The essential of the thymus in CT evaluation: normal and pathological findings

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Learning objectives

1. To present and illustrate the thymic CT morphology in relation to age.
2. To list and discuss the CT features in thymic pathology.
3. To review the classification of thymic epithelial tumors.
4. To discuss the differential diagnosis of anterior mediastinal masses.
Background

Thymic function, embryology, histology and anatomy

The thymus is a central lymphoid organ that plays an important role in the maturation of the immune system, especially regarding the cellular immunity during childhood [1].

The thymus arises in the sixth gestational week from the third and fourth branchial pouches and undergoes a descensus process towards its final location, in the anterior mediastinum, behind the sternum and anterior to the pericardium and great vessels, and may extend longitudinally from the lower pole of the thyroid gland to the diaphragm [2]. At first, the thymus gland is purely epithelial, but in the tenth gestational week it is populated with lymphoid cells migrated from the fetal liver and bone marrow [3]. Histologically, the cortex of the thymus consists mainly of lymphocytes, whilst the medulla contains primarily epithelial cells. Other types of cells are also present, such as myoid cells, which may play a role in the pathogenesis of myasthenia gravis [3].

Thymic morphology has great variability. In young adults, it is frequently bilobated, but may also be unilobated or trilobated [2]. Fig. 1 on page 8

Fig. 1: Thymic morphology and histology [4, 5].

As the function of the thymus decreases with age, the epithelial component atrophies. Throughout a process of fatty involution, the shape of the gland modifies and its size and density decrease.

In the context of continuously changing thymic morphology, it is important to be familiar with the CT aspects of the normal thymus and its main pathology.

**CT protocol in the evaluation of the thymus gland**

In the evaluation of the mediastinum, CT is the standard imaging technique. It is commonly performed as part of a general thoracic examination. The protocol requires thin-section multislice acquisition (0.75-1.5 mm) with reconstructed axial images of 5 mm and multiplanar reformation. Noncontrast and contrast-enhanced CT is indicated to evaluate a mediastinal mass, in purpose to appreciate enhancement characteristics of the lesion and vascular invasion [6,7]. For adults, intravenous non-ionic iodinated contrast media should be injected in volumes of 100-150 ml, at flow rates of 3-5 ml/sec in order to evaluate tumor vascularity and mediastinal vessels [6].

**Thymic pathology**

Anterior mediastinal pathology includes a wide variety of lesions. The most common entities can be summarized using the mnemonic "4T" which stands for:

- thymoma,
- teratoma,
- thyroid tumors/goiter and
- terrible lymphoma

Anterior mediastinal pathology involving the thymus includes also:

- thymic hyperplasia,
- cysts, epithelial tumors,
- germ cell tumors and
- hematologic malignancies.

1. **Thymic hyperplasia**

There are two histological forms of thymic hyperplasia: true hyperplasia and lymphoid hyperplasia.

True thymic hyperplasia, or rebound hyperplasia, is frequently related to chemotherapy, radiation or corticosteroid therapy, major surgery, burns or infections [1]. Under stress, the thymus becomes atrophic. After the cessation of the infliction, frequently in 6-9 months, it grows back to the original size, or even larger [7].
Lymphoid hyperplasia is characterized by an increased number of lymphoid follicles in the medulla and is associated with immunologically mediated disorders such as myasthenia gravis (MG), systemic lupus erythematosus, rheumatoid arthritis or Graves' disease [1].

2. **Thymic cyst**

Thymic cysts may be congenital or acquired through thoracotomy or cystic changes in thymic epithelial tumors, lymphomas or germinal cell tumors [2].

3. **Thymic epithelial tumors**

Thymic epithelial tumors arise from thymic epithelium and include noninvasive/invasive thymoma and thymic carcinoma. Whilst noninvasive thymoma is an encapsulated tumor without capsular effraction, invasive thymoma and thymic carcinoma may exhibit local invasiveness, lymphadenopathies and metastases.

The WHO classification of thymic epithelial tumors is a histologic classification and correlates with prognosis [10].

