The thymus: A pictorial review of thymic pathology

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Learning objectives

1. Discuss the dynamic nature of the thymus.
2. Provide a comprehensive review of both benign and malignant thymic disease.
3. Highlight the computed tomography characteristics of thymic disorders.
4. Review the staging schemes for thymomas.

Background

The thymus is a bilobed lymphatic organ located in the anterior mediastinum. It is important in the development of the T cells, a component of cellular immunity. The thymus evolves over time with its appearance changing as individuals age. Knowledge of this evolution is important so that normal thymus is not misdiagnosed as a mass leading to unnecessary interventions.

The thymus originates from two ectodermal diverticuli arising from the third and fourth brachial clefts [1]. These migrate caudally and medial to the anterior mediastinum. Although almost all thymic tissue is located in the anterior mediastinum, ectopic thymic tissue may be present along this path. In the anterior mediastinum the diverticuli develop into two distinct lobes which are enclosed in a capsule.

The thymus enlarges until puberty at which time undergoes involution with the replacement of glandular tissue by fat. The fatty involution is easily seen with computed tomography (CT). Fatty replacement is complete by the sixth decade and is complete in 50% of individuals by the age of 40. Although age specific measurements have been performed, qualitative assessment of thymic gland shape is sufficient in most cases for diagnosing mass lesions of the thymus. Multilobulatity of the thymus has been shown to be fairly sensitive in detecting thymic masses. Focal alteration of the lateral mediastinal border by the thymus is also concerning for the presence of thymic mass [1].

Imaging findings OR Procedure details

Thymic Hyperplasia:
Thymic hyperplasia is subdivided into two histologic types; true thymic hyperplasia and lymphoid hyperplasia. In true thymic hyperplasia the histologic pattern is normal with normal thymic elements being present in normal proportions. This form of hyperplasia is seen in patients who are recovering from stress such as pneumonia, burns, chemotherapy, radiation therapy and corticosteroid treatment. The thymus gland may shrink in size during periods of stress. During recovery from these stressful conditions the thymus usually returns to its original normal size. In some patients the thymus grows larger than normal. This hyperplastic enlargement of the thymus is known as thymic rebound [1]. Appreciation of post chemotherapy thymic enlargement is important so that patients are not mis-diagnosed as having an enlarging mediastinal mass. Fig. 1 on page 5

Hyperplasia typically demonstrates diffuse symmetric enlargement of the gland while tumors tend to appear as a focal mass [1]. While it may be fairly straightforward in patients whose disease rarely involves the anterior mediastinum, such as testicular carcinoma, it is more problematic in those patients with diseases such as lymphoma that frequently involve the anterior mediastinum. In these patients it may not be possible to separate recurrent disease from thymic hyperplasia [3]. Thymic rebound may be a positive prognostic indicator in patients receiving chemotherapy. In one study, patients with thymic hyperplasia had a 93% disease-free survival as compared to a 78% disease free survival in those patients who did not develop thymic hyperplasia [3].

In lymphoid hyperplasia the medulla show increased lymphoid follicles while the cortex atrophies. This form of thymic hyperplasia is encountered in 65% of patients with myasthenia gravis [4]. It is also seen in a number conditions including with systemic lupus erythematosus, scleraderma, rheumatoid arthritis, Graves disease, thyrotoxicosis and Addison's disease [1].

**Thymic Cyst:**

Thymic cysts are uncommon lesions involving the thymus which may be congenital or acquired. Congenital thymic cysts tend to be unilocular, contain thin fluid and show no evidence of inflammation on histological examination [5]. Fig. 2 on page 6

Acquired cysts are usually multilocular and arise from an inflammatory process. The fluid within them is thick and the wall of the cyst demonstrate significant inflammation on histopathologic examination [5]. Thymic cysts have been reported associated with Sjogren's syndrome, myasthenia gravis, aplastic anemia, systemic lupus erythematosis, HIV infection and surgical trauma. On CT acquired cysts may appear unilocular or multilocular and a cyst wall is always evident with the majority of cysts having associated soft tissue.

**Thymoma:**
Thymic epithelial tumors include thymoma and the less common thymic carcinoma [1]. These neoplasms, although rare, are the most common primary tumor of the anterior mediastinum. They have no gender predilection and occur most commonly in the fifth and sixth decades of life. Increasingly asymptomatic thymomas are being found on chest CT. When symptoms are present they are due to either mass effect or invasion of adjacent structures. Superior vena cava syndrome due to compression or invasion of the superior vena cava or dyspnea due to diaphragm paralysis secondary to phrenic nerve invasion are encountered. Chest pain, dyspnea and cough are common symptoms. Thymomas have been associated with over 30 different diseases [1]. Myasthenia gravis is the disease that has the most well recognized association with thymoma. Symptoms of myasthenia gravis are encountered in up to half the patients with thymomas and 10%-20% of patients with myasthenia gravis have thymomas.

