

## Microscopic thymoma and parathyroid adenoma: rare combination of two distinct pathologies

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### Abstract

While there is an intimate anatomical and embryological relationship between the inferior parathyroid gland and thymus, concurrent pathology is rare. Three cases have been reported in the literature of a parathyroid adenoma in conjunction with a thymoma. We present a case report of a 60-year-old female with a past medical history of hypercalcemia subsequently found to have primary hyperparathyroidism. Sestamibi scan of the parathyroid revealed increased uptake in the lower left neck consistent with a parathyroid adenoma. A standard transverse neck incision was performed with exploration of the lower left thyroid pole. Further dissection was required to identify the parathyroid gland which was intimately associated with thymic tissue in the superior mediastinum. Both thymic tissue and the parathyroid gland were sent for pathology. Permanent pathology subsequently revealed a parathyroid adenoma with an incidental spindle cell thymoma. The embryological relationship of the inferior parathyroid glands and the thymus is well known as both are derived from the third branchial pouch. However, there are only 3 other previous reports of parathyroid adenoma associated with a thymoma in the current literature. Interestingly, up to 16% of parathyroid adenomas are found in the mediastinum, and the current literature states the incidence of thymoma varies from 10-42%.

### Introduction

While there is an intimate anatomical and embryological relationship between the inferior parathyroid gland and thymus, concurrent pathology is rare. Three cases have been reported in the literature of a parathyroid adenoma in conjunction with a thymoma. Eighteen percent of atypical parathyroid adenomas are found in the anterior mediastinum.<sup>1</sup> Jaskowiak *et al.* reviewed surgi-

cal cases of 215 operations for primary hyperparathyroidism and found that 14/222 operations required cervical thymectomy.<sup>1</sup> We report a case of a patient who underwent neck exploration for a parathyroid adenoma who was incidentally found to have a microscopic thymoma after thymectomy.

### Case Report

AL is a 60 year old female who initially presented to the Endocrinology Clinic with a chief complaint of hypercalcemia. The patient had been followed 2 years prior to the clinic visit with interval calcium checks. Patient complained of constipation but denied depression or a history of psychosis. A bone mineral density test prior to presentation on 2/18/2011 revealed t score of -2.5 in the left hip and -2.21 in the lumbar spine consistent with osteoporosis. Patient had subsequent testing which revealed a calcium of 12.8 mg/dL (normal range: 8.6-10.6 mg/dL), PTH of 142.0 pg/mL (normal range: 12.0-88.0 pg/mL), and a Vitamin D of 8. She was started on Vit-D2 therapy at 50,000 units weekly and repeat laboratory testing revealed a Vitamin D of 44 after several months of therapy. The patient was then referred to the Otolaryngology Clinic for evaluation for parathyroidectomy. Patient presented with a 99mTc/99mTc-MIBI scintiscan scan from 2/18/11 which was interpreted as increased uptake below the left thyroid lobe consistent with an ectopically located parathyroid adenoma. Patient also had a thyroid ultrasound performed at that time which was interpreted as normal. Pre-operatively, a PTH level of 132.1 pg/mL (normal range: 12.0-88.0 pg/mL) was found. Utilizing a lower anterior neck incision, a four gland exploration was undertaken. After a thorough dissection was undertaken which included exploration of retroesophagus and carotid sheath, a mass was palpated in the upper mid mediastinum, adjacent to the innominate artery. The mass was somewhat fixed to surrounding thymic tissue and removed along with a cuff of thymus. This was sent off for frozen pathology and a rapid PTH was sent with an expected drop to a PTH of 16.4 pg/mL (normal range: 12.0-88.0 pg/mL). Patient had subsequent resolution of her hypercalcemia and was asymptomatic after surgery. Permanent pathology revealed a 2.3 gram parathyroid adenoma (Figure 1) along with a thymoma. The case was then presented at combined Head and Neck Tumor Board where recommendations were made for annual chest CT scanning without adjuvant treatment. The patient underwent an outpatient neurological examination by a neurologist and was found to not have symptoms of myasthenia gravis.