<table>
<thead>
<tr>
<th>WHO Classification</th>
<th>Suster- Moran Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type- A thymoma</td>
<td>Thymoma</td>
</tr>
<tr>
<td>Type- AB thymoma</td>
<td></td>
</tr>
<tr>
<td>Type- B1 thymoma</td>
<td>Atypical thymoma</td>
</tr>
<tr>
<td>Type- B2 thymoma</td>
<td>Thymic carcinoma</td>
</tr>
<tr>
<td>Type- B3 thymoma</td>
<td></td>
</tr>
<tr>
<td>Type- C thymoma</td>
<td></td>
</tr>
</tbody>
</table>

*Table 1. WHO classification of thymic epithelial tumors [10].*

The Masaoka staging system is based on the presence of invasion and also correlates with the prognosis [7].

<table>
<thead>
<tr>
<th>Stage</th>
<th>Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>Micro- and macroscopically encapsulated.</td>
</tr>
<tr>
<td>Stage IIa</td>
<td>Macroscopic invasion of the surrounding fatty tissue or mediastinal pleura.</td>
</tr>
</tbody>
</table>
Stage IIb: Microscopic invasion of the capsule.
Stage III: Macroscopic invasion of the pericardium, great vessels or lung.
Stage IVa: Pleural or pericardial dissemination.
Stage IVb: Lymphogenous or hematogenous metastatic disease.

Table 2. Masaoka staging system [7].

4. Germinal cell tumors

Germinal cell tumors originate from multipotent primitive germ cells. These tumors mainly arise in the gonads, but may also be present in the midline of the body, from the pineal gland to the sacrococcygeal region, arising from germ cells misplaced during their migration from the yolk endoderm to the gonads in embryogenesis [11]. The most common extragonadal site is the anterior mediastinum, and the average age of presentation is between the second and fourth decade of life [7].

Germ cell tumors can be subdivided into benign lesions, such as mature teratoma (the most frequent subtype) and malignant tumors; seminoma and nonseminomatous germ cells tumors [7]. Malignant tumors occur mostly in men and may secrete tumor markers: human chorionic gonadotropin (hCG) in pure seminomas and #fetoprotein (AFP) in nonseminomatous germ cell tumors [11].

5. Thymic lymphoma and leukemia

Thymic involvement usually occurs secondary to widespread disease, but may also be isolated. The thymus gland is more commonly affected in Hodgkin disease, frequently in young patients (average age of 30 years) [2].

<table>
<thead>
<tr>
<th>Pathology</th>
<th>CT aspects</th>
<th>Diagnostic features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Thymic hyperplasia</td>
<td>Symmetrical enlargement of the thymus, NO contour irregularities or focal masses.</td>
<td>Differentiation between thymic hyperplasia and neoplasms on CT alone is not possible in some cases; chemical shift MRI might be useful.</td>
</tr>
<tr>
<td>Thymic cyst</td>
<td>Fluid/parafluid (may exhibit higher densities), well outlined mass ± wall calcifications.</td>
<td>MRI should be performed [9].</td>
</tr>
<tr>
<td>Condition</td>
<td>Description</td>
<td>Clinical/Laboratory Findings</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>-----------------------------------------------------------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td>Thymoma</td>
<td>Round/lobulated, well outlined, homogenous/slightly heterogeneous mass, ± calcifications.</td>
<td>Clinical aspects: MG or other paraneoplastic syndromes. Biopsy may be required [9].</td>
</tr>
<tr>
<td>Invasive thymoma</td>
<td>Lobulated, homogeneous/slightly heterogeneous mass, local invasiveness.</td>
<td>Requires biopsy [9].</td>
</tr>
<tr>
<td>Thymic carcinoma</td>
<td>Large, heterogeneous mass, locally invasive, lymphadenopathies or distant metastases.</td>
<td>Requires biopsy [9].</td>
</tr>
<tr>
<td>Teratoma</td>
<td>Heterogeneous mass with fat, fluid, soft tissue and calcar components.</td>
<td>Imaging alone may suffice [9].</td>
</tr>
<tr>
<td>Seminoma</td>
<td>Large, lobulated, homogenous mass with local invasiveness, lymph node and systemic metastases.</td>
<td>Clinical context: young male. Laboratory findings: hCG. Biopsy is required [9].</td>
</tr>
<tr>
<td>Nonseminomatous germ cell tumor</td>
<td>Large, lobulated, heterogeneous mass with local invasiveness and lymphogenous and hematogenous metastases</td>
<td>Clinical context: young male. Laboratory findings: AFP. Biopsy is required [9].</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Lobulated mass with mild contrast enhancement, local invasiveness, surrounding the great vessels but WITHOUT invasion. Lymphadenopathies.</td>
<td>Clinical: &quot;B&quot; symptoms. Cytology and biopsy [9].</td>
</tr>
</tbody>
</table>

*Table 4: Differential diagnosis amongst thymic masses.*
Fig. 1: Thymic morphology and histology [4, 5].

