The thymus in myasthenic patients: CT- pathologic correlation.

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Purpose

1. To correlate computed tomographic appearance of the thymus with results from histologic examination of thymic tissue in patients with generalized myasthenia gravis (MG) or myasthenic syndrome who underwent thymectomy.

2. To analyzed the global variation in shape, size and density of the normal thymus.

3. To describe different CT aspects in patients with thymic lymphoid follicular hyperplasia and thymoma.

Methods and Materials

We made a retrospective study, based on case series report, between January 1996 and May 2010.

From 1695 patients with generalized myasthenia gravis or myasthenic syndrome explored by CT, we included in this study 463 subjects (27.31%) who were operated with histologic evaluation available.

All the patients had passed a secvential or spiral CT scan obtained in deep-inspiration breath-hold. Secvential CT scans were performed using 1 cm collimation, contiguous throughout the thorax; contiguous 0.3-0.5 cm collimation slices were obtained for densitometric characterization of micronodules. Spiral CT scans were performed using the following protocols: monoslice scanner (collimation 7 mm; pitch 1-1.5; section width 5 mm) and multislice scanner (collimation 0.75 mm; feed/rotation 11.3 mm; slice width 5.0 mm).

Intravenous administration of nonionic iodinated contrast media was used occasionally in separating the thymus from the aorta, superior vena cava and pulmonary artery. We used iodinated contrast media with 350-370-400 mg iodine/ml, 1 ml/kg, with a flow rate of 3 ml/sec.

We analyzed the global variation in shape, size and density of the normal thymus and visualized different CT aspects in patients with histological normal thymus.

Results
All patients from our study had associated myasthenia gravis or myasthenic syndrome. **463 (27.31%) subjects had histologic evaluation.** The relationship between CT results and histopathologic findings are summarized in the table (Fig. 1 on page 6).

In this study female patients were affected two times more than male patients.

The thymus achieves its maximal weight between 12 and 19 years; between 20 and 60 years, regression in size occurs, together with replacement by adipose. [1]

Computed tomography is the study of choice for evaluating disease in the anterior mediastinum. [2]

In our study, the thymus was seen in 85% of patients under the age of 29 years, 50% of patients between 29 and 49 years, and in 15% of patients over 50 years of age.

The normal thymus on CT scans varied with the patients’ age.

**The shape of normal thymus in adults.**

Baron individualized three configurations of the normal thymus:

- **"arrowhead" configuration,** when the two lobes are confluent, in 62% of cases;
- **two separate lobes,** the shapes may be characterized as ovoid, elliptical, triangular, or semilunar, in 32% of cases;
- **one lobe visualized,** in 6% of cases.

We visualized different CT aspects in patients with normal histological thymus appearance (Fig. 2 on page 6).

In 80% of cases, in our study, the thymus appear as an "arrowhead" configuration (Fig. 3 on page 7) and as two separate lobes in 17% of cases (Fig. 4 on page 8). In 3% of cases only one of the lobes could definitely be identified (Fig. 5 on page 9).

**The size of normal thymus in adults.**

The width (longest axis of the lobe as visualized on a transverse scan) and the thickness (the largest dimension perpendicular to the long axis of the lobe) of each lobe of the thymus were measured. [3]

When visualizing an "arrowhead" configuration, the thymus must be divided in the midline into a right and left lobe to obtain measurements of the width of each lobe (Fig. 6 on page 10). [3]
The width decreases in older patients, but a large variation exists within each age group. The thymus becomes narrower with increasing age, a wide variation of the thickness exist in different age groups. [3]

The maximum thickness was 1.8 cm in patients under age 20 years and 1.3 cm in patients over age 20 years. [4]

No significant change in thickness could be found in our series, after CT exam and histopathological correlation, with respect to the age of the patients.

**The density of normal thymus in adults.**

The mean attenuation value of the thymus was obtained and compared with that of the chest wall muscles. The CT attenuation values decrease with aging.

In patients under 25 years of age, the thymus is isodense or with a higher density than the chest wall musculature; between 25 and 49 years the thymus appear with lower density than that of associated soft tissues because of progressive fatty infiltration; patients over 50 years of age had a thymic density approaching to the fat (Fig. 7 on page 11). [3]

CT scan revealed a lobular architecture of the thymus with fatty replacement visible between the lobules. [3]

In our study, remnant of thymic tissue was characterized as normal if areas with linear streaks of soft-tissue attenuation were present and did not produce a focal lateral convexity along the mediastinal boundary. According to the litterature [5] rounded anterior mediastinal areas of soft-tissue attenuation were considered to represent normal residual thymus rather than a small mass when they did not exceed 7 mm in diameter (Fig. 8 on page 12).