Two main classification and staging systems are used with thymic tumors, the Masaoka staging system and the WHO classification scheme [1]. The Masaoka system is based on surgical findings including the presence of invasion and metastasis. Fig. 3 on page 7 The WHO classification scheme is based on histologic features of the tumor. (Table 1) Fig. 4 on page 8 The WHO scheme correlates with the likelihood of invasion. Types A and AB typically are encapsulated without evidence of invasion and tend to have a benign clinical course. Fig. 5 on page 8 Type B has a greater likelihood for invasion. Fig. 6 on page 9 Type C is almost always invasive and has the worst survival rate. Fig. 7 on page 9

On CT, thymic epithelial tumors appear as soft tissue masses in the anterior mediastinum [6]. They vary in size and can have smooth or lobulated borders. They tend to be homogeneous in density Fig. 8 on page 10 although may be inhomogeneous when necrosis, Fig. 9 on page 10 hemorrhage or cystic change Fig. 10 on page 11 has occurred. If the tumor has extended beyond the capsule there is evidence of invasion into the mediastinal fat or adjacent structures. Fig. 11 on page 12 If the tumor has grown to the pleural surface, pleural seeding may be present and is manifest by pleural nodules or masses that are almost always ipsilateral to the mediastinal mass. Fig. 12 on page 13 Pleural effusions are uncommon. Vascular involvement is present when irregular vessel contour, vascular encasement, vascular obliteration or endoluminal soft tissue is present. Extension into the cardiac chambers can occur.

The CT findings correlate with the invasiveness of the tumor and its clinical prognosis. Tomiyama et al. found that smooth contours and round shape are commonly seen in type A tumors which have a good clinical outcome following surgery [7]. The presence of calcification within the mass suggests type B histology. Irregular contours suggests a type C tumor. Fig. 13 on page 14 Jung et al. reported that thymic tumors with a high risk of invasion, types B and C, are more likely to have lobulated borders, as well as invasion of mediastinal fat and adjacent vessels [8]. Fig. 14 on page 15 Recurrence
of tumor and metastasis are associated with lobulated or irregular contours, oval shape, mediastinal or great vessel invasion and pleural implants.

**Thymolipoma:**

Thymolipomas are rare slow growing benign tumors of the thymus [9]. They account for 2-9% of thymic neoplasms. The tumors are rarely associated with myasthenia gravis. Histologically thymolipomas consist of mixture of normal appearing thymic tissue and mature adipose tissue. Thymolipomas can grow very large. The combination of size and malleable nature tends to cause the tumors to migrate caudally and appear more inferior than the expected location of the thymus. They may be associated with a pedicle which extends more superiorly in the anterior mediastinum. It's soft consistency allows it to conform to the shape of adjacent cardiomedistinal structures. On CT the masses appear as a mixture of fat and soft tissue attenuation. The soft tissue component may appear as whorls within the fat. **Fig. 15 on page 16** Although microscopic calcification may be present, calcifications are not seen on CT [9].

**Thymic Carcinoid:**

Thymic carcinoid is a rare malignant tumor of the thymus [10]. It is encountered three times as often in men as compared to women. The median age of presentation is 43 years. Histologically thymic carcinoids are similar to atypical bronchial carcinoids and tend to exhibit aggressive behavior. Approximately a third of the patients present with symptoms related to mass effect or invasion of mediastinal structures while the remainder are found incidentally. In approximately one-half of patients the carcinoids are functionally active with clinical manifestations of hormone syndromes. Cushing syndromes (33% - 49%) and type 1 MEN syndrome (19% - 25%) are the most common syndromes encountered. Carcinoid syndrome has not been reported with thymic carcinoids. Thymic carcinoids are aggressive tumors that tend to metastasize widely and recur locally. Thymic carcinoids appear as large anterior mediastinal masses. The lesions may be localized or show evidence of invasion of adjacent structures. **Fig. 16 on page 16** Radiographically they are indistinguishable from thymomas. Octreotide radionuclide imaging of the thymus may be helpful in evaluating patients with MEN because it accumulates in both thymomas and carcinoids which are both encountered in the syndrome but not in thymic hyperplasia.