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### Discussion

The association of a thymoma with a parathyroid adenoma or hyperparathyroidism is rare in the current literature. There have been 3 documented cases in the literature. Embryology would dictate that this condition would be more common. The inferior parathyroid glands and the thymus are both derived from the third branchial pouch.<sup>2</sup> As they descend into their final anatomical location, parathyroid glands can move variably into the superior mediastinum along the thyrothymic ligament. Jaskowiak *et al.* evaluated 288 patients with persistent or recurrent hyperparathyroidism. They found that the most common ectopic site for an abnormal gland was within the thymus or mediastinum. They found 37 lesions (16.7%) had descended down into the mediastinum.<sup>1</sup> The overall incidence of thymomas in the general population is about 0.13 per 100,000 persons.<sup>3,4</sup> Thymomas are epithelial neoplasms characterized by an admixture of epithelial cells and mature lymphocytes. Most thymomas are completely surrounded by a fibrous capsule.<sup>5,6</sup> Microscopic thymoma is a rare variant of thymoma, characterized by multifocal proliferation of epithelial cells. Microscopic thymoma is grossly invisible. It may arise in the cortical or medullary compartment of the thymic gland. It has been found in the thymic glands of patients with myasthenia gravis (15% of cases) or without myasthenia gravis (4% of cases). These

tumors are non-encapsulated and composed of bland-looking, pleomorphic, plump spindle cells or polygonal cells usually with a few if any intraepithelial lymphocytes. So authors consider them as nodular hyperplasia or a thymic tumorlet. Microscopic thymomas can occur adjacent to a macroscopic thymoma; however, the role as a precursor lesion is still unresolved.<sup>7-9</sup> Patients with myasthenia gravis have symptoms of varying degrees of weakness of the skeletal muscles that increase during periods of activity and improves after periods of rest. The parathyroid adenoma is the most common cause of primary hyperparathy-

roidism. Due to diversity in pathologic interpretation and patient population, the incidence ranges from 30% to 90%. Parathyroid adenomas may occur in any of the 4 parathyroid glands but more commonly occur in the inferior parathyroid glands.<sup>2</sup>

There have been 5 previous reports in the literature describing the association of a thymoma with hyperparathyroidism. There have also been several reports of thymic tissue secreting ectopic PTH.<sup>10</sup> The first case of thymoma accompanied by hyperparathyroidism was described by Palmer *et al.* in 1978. They described a case of a thymoma associated with myasthenia gravis and hyperparathyroidism.<sup>11</sup>

Byrne in 1989 described an associated case of thymoma with myasthenia gravis and hyperparathyroidism. They described a case of four gland parathyroid hyperplasia in their patient. The patient underwent thymectomy and excision of three and a half parathyroid glands. Pathologic examination revealed a lymphocytic thymoma and nodular hyperplasia of the parathyroid glands.<sup>12</sup>

Suzuki *et al.* described a case of non-invasive thymoma accompanied by hyperparathyroidism without the presence of myasthenia gravis. Their patient was a 50-year-old female with a concomitant right superior parathyroid adenoma along with a noninvasive thymoma.<sup>13</sup>

Triggiana *et al.* described a case of a 46-year-old patient with a widely invasive malignant thymoma with myasthenia gravis and primary hyperparathyroidism due to a parathyroid adenoma. The patient initially underwent wide local excision with attempted post-operative radiation therapy for a WHO Type B3 thymoma. After routine laboratory evaluation revealed a serum calcium of 10.9 mg/dL (normal range: 8.5-10.1 mg/dL), the patient had a PTH drawn with a level of 270.0 pg/mL (normal range: 10-65 pg/mL). After pre-operative imaging localized a lesion to the right lower lobe, the patient underwent an uneventful right parathyroidectomy with resolution of her hyperparathyroidism.<sup>6</sup>

Maria *et al.* described a case of a 68-year-old female initially diagnosed with primary hyperparathyroidism who underwent a routine transcervical approach for parathyroidectomy. An incidental oval mass was found in the superior mediastinum while the left lower parathyroid adenoma was removed. The oval mass was also removed, and histopathological analysis revealed a WHO Type A thymoma.<sup>4</sup>

Palin *et al.* also described a 67-year-old patient with a parathyroid adenoma who presented with myasthenia gravis without a thymoma.

There have also been various case reports involving PTH-related protein or PTH production by the thymoma itself. Suzuki *et al.* again reported a PTH-related-protein-producing thymic carcinoma that initially presented as a

giant extrathoracic mass.

