REVIEW

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Mediastinal parathyroid adenomas and their surgical implications

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ABSTRACT

Primary hyperparathyroidism is a relatively common problem encountered by any endocrine surgical unit. Ectopic parathyroid adenomas have been known to be a common cause of persistent hyperparathyroidism after surgery. A common site of the missed ectopic gland will be that in the mediastinum. However, with the increasing improvement in available imaging, it is likely that this can be diagnosed preoperatively. The surgical approach to the mediastinal parathyroid has also changed vastly over the last decade from maximally invasive to minimally invasive with minimal complications. We provide a review on the entity of mediastinal parathyroid adenomas and their surgical implications.

KEYWORDS

Parathyroid – Mediastinum – Surgery

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Primary hyperparathyroidism is a relatively common problem encountered by the endocrine surgeon. Most patients present with asymptomatic[1] or incidental disease. Parathyroidectomy is the treatment of choice with a cure rate of 96–98% in expert centres.[2] A common cause of failure is inadequate resection of the parathyroid adenoma, parathyroid hyperplasia and an ectopic location of the parathyroid gland. Most ectopic glands are found in the superior mediastinum in the thymus gland and can be excised via a cervical incision. However, parathyroid adenomas found deeper in the mediastinum remain a challenge.

A mediastinal parathyroid is defined as a parathyroid found completely below the level of the clavicle. The first report of a mediastinal parathyroid adenoma (MPA) was in 1932 by Churchill.[3] The patient had undergone six prior unsuccessful cervical explorations and had severe osteitis fibrosa cystica until the ectopic gland was removed successfully through the transsternal approach. Since then, advances in diagnostic imaging and surgical approaches have improved patient outcomes dramatically. This present review focuses on MPAs and attempts to provide sufficient understanding about their clinical presentation, the optimal diagnostic approach and surgical implications.

A comprehensive literature search was performed on MEDLINE® for articles published in English between January 1980 and June 2012. Studies outlining the incidence, investigations and clinical management were retrieved.

Epidemiology

MPAs are part of the clinical entity of ectopic parathyroid glands, which are a result of aberrant migration of the parathyroid during development. Owing to the different embryological origin and more extensive migration, the inferior parathyroid glands are more frequently ectopic than the superior ones.

Ectopic inferior parathyroids are most frequently found in the anterior mediastinum, usually embedded in the thymus gland, while superior parathyroids are generally found in the posterosuperior mediastinum. Less commonly, MPAs may be located in the aortopulmonary window, and rarely in the pericardium and right dome of the diaphragm.

The prevalence of ectopic parathyroids ranges from 28% to 42% in autopsy series, from 6.3% to 16% in surgical series of patients who were operated on for primary hyperparathyroidism and even up to 45% in patients who underwent re-exploration.[4] Imaging studies have reported low incidence (1.4%) of ectopic parathyroid adenomas in patients who underwent investigation for primary hyperparathyroidism. The actual prevalence of MPA is unknown but has been reported to be 6–30%.[5]

Clinical presentation

MPAs have been reported to be associated with more severe clinical manifestations[6] of primary hyperparathyroidism, presenting with higher calcium levels and more frequently with bone disease. This could be partly due to delayed diagnosis and localisation as most of them are diagnosed in patients who present with persistent hypercalcaemia after surgery for primary hyperparathyroidism. Rarely, a MPA may result in thoracic bleeding[7] or cause obstructive symptoms[8] resulting in stridor or vocal cord palsy from its large size or extracapsular haematoma.

Localisation

Preoperative localisation studies are essential before mediastinal exploration for parathyroid adenomas. However, the optimal approach to preoperative localisation has not been determined. Technetium sestamibi imaging has been used for detection of parathyroid adenomas with a reported sensitivity of 80–90%.[9] Negative imaging can be due to double adenomas and asymmetric hyperplasia. False positive results in the mediastinum can be due to metastatic lung cancer, thymoma, seminoma or lymphoma.[10]

Unlike parathyroid adenomas in the neck, ultrasonography has not been proven to be useful in detecting MPAs. Instead, computed tomography (CT) and magnetic resonance imaging (MRI) may help to identify the MPA and provide valuable information with regard to its anatomical location in relation to other structures. Single photon emission CT alone or in combination with CT can further improve localisation with a sensitivity of up to 96%.[11] Four-dimensional CT has also been reported to be used in up to 93% of cases.[12]

The latest imaging modalities include dual energy CT and positron emission tomography (PET) MRI. Dual energy CT may provide more information by acquiring two datasets showing different attenuation values and may quantify iodine contrast uptake in soft tissue.[13] It has been reported to be successful in identifying parathyroid adenomas in cases of negative results by routine methods. Other modalities such as PET CT[14,15] and PET MRI[15] may be useful in cases where conventional imaging has failed.