**Thymic hyperplasia.**

There are two distinct histologic types of thymic hyperplasia: true thymic hyperplasia and lymphoid hyperplasia, both manifest as diffuse symmetric enlargement of the thymus, so that it is difficult to distinguish between the two types on the basis of imaging findings alone. [4]

Lymphoid hyperplasia is characterized by the presence of numerous lymphoid follicles with active germinal centers within thymic medulla. [5]

This condition is most commonly associated with myasthenia gravis, being seen in up to 65% of cases. [4] Controversy exists as to the incidence of lymphoid-gemminal centers in the thymus of normal individuals. [6]
In contrast, hypertrophic thymus is a CT diagnosis that should be always correlated with patient’s age and clinical context. Hypertrophic thymus can be found in normal patients and does not mean a pathological thymus (Fig. 9 on page 14).

Different aspects was noted on CT scans in all 271 patients with thymic lymphoid follicular hyperplasia (Fig. 10 on page 13): remaining thymic mass (57.56%), remnant of thymic tissue (16.97%), fatty infiltration of the thymus (11.44%) and tumoral thymus (14.02%). (Fig. 11 on page 15)

Thymomas.

Thymomas are primary epithelial neoplasms that can be completely encapsulated or locally invasive. Encapsulated thymomas are confined within a thick fibrous capsule. Invasive thymomas are histologically identical to encapsulated thymomas but have microscopic evidence of growth outside the tumor capsule. [7]

Because histologic features of malignancy are absent, the term invasive thymoma is preferred over malignant thymoma. Invasive thymoma is a separate entity from thymic carcinoma, which is a histologically malignant neoplasm arising from thymic epithelial cells. [7]

On CT scans, thymomas are generally seen as homogeneous, soft-tissue masses located in the anterior mediastinum, usually projects to one side of the mediastinum, vary in size, and can have smooth and lobulated borders (Fig. 12 on page 16).

The mass may be partially or completely outlined by fat or may completely replace the anterior mediastinal fat (Fig. 13 on page 17). The absence of fatty planes between the mass and mediastinal structures does not necessarily denote the presence of invasion. On scans obtained after intravenous administration of contrast material, the mass enhances homogeneously, unless necrosis and hemorrhage are present. [7]

Areas of decreased attenuation corresponding to cystic changes. Calcification within a thymoma may be detected on plain radiographs. The pattern of calcification is commonly linear, thin, and peripheral and corresponds to calcium deposition in the tumor capsule. Calcified foci may also be seen scattered throughout the tumor. [7, 8] Calcification, even if subtle, can be easily detected with CT (Fig. 14 on page 18). [8]

With increasing age, the thymus undergoes fatty involution, which makes the detection of thymoma easier in patients over 40 years of age. In contrast, detection of small thymomas in younger patients with residual thymic tissue may be difficult with CT. [7, 8]

The presence of irregular borders between the mass and the adjacent lung suggests the presence of invasion. [7] CT is very sensitive in the detection of involvement of the adjacent lung and in the evaluation of pleural and extrapleural seeding by the tumor.
In 69 patients with surgically proved thymomas, CT scan (Fig. 15 on page 19) showed: tumoral thymus (81.16%), remaining thymic mass (8.70%), remnant of thymic tissue (8.70%) and fatty infiltration of the thymus (1.44%). (Fig. 16 on page 20)

**Total replacement of the thymus by fat.**

In 58 patients with total replacement of the thymus by fat on CT scan (Fig. 17 on page 21), histopathological evaluation revealed: normal thymus in 9 patients (15.52%), thymic atrophy in 9 patients (15.52%), thymic hyperplasia in 31 patients (53.45%), fatty infiltration in 8 patients (13.79%) and thymoma in 1 patient (1.72%). (Fig. 18 on page 22)