Findings and procedure details

A retrospective study of 15 years including 180 patients, aged 1-80 years who have undergone a thoracic CT exam, performed without and with contrast injection, followed by MPR reconstructions in coronal and sagittal plane, for suspicion of anterior mediastinal masses or in the context of myasthenia gravis/myastheniform syndrome.

In the current study, 60 patients had normal thymic features, whilst 120 patients presented with anterior mediastinal masses.

The dominant pathologies were lymphoma and thymoma.

NORMAL THYMUS

Normal CT features of the thymus gland

The thymus is located in the anterior mediastinum, and extends approximately 1.7 cm superiorly to the innominate vein, and inferiorly to the pulmonary arteries in adults. In infants, it may reach the diaphragm [7]. Its maximum anteroposterior diameter before the age of 20 years is 18 mm, whilst after this age it is 13 mm [7]. Before puberty, the shape is quadrilateral or triangular with convex lateral borders. In adults, the shape remains triangular or arrowhead, but the margins become linear or concave. The structure is homogenous, with soft tissue attenuation in the pediatric population. After puberty, the density decreases, and the structure becomes slightly heterogeneous. Frequently, after the age of 40 years, complete fatty involution occurs. Residual thymic tissue may also be present, in the form of linear or oval-shaped tissue attenuating mass in the thymic loch [8]. Fig. 2 on page 28
Fig. 2: Age related normal aspects of the thymus.

References: Department of Radiology and Medical Imagistics, Fundeni Clinical Institute/ Bucharest

THYMIC PATHOLOGY

Thymic hyperplasia

On CT, rebound hyperplasia is a diffuse, symmetric enlargement of the thymus, without contour irregularities or focal masses. The structure might be slightly heterogeneous through the presence of areas of intralesional fat [9]. Fig. 3 on page 28
Fig. 3: F, 50 yo, history of chemotherapy for neuroendocrine pancreatic tumor. CT aspects: diffuse enlargement of the thymus, WITHOUT contour irregularities or focal masses.

References: Department of Radiology and Medical Imagistics, Fundeni Clinical Institute/ Bucharest 2017

In lymphoid hyperplasia, the thymus may have a normal appearance, increased size, or even a focal mass [7].

**Thymic cysts**

On CT, the thymic cyst frequently presents as a fluid/parafluid lesion [2], but may also have higher densities (depending on the presence of blood products). It is round or oval shaped, with thin walls with or without calcified rims. It shows no solid components or contrast enhancement. *Fig. 4 on page 29*
Fig. 4: M, 65 yo, myasthenia gravis. CT aspects: oval shaped parafluid mass, with thin walls and calcified rims. NO contrast enhancement.

References: Department of Radiology and Medical Imagistics, Fundeni Clinical Institute/ Bucharest 2015

**Thymic epithelial tumors**

Thymoma presents as a round, oval or lobulated, well outlined, soft tissue mass, frequently homogenous but may include calcifications, cystic or necrotic areas [2]. Fig. 5 on page 30
Fig. 5: M, 78 yo, myasthenia gravis. CT aspects: oval shaped, well outlined, soft tissue mass, nodular calcifications included.

References: Department of Radiology and Medical Imagistics, Fundeni Clinical Institute/ Bucharest 2014

Indicators of invasiveness in the context of thymoma are infiltration of the fat planes, invasion of the great mediastinal vessels and pleural involvement (thickening, nodularity or effusion) [3]. *Fig. 6 on page 31*
Fig. 6: F, 42 yo, myasthenia gravis. CT aspects: lobulated, well outlined, anterior mediastinum mass, with heterogeneous contrast enhancement (necrotic areas), undelimited and with compression of the ascending aorta and right pulmonary artery, surrounding the superior vena cava (more than 67% of the circumference).

References: Department of Radiology and Medical Imagistics, Fundeni Clinical Institute/ Bucharest 2017
Thymic carcinoma frequently presents as a large multilobulated soft tissue mass, with heterogeneous enhancement, local invasiveness (of the mediastinal fat, great vessels, pleura or lung), associated lymphadenopathies and hematogenous dissemination [7].