Management

Surgery remains the only cure for patients with primary hyperparathyroidism. Before the advent of effective parathyroid imaging, MPA was not diagnosed preoperatively. Typically, the patient would have undergone a four-gland exploration, partial thyroidectomy and thymectomy, and eventually a median sternotomy, resulting in increased morbidity. The advances in imaging techniques have thankfully changed such an approach.

In the past, MPAs have been accessed via a median sternotomy[16] or a thoracotomy. These approaches have been reported to be associated with significant complications including phrenic and recurrent laryngeal nerve injuries, innominate vein laceration, wound infections, mediastinitis and death. With the advent of minimally invasive surgery, however, it has been possible to negate most of these complications.

Since the first account of thoracoscopic excision of a mediastinal parathyroid by Prinz *et al* in 1994,[17] many case series have reported success in using the same approach. The literature review by Alesina *et al* has shown that video assisted thoracoscopic surgery (VATS) is a feasible and safe approach with overall low morbidity and mortality.[18] The overall success rate was reported as up to 98–100%. Nevertheless, the success of thoracoscopy is dependent on accurate preoperative localisation, which helps determine which side of the chest to access. Some centres have reported success in VATS parathyroidectomy as a day-case procedure.

Many questions still remain in terms of the optimum management of this condition. First, few reports have addressed the issue of the optimal surgical approach for MPAs. While most MPAs can be resected via a cervical incision, it is not possible in 1–2% of cases. The difficulty lies in determining the best approach for each patient. Iihara *et al* attempted to answer this question in their retrospective analysis of 14 patients.[19] They suggested the level of the aortic arch on the horizontal chest CT should be used as a landmark for guiding a suitable surgical approach. Those adenomas found above the aortic arch in the superior mediastinum can be treated successfully by a transcervical approach while those found in the middle or posterior mediastinum below the level of the aortic arch should be approached transthoracically.

Second, although several intraoperative adjuncts have been reported in the literature to help localise the mediastinal parathyroid gland, no large trial or study has been done to determine their role. The use of a gamma probe intraoperatively could help identify the parathyroid gland, and has been suggested by some to reduce unnecessary dissection and decrease operating time.[19] On the other hand, others have suggested that the use of a gamma probe in the mediastinum is limited owing to accumulation of radioisotopes in the myocardium.[20] Conversely, intraoperative parathyroid hormone monitoring has been found to be useful as it may help reduce the failure rate of surgery and prevent unnecessary re-exploration.[21] Frozen section can also be used to confirm excision of the gland.

Lastly, as MPAs were previously seldom diagnosed before surgical exploration, most patients are submitted to mediastinal exploration only after a failed neck exploration. This practice is evolving because of the vast improvement in imaging for localising the glands prior to surgery. Some have challenged the notion that a negative bilateral neck exploration should be undertaken before considering a mediastinal or thoracic approach. A case series reported by Randone *et al* shows that positive localisation of ectopic glands in the mediastinum can allow for a more focused approach and avoid unnecessary neck exploration.[22]

For patients who are poor surgical candidates, angiographic ablation has been described.[23] This consists of injecting extra contrast material into the supplying vessel, resulting in ischaemia of the parathyroid gland. Results have been variable, however, with failure rates of up to 40%. Alternatively, medical therapy such as cinacalcet can be used to treat hyperparathyroidism.

Conclusions

MPA is a unique clinical entity in primary hyperparathyroidism where difficulties lie in preoperative diagnosis and surgical approach to such cases. Nevertheless, the advances in imaging modalities and surgical techniques have made exciting changes to the management of MPA. The possibility of a minimally invasive single gland approach becoming the standard of care for such patients is a future we can look forward to.

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