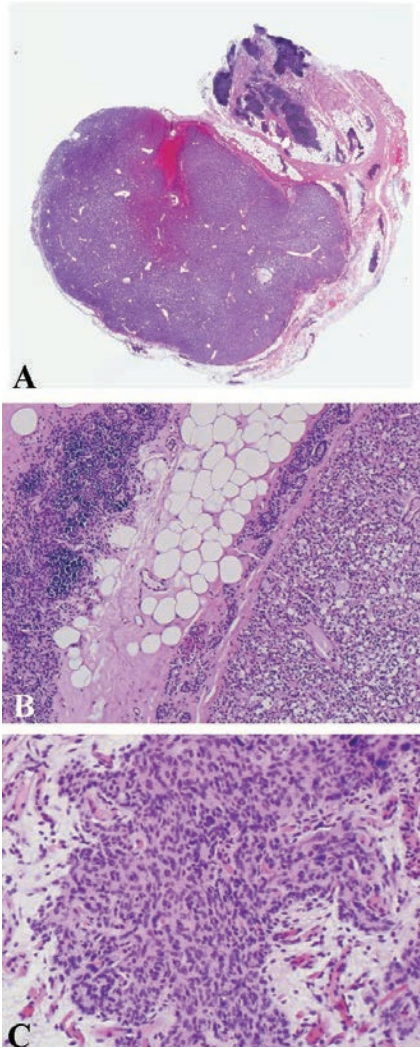
Rizzoli *et al.* described a case of a thymoma excreting PTH.<sup>10,14</sup> Association of thymic tissue with parathyroid adenomas is not uncommon in literature and is a frequent site of ectopic parathyroid tissue. This is explained by the common embryologic origin of the thymus and the parathyroid glands from the III and IV pharyngeal pouches.<sup>12</sup> As the inferior parathyroid glands and thymus descend, there is a chance that one or both of the glands can travel into the superior mediastinum. It is not uncommon to operate in the mediastinum in search of parathyroid glands.

Jaskowiak *et al.* found the thymus to be the single most common true ectopic site, either in the low neck or in the superior mediastinum. This occurred in 16.7% of their reoperative series.<sup>2</sup> We present an uncommon case of a microscopic thymoma associated with a parathyroid adenoma. Our patient was otherwise asymptomatic from the thymoma and did not exhibit any signs or symptoms of myasthenia gravis. Although, this is a rare occurrence, the surgeon should be aware of implications of the thymus with parathyroid glands and the possible association.

Eloy *et al.* described a case of a 25-year-old female with primary hyperparathyroidism in which pre-operative <sup>99m</sup>Tc/<sup>99m</sup>Tc-MIBI scintiscan localized the parathyroid adenoma in the thymus.<sup>15</sup> Rarely, pre-operative imaging including <sup>99m</sup>Tc/<sup>99m</sup>Tc-MIBI scintiscan will pick up a concomitant thymoma during evaluation of primary hyperparathyroidism.<sup>16</sup> Often, thymomas are treated surgically with full removal. The lower histological subtyping incurs a good prognosis.<sup>3</sup> The surgeon should be aware of abnormal findings in the superior mediastinum and lower neck during surgery. Some authors believe that thymectomy surgery should warrant investigation of the parathyroid glands for possible association.<sup>1</sup> This will avoid further interventions.

## Conclusions

While thymomas and parathyroid adenomas appear to be relatively common pathologies, especially in the upper mediastinum and lower central neck; there appears to be very few reports of co-existing pathology. The head and neck surgeon should be aware of both pathologies when operating in the upper mediastinum, especially in reoperations for primary hyperparathyroidism. As described earlier, the thymus tissue is the most common ectopic site for parathyroid adenomas. As we continue to operate on patients with parathyroid adenomas and our diagnostic imaging improves, we may find more concomitant cases involving thymomas and parathyroid adenomas.



**Figure 1.** A) Parathyroid adenoma with residual compressed normal parathyroid gland and adjacent thymic tissue (scanning power); B) high power view showing part of the thymic gland (arrow head) and parathyroid adenoma surrounded and separated from residual normal parathyroid (dashed arrow) by a thin fibrous capsule (large arrow) (Hematoxylin & Eosin, 100 $\times$ ); C) microscopic thymoma, composed of spindle to oval cells with bland nuclei, forming a solid sheet without any pattern (Hematoxylin & Eosin, 200 $\times$ ).

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