Fig. 7 on page 32
**Fig. 7:** F, 61 yo, dermatomyositis and anterior thoracic pain. CT aspects: large, lobulated thymic mass (T), heterogeneous, with central necrosis and nodular calcifications, invading the anterior thoracic wall (white arrow), with hypervascular hepatic metastases (arrowhead).

**References:** Department of Radiology and Medical Imagistics, Fundeni Clinical Institute/ Bucharest 2018

**Germinal cell tumors**

The CT aspects of germinal cell tumors are highly variable depending on the subtype of tumor. Thus, a mature teratoma is intensely heterogeneous, frequently associating cystic, fat, soft tissue and calcium densities, seminomas are generally homogenous and nonseminomatous germ cell tumors are heterogeneous due to necrosis and hemorrhage [11]. Table 3, *Fig. 8 on page 33*, *Fig. 9 on page 34*

<table>
<thead>
<tr>
<th>Mature teratoma</th>
<th>Seminoma</th>
<th>Nonseminomatous tumors</th>
</tr>
</thead>
<tbody>
<tr>
<td>Round/ lobulated mass.</td>
<td>Large, lobulated, well</td>
<td>Large, lobulated, well</td>
</tr>
</tbody>
</table>
Heterogeneous: tissue, cystic (fluid, lipid, mixt components), calcar elements (calcifications, bone, teeth).

Contrast enhancement of the capsule and septa.

Extension towards ONLY one side of the median line.

Frequently homogenous.

Extension towards BOTH sides of the median line.

Local invasiveness.

Lymphogenous and hematogenous metastatic disease.

Outlined.

Heterogeneous: diminished/no central enhancement (necrosis, hemorrhage), important peripheral contrast enhancement.

Local invasiveness.

Lymphogenous and hematogenous metastatic disease.

Pleural/pericardial effusions.

Table 3. Main CT aspects in germinal cell tumors [11].
Fig. 8: M, 51 yo, anterior thoracic pain. CT aspects: lobulated, well outlined anterior mediastinal mass (M), with central necrosis, without visualization of the left innominate vein and tumor thrombosis at the confluence of the innominate veins (white arrow), including the brachiocephalic artery, left common carotid and subclavian artery, invading the anterior wall of the pulmonary trunk.

References: Department of Radiology and Medical Imagistics, Fundeni Clinical Institute/ Bucharest 2010
Fig. 9: M, 25 yo, thoracic pain, dry cough, fever, elevated #- fetoprotein. CT aspects: large, lobulated, well outlined anterior mediastinum mass (M), with extension towards the left side of the median line, highly heterogeneous, with central necrotic and hemorrhagic areas (white arrow) and peripheral contrast enhancement, nodular calcifications, hemothorax (arrowhead).

References: Department of Radiology and Medical Imagistics, Fundeni Clinical Institute/ Bucharest 2018

**Thymic lymphoma and leukemia**

Thymic involvement in lymphoma or leukemia presents as a soft tissue lobulated thymic mass, frequently homogenous (may also include cystic or necrotic changes), with mild contrast enhancement and local invasiveness, surrounding the great vessels but commonly without invasion. An important imagistic feature is the presence of associated lymphadenopathies. *Fig. 10 on page 35, Fig. 11 on page 36 and Fig. 12 on page 37*
**Fig. 10:** F, 24 yo, anterior thoracic pain. CT aspects: large, homogeneous anterior mediastinum mass (M), in contact with the great mediastinal vessels, invading the fat planes, with important mass effect and posterior displacement of the mediastinal vessels, associated lymphadenopathies (white arrow).

**References:** Department of Radiology and Medical Imagistics, Fundeni Clinical Institute/ Bucharest 2011
**Fig. 11:** M, 50 yo, dysphonia, dyspnea, cough, thoracic pain. CT aspects: large, lobulated, slightly heterogeneous (necrotic areas) mass (M), originating in the anterior mediastinum, with middle and posterior mediastinum extension, surrounding the great vessels but WITHOUTH invasion, associated bilateral pleurisy (Pl) and pericarditis (P).

**References:** Department of Radiology and Medical Imagistics, Fundeni Clinical Institute/ Bucharest 2018
**Fig. 12**: M, 8 yo, weight loss (5 kg in 4 weeks), cervical lymphadenopathies. CT aspects: large, well outlined, homogeneous anterior mediastinum mass (M), invading the fat planes adjacent to the great vessels and pericardium, pleural (Pl) and pericardial effusion (P).