**Images for this section:**

<table>
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<th>Histopathological evaluation</th>
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<td>Remaining thymic mass</td>
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<td>thymoma 3.00%</td>
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<td>thymolipoma 3.00%</td>
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<td>Remnant of thymic tissue</td>
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<td>Total replacement of the thymus by fat</td>
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<td>thymoma 59.57%</td>
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**Fig. 1:** The relationship between CT results and histopathologic findings.
Fig. 2: The shape of normal thymus in adults.
Fig. 3: "Arrowhead" configuration, when the two lobes are confluent. 17-y/o female with myasthenia gravis; CT scan shows remaining thymic mass with density similar to muscle; pathologic diagnosis - thymic hyperplasia.
**Fig. 4:** "Bilobed thymus" with two separate lobes. 22-y/o male with myasthenia gravis; CT scan shows diffusely enlarged thymus with higher density than the chest wall musculature (arrows); pathologic diagnosis - benign thymoma.
**Fig. 5:** One lobe visualized. 31-y/o female with myasthenia gravis; CT scan shows remaining thymic mass; pathologic diagnosis - thymic hyperplasia.
Fig. 6: Measurement of thymic size in a bilobed and arrowhead-shaped organ. The width (W) - longest axis of the lobe as visualized on a transverse scan. The thickness (T) - the largest dimension perpendicular to the long axis of the lobe.
**Fig. 7:** Progressive fatty infiltration of the thymus. (A) 20-y/o female with myasthenia gravis; CT scan shows remanining thymic mass with density similar to muscle; pathologic diagnosis - thymic hyperplasia. (B) 28-y/o female, with myasthenia gravis; CT scan shows remanining thymic mass with early fatty infiltration; pathologic diagnosis - thymic hyperplasia. (C) 32-y/o female with myasthenia gravis; CT scan shows remnant of thymic tissue; pathologic diagnosis - thymic atrophy. (D) 46-y/o female with myasthenia gravis; CT scan shows replacement of the thymus by fat; pathologic diagnosis - thymic atrophy.
Fig. 8: Residual thymus. 22-y/o female, with myasthenia gravis; CT scan shows remnant of thymic tissue (arrows) with partial fatty infiltration; pathologic diagnosis - thymic atrophy.
Fig. 9: CT aspects in all patients with thymic lymphoid follicular hyperplasia.
Fig. 10: Residual thymus. 17-y/o male, with myasthenia gravis; CT scan shows irregularly shaped structure anterior to ascending aorta with density similar to muscle; pathologic diagnosis - thymic hyperplasia.
Fig. 11: CT aspects in patients with thymic lymphoid follicular hyperplasia. (A) 27-y/o female with myasthenia gravis; CT scan shows remaining thymic mass; pathologic diagnosis - thymic hyperplasia. (B) 25-y/o female with myasthenia gravis; CT scan shows remnant of thymic tissue with partial fatty infiltration, pathologic diagnosis - thymic hyperplasia. (C) 42-y/o male with myasthenia gravis; CT scan shows replacement of the thymus by fat; pathologic diagnosis - thymic hyperplasia. (D) 38-y/o male with myasthenia gravis; CT scan shows tumoral mass in the prevascular space on the left side; pathologic diagnosis - thymic hyperplasia.
Fig. 12: Thymoma. 46-y/o female with myasthenia gravis; CT scan shows an tumoral nodule in the prevascular space; pathologic diagnosis - benign thymoma.
**Fig. 13:** Thymoma. 22-y/o female with myasthenia gravis; CT scan shows an tumoral thymus, pathologic diagnosis - benign thymoma.
Fig. 14: Thymoma. 29-y/o male with myasthenia gravis; contrast-enhanced CT scan shows an tumoral thymic mass with areas of necrosis and calcified foci (arrows); pathologic diagnosis - thymoma.
Fig. 15: CT aspects in all patients with thymoma.
**Fig. 16:** CT aspects in patients with thymoma. (A) 33-y/o male with myasthenia gravis; CT scan shows tumoral nodule in the prevascular space; pathologic diagnosis - benign thymoma. (B) 19-y/o female with myasthenia gravis; CT scan shows remaining thymic mass with density similar to muscle; pathologic diagnosis - benign thymoma. (C) 29-y/o male with myasthenia gravis; CT scan shows remnant of thymic tissue; pathologic diagnosis - benign thymoma. (D) 37-y/o male with myasthenia gravis; CT scan shows replacement of the thymus by fat; pathologic diagnosis - benign thymoma.
Fig. 17: Different pathologic aspects in all patients with partial or total replacement of the thymus by fat on CT scan.

Fig. 18: Different pathologic aspects in patients with fatty infiltration of the thymus. (A) 24-y/o female with myasthenia gravis; CT scan shows remaining thymic mass and early
fatty infiltration with separation of thymic lobules; pathologic diagnosis - thymic atrophy. (B) 27-y/o female with myasthenia gravis; CT scan shows fatty infiltration of the thymus with separation of thymic lobules; pathologic diagnosis - fatty infiltration of the thymus.
Conclusion

1. CT exam is the imaging method of choice following standard chest radiography when thymic pathology is suspected especially in the assessment of patients with myasthenia gravis.

2. We propose the following CT entities concerning thymic space: normal findings with respect to the chronological age of the patients (includes remaining thymic mass, remnant of thymic tissue, fatty infiltration of the thymus), diffuse enlargement of the thymus and thymic focal mass.

3. CT can be useful in differentiating non-invasive from invasive thymomas, but has limited value in differentiating thymomas from lymphoid follicular hyperplasia. On occasion, CT may suggest the histologic nature of a thymic lesion.

4. CT findings may serve as predictors of postoperative recurrence or metastasis in thymic epithelial tumors cases.

References


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