**Images for this section:**
**Fig. 1:** Figure 1A shows normal thymic tissue in a young adult recently diagnosed with a lower extremity sarcoma. Figure 1B shows marked thymic enlargement after chemotherapy.
**Fig. 2:** Figures 2A-B show a homogeneous cystic mass adjacent to the right cardiomesdiastinal border. The PET images in 2C-D show no significant metabolic activity within the lesion.
**Table 1**

**Masaoka-Koga Staging System**

<table>
<thead>
<tr>
<th>Stage</th>
<th>Definition</th>
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</thead>
<tbody>
<tr>
<td>I</td>
<td>Grossly and microscopically completely encapsulated tumor</td>
</tr>
<tr>
<td>IIa</td>
<td>Microscopic transcapsular invasion</td>
</tr>
<tr>
<td>IIb</td>
<td>Macroscopic invasion into thymic and surrounding fatty tissue or grossly adherent to but not breaking through medistinal pleura or pericardium</td>
</tr>
<tr>
<td>III</td>
<td>Macroscopic invasion into neighboring organs</td>
</tr>
<tr>
<td>IVa</td>
<td>Pleural or pericardial metastases</td>
</tr>
<tr>
<td>IVb</td>
<td>Lymphogenous or hematogenous metastasis</td>
</tr>
</tbody>
</table>

**Fig. 3**

**Table 2**

**WHO Classification Scheme for Thymic Epithelial Tumors**

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>A</td>
<td>Medullary</td>
</tr>
<tr>
<td>AB</td>
<td>Mixed</td>
</tr>
<tr>
<td>B1</td>
<td>Lymphocyte rich, predominately cortical</td>
</tr>
<tr>
<td>B2</td>
<td>Cortical</td>
</tr>
<tr>
<td>B3</td>
<td>Epithelial</td>
</tr>
<tr>
<td>C</td>
<td>Thymic carcinoma</td>
</tr>
</tbody>
</table>

**Fig. 4**
Fig. 5: 55 yo female with encapsulated thymoma, type A. The tumor contains areas of necrosis with the capsule clearly demarcated from adjacent mediastinal structures.

Fig. 6: 39 yo female with a type B3 thymoma. (a) The mass can not be separated from the right atrium which it deforms. (b) Pleural soft tissue mass is present along the right diaphragm representing pleural metastases.
Fig. 7: Figure 7A shows a large heterogeneous anterior mediastinal mass compressing and likely invading the main pulmonary artery. Pathology demonstrated thymic carcinoma. Figure 7B shows pericardial and pleural effusions present in this patient. Figure 7C shows extensive hepatic metastatic disease.

Fig. 8: 29 yo female with an incidentally found thymoma, type B1. Homogeneous density mass that has no clear separation from the right atrium.
Fig. 9: Figures 9A-B show a large anterior mediastinal mass, located asymmetric to the left. This demonstrates marked peripheral enhancement with central necrosis. There is a clear fat plane between the mass and the mediastinal structures; no invasion is present. Findings are consistent with encapsulated thymoma. Bilateral pleural effusions are present, which is an unusual finding with encapsulated thymoma.
Fig. 10: 64 yo female with a type A thymoma. Encapsulated mass has clear separation from adjacent structures and contains a large cystic component.
Fig. 11: Thymoma, type B2, that invades the mediastinal fat and is inseperable from adjacent vascular structures.
Fig. 12: Thymoma, type B1, that abuts the pleural surface. Ipsilateral pleural metastases are seen posteriorly.
Fig. 13: Thymoma, type C, with irregular margins along its' posterior surface.
Fig. 14: Large thymoma, type B3, that has a lobulated contour. Mass invades mediastinal fat and is inseperable from aorta, brachiocephalic artery and superior vena cava.

Fig. 15: The CXR in Figure 7A shows a large extending into the bilateral hemithoraces. Figures 7B-C show a large anterior mediastinal mass occupying a majority of the left hemithorax. Fat density constitutes at least 50% of the mass.
Fig. 16: The patient presented with symptoms of Cushing's syndrome, including central obesity, striae, moon face, buffalo hump, and hyperglycemia. The CXR in Figure 8A shows abnormal density in the lower right paratracheal region. Figures 8B-D show an irregular anterior mediastinal mass, consistent with biopsy-proven thymic carcinoid. This mass abuts and possibly invades the left brachiocephalic vein (8B), contains a small focus of calcification (8C), and appears to invade the pericardium and right atrium (8D).
Conclusion

A variety of both benign and neoplastic conditions may involve the thymus. Knowledge of the dynamic nature of the thymus and the CT characteristics of benign thymic conditions is important to prevent unnecessary interventions. Imaging is very important in the diagnosis and staging of thymic tumors. Familiarity with the CT findings that correlate with prognosis and likelihood of invasion help plan therapy and predict outcome.

References

Personal Information