**References**: Department of Radiology and Medical Imagistics, Fundeni Clinical Institute/ Bucharest 2017

**DIFFERENTIAL DIAGNOSIS**

Differential diagnosis of the anterior mediastinum masses can be summarized using the mnemonic "4T": thymoma, teratoma, thyroid tumors/goiter, and terrible lymphoma.

Other differential diagnoses

- **Goiter** can be diagnosed certainly by CT alone. It appears as a lobulated anterior mediastinum mass, frequently in continuity with the thyroid gland, with high attenuation on non-contrast CT (70-85 UH) and prolonged contrast enhancement. It is commonly inhomogeneous due to cystic changes and calcifications [9].
- **Lymph node involvement** secondary to extramediastinal malignancies [12].
- **Ascending aorta aneurysms** [14]. *Fig. 13 on page 38, Fig. 14 on page 39 and Fig. 15*

*Fig. 13*: F, 49 yo. CT aspects: lobulated, heterogeneous, high native attenuation, contrast enhancing anterior mediastinal mass, in continuity with the thyroid gland (white arrow).

*References*: Department of Radiology and Medical Imagistics, Fundeni Clinical Institute, Bucharest 2013.
Fig. 14: M, 80 yo, diagnosed with hepatocarcinoma. CT: lymphadenopathies of the anterior mediastinum (white arrow), right pleural effusion (PI).

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**Fig. 15:** F, 68 yo. EKG gating Angio-CT of the thoracic aorta: Important ascending aorta dilation, with no intraluminal defects (white arrow).

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In particular cases, secondary mediastinal involvement such as:

- **lun**g malignancies with mediastinal extensions or
- **anterior** mediastinal plasmacytoma [13] should be taken into consideration. *Fig. 16 on page 41*, *Fig. 17*
**Fig. 16:** Fig. 14. F, 63 yo, anterior thoracic pain, dyspnea. CT aspects: round, well defined with slightly irregular contours, heterogeneous mass (M) involving the left pulmonary hilum and the anterior mediastinum, nodular calcifications. Histopathologic diagnosis: squamous cell pulmonary carcinoma.

**References:** Department of Radiology and Medical Imagistics, Babes Vodora Clinical Institute, Bucharest.
**Fig. 17**: M, 73 yo, diagnosed with multiple myeloma. CT aspects: large, lobulated, homogeneous anterior mediastinum mass (M), with extension to the middle mediastinum, left pleural effusion (Pl), associated bone lesions and right chest wall mass (white arrow).

**References**: Department of Radiology and Medical Imagistics, Fundeni Clinical Institute/ Bucharest 2012

**STRUCTURED REPORT**

*The structured CT report* in patients with myasthenia gravis, miasteniform syndrome or suspicion of anterior mediastinal mass should include:

1. **Information regarding the anterior mediastinal mass**:
   - Location;
   - Size;
   - Contours: well outlined/ poorly outlined, regular/ irregular contours;
   - Structure: homogeneous/ heterogeneous ± cystic components, calcifications, necrotic or hemorrhagic areas;
• Contrast enhancement features;
• Signs of invasion: infiltration of the fat planes, invasion of the great mediastinal vessels and pleural involvement (thickening, nodularity or effusion);

2. Presence of associated lymphadenopathies;
3. CT signs of metastatic disease;
4. Other associated lesions - incidentaloma;
5. Aberrant anatomy/variants.
Fig. 2: Age related normal aspects of the thymus.

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Fig. 3: F, 50 yo, history of chemotherapy for neuroendocrine pancreatic tumor. CT aspects: diffuse enlargement of the thymus, WITHOUT contour irregularities or focal masses.

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Conclusion

- In the context of continuously changing thymic morphology, it is important to be familiar with its normal CT aspects. Its shape is quadrilateral/triangular with convex lateral borders before puberty and triangular with straight or concave lateral borders after puberty. The size and density of the gland decrease with age.

- The main differential diagnosis of masses involving the anterior mediastinum may be summarized by the mnemonic "4T": thymoma, teratoma, thyroid tumors/goiter and terrible lymphoma.

- Whilst some of the anterior mediastinal masses may be diagnosed with certainty on CT alone, most of them require correlation with clinical and laboratory data, patient history and histopathological confirmation. Even so, CT imaging plays a key role in establishing a presumptive diagnosis, further testing indications and patient management.
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References


