of renal failure and sepsis secondary to candida endocarditis following successful operation. The second patient died of a fulminant staphylococcal infection 2 days postoperatively following successful surgery for hyperplasia of the MEN type IIa variety. Complications included: 3 sternal incision infections and 1 Horner's syndrome. All 3 patients with sternal incision infections underwent cervical exploration followed by mediastinal exploration. No patient suffered long-term sequelae from a sternal incision infection.

Of the 4 patients with hyperplasia, 2 had persistent disease and the others did not require calcium at discharge. Of the 26 patients with adenoma who were successfully treated, 10 required vitamin D and 14 required oral calcium medication at discharge. One patient is permanently hypoparathyroid, and has no cryopreserved tissue. Two patients underwent autologous cryopreserved parathyroid grafts to correct hypoparathyroidism. Both grafts are working. One autografted after 4 1/2 years of cryopreservation is, to our knowledge, the longest successful cryopreservation of human parathyroid tissue [14]. All other patients with mediastinal parathyroid adenomas are normocalcemic and off medications.

Discussion

Median sternotomy is not a common incision in reoperative parathyroid surgery. Scholz et al. described a large series of mediastinal hyperfunctioning parathyroid tumors in 1972 [15]. Their patients' parathyroid tumors were larger than ours, but one-

Table 3. Size of abnormal parathyroid tissue.

Number of abnormal glands removed	Small ($<1 \times 1$ cm)	Medium ($>1 \times 1$ $<2 \times 2$ cm)	Large ($>2 \times 2$ cm)	Parathyroid tissue found by pathologist (not surgeon)
30	11	14	5	10 (33%)

third were small and located within the thymus. In a more recent series from the same institution, 11 of 51 patients underwent median sternotomy, and 6 adenomas (no hyperplasia) were found in the mediastinum. All 6 were intrathymic, and the success rate was 64% [7]. Wang's experience was nearly identical to ours. He removed 21 abnormal mediastinal parathyroid glands. Fourteen (67%) were within the thymus. The remaining 7 were behind the thymus, anterior to the great vessels [8]. Subsequently, Wang has described 6 patients with hyperfunctioning supernumary glands, all of whom had intrathymic parathyroid adenomas [16].

We have a large experience with median sternotomy for primary hyperparathyroidism. The subgroup of patients who underwent median sternotomy are slightly different from the population of other patients who underwent reoperative parathyroid surgery. They appeared to have more severe symptoms than the entire population. More than half of these patients had nephrolithiasis, and the remainder had documented bone disease. In addition, unlike the entire reoperative population in whom 39% had hyperplasia [9], only 4 of 33 had this diagnosis. The majority of patients (88%) in this series had a diagnosis of adenoma.

From our experience, it appears that most patients with parathyroid hyperplasia who are undergoing reoperation for recurrent or persistent hypercalcemia can be successfully managed through a cervical incision. We recommend reexploring the neck in these patients unless there is bona fide evidence for deep mediastinal abnormal parathyroid tissue. We recommend excising the cervical extent of the thymus in these patients since 20% of lower glands will be present there [17].

The preoperative invasive localization studies that we performed, including selective arteriography, selective venous sampling with parathyroid hormone determination, CT, and NMR, localized abnormal parathyroid tissue to the mediastinum in 67% of these patients. Selective arteriography has been the most helpful; it accurately imaged the size and shape of the abnormal tissue in 42% of our patients. This experience has been previously described [18], and the technique has been performed safely. Others have reported grave complications associated with selective arteriography [7], but we have not seen this. In

addition, 15 patients with mediastinal parathyroid adenomas have been successfully ablated with transcatheter staining by contrast material [13]. Several patients have failed catheter ablation and are included in this report. There was 1 false-positive thymic vein step-up, and 2 false-positive NMR and CT scans which produced median sternotomies. Nevertheless, preoperative localization studies for mediastinal parathyroid glands helped our exploration in two-thirds of our patients.

We always review the prior operative records and pathological material. However, we have often found the operative record to be incomplete and misleading. Generally, we reexplore the neck first, but we rely heavily on the localization studies. If, following a failed cervical exploration, an abnormal gland is localized to the mediastinum by selective arteriogram or thymic venous step-up, we recommend an immediate median sternotomy with mediastinal exploration. This strategy resulted in a needless median sternotomy in 1 patient. However, 10 patients in whom only a median sternotomy was performed underwent removal of the abnormal parathyroid tissue without complication in every case. In the patients who had a prolonged operation with standard cervical exploration followed by median sternotomy, 4 of 22 patients had postoperative complications for a complication rate of 18%. Two of these patients had preoperative localization data that pointed to the mediastinum. Increased duration of operation increases intra- and postoperative complications.

The fact that the abnormal parathyroid gland was located within the thymus in a majority of cases, and that often the surgeon was unable to identify it during the mediastinal exploration, supports the need for total thymectomy. We perform total thymectomy in every patient who undergoes median sternotomy for primary hyperparathyroidism. The abnormal gland is small in some patients, explaining why the surgeon may not identify it without doing a thymectomy. If abnormal tissue is not present in the thymus, then the surgeon must explore behind the thymus along the aortic arch. Five of the abnormal glands found had a relationship to the aortic arch. One gland was just to the right of the arch, the remaining glands were to the left (Fig. 1). This is a difficult area to explore, but it

is necessary since 17–33% of the time the abnormal gland will be in this area [8]. Others have suggested that mediastinal parathyroids may be inside the pericardium [15]. We do not open the pericardium, because it is embryologically impossible for the parathyroid gland to be within it [19]. Our sequence of mediastinal exploration for hyperparathyroidism is total thymectomy, then diligent exploration around the aortic arch. If abnormal parathyroid tissue is still not found, one should return to the neck and consider undescended parathymus and thyroidectomy.

Despite the fact that these abnormal mediastinal parathyroid glands may be small, it is important for the surgeon to save and cryopreserve them. We developed this technique in reoperative patients, because there is no assurance that the patient will have remaining normal functioning parathyroid tissue [20]. Thirty percent of these patients required vitamin D at discharge, and 42% required oral calcium medications. Long-term follow-up in the patients with mediastinal adenomas demonstrated that 3 patients were hypoparathyroid. Two patients received cryopreserved autologous adenomatous parathyroid grafts in their forearm musculature. Both of these autografts have functioned normally. The third patient remains permanently hypoparathyroid on vitamin D and calcium replacement.

Median sternotomy was performed in 33 patients undergoing reoperation for primary hyperparathyroidism. It was necessary in 25 patients (76%). It was needed to remove abnormal deep mediastinal parathyroid glands in 23 patients (70%). It was necessary to repair a proximal carotid laceration in 1 patient and remove a concomitant thymic cyst in another patient. It was not helpful in 8 patients (24%) since the abnormal tissue was either subsequently found in the neck or not found at all.

Résumé

Trente-trois sujets ont subi une sternotomie médiane lors de réinterventions pour hyperparathyroïdisme persistant ou récidivant. L'exploration radiologique avait permis de localiser correctement le tissu anormal au niveau du médiastin chez 21 patients et la chirurgie fut suivie de succès chez 19 d'entre eux. Chez 12 malades chez qui le siège de la tumeur n'avait pu être défini, l'intervention permis de découvrir et de traiter avec succès 9 d'entre eux. Vingt-six des 29 malades qui présentaient un adénome parathyroïdien furent guéris alors que seulement 2 sur 4 des sujets qui étaient porteurs d'une hyperplasie parathyroïdienne furent traités avec succès. La sternotomie pour pratiquer l'exploration du tissu parathyroïdien anormal s'est montrée nécessaire dans seulement 70% des cas. Le tissu

anormal fut découvert dans le thymus (21), derrière le thymus (6), dans la thyroïde (4) ou ailleurs. Les glandes parathyroïdes incluses dans le thymus étaient d'un diamètre inférieur à 1 cm et ne furent découvertes que par l'anatomo-pathologiste, ce fait plaçant en faveur de la thymectomie totale lorsque les glandes restantes ne sont pas découvertes par l'exploration complète. Les taux respectifs des complications et de la mortalité furent de 12% et de 6%.

Resumen

Treinta y tres pacientes fueron sometidos a esternotomía mediana para reoperación por hiperparatiroidismo persistente o recurrente. Los estudios radiológicos localizaron en forma correcta el tejido anormal en el mediastino en 21 pacientes, y la cirugía fué exitosa en 19 de ellos. En los 12 pacientes sin localización preoperatoria la cirugía fué exitosa en 9. Veintiseis de 29 pacientes con diagnóstico de adenoma paratiroideo fueron operados exitosamente, mientras sólo 2 de 4 pacientes con hiperplasia tuvieron operaciones exitosas. La esternotomía fué necesaria para la resección de tejido paratiroideo anormal en sólo 70% de los pacientes. Glándulas paratiroides anormales fueron halladas en el timo (21), sobre el arco aórtico y posterior al timo (6), en la glándula tiroidea (4) y en otras ubicaciones ectópicas. Los paratiroides anormalmente presentes en el timo generalmente fueron de menos de 1 cm de diámetro y fueron halladas por el patólogo sólo después de disecar la totalidad del timo, lo cual señala la necesidad de realizar timectomía total. La tasa de complicaciones fué de 12% y la de mortalidad de 6%.

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Invited Commentary

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The first large series of mediastinal hyperfunctioning parathyroid tumors was reported by Nathaniels et al. in 1970 [1]. From this report and from other surgical papers published subsequently [2-6] as well as from anatomic studies [7-9], the following conclusions can be drawn: (a) there is a substantial number of normal parathyroid glands as well as parathyroid tumors located in the mediastinum (2-20%), mostly within or close to the thymus [1, 6, 7-9]; (b) most mediastinal parathyroid tumors can be removed from the neck mainly by partial or complete cervical thymectomy [10, 11]; (c) during reoperative surgery most tumors are found in the neck [3-5, 12]; and (d) item (b) is also true for reoperative surgery and only a small percentage of patients (2-22%) require sternotomy [3-5].

Norton and coauthors describe a subgroup of the largest experience of reoperations reported in the literature. Among 175 patients reoperated on for

persistent or recurrent hyperparathyroidism, 45 (26%) had a mediastinal tumor. In 12 patients these were removed from the neck, in 33 (19%) a sternotomy was performed (in 11 sternotomy only, in 22 neck explorations + sternotomy). The success rate was 85% for all patients and must be considered excellent.

The central question raised by this article is the indication for sternotomy. The authors open the sternum if an attempt to find the tumor in the neck or to remove the mediastinal tumor from above was not successful, or if preoperative localization procedures visualized a tumor in the mediastinum. While the first indication is accepted in the literature, the second deserves to be discussed. How can one be sure that the lesion shown by radiological means is really a parathyroid tumor? Even these authors report 3 false-positive localization procedures, although they work together with superb radiological experts. How can we be certain we are dealing with a single adenoma? Most reports on previous operations are misleading, as the authors mention. Eight (24%) unnecessary sternotomies may be a sign of a too liberal indication, even if 10 of the 11 "pure" sternotomies were successful. Wang [7] reports 4 patients in whom the missing