Clinical and Radiologic Review of the Normal and Abnormal Thymus: Pearls and Pitfalls[1]

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ONLINE-ONLY CME

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LEARNING OBJECTIVES

After reading this article and taking the test, the reader will be able to:

- Discuss the embryology, anatomy, and dynamic physiology of the thymus.
- Identify anatomic variations and dynamic changes of the thymus along with thymic pathologic conditions.
- Describe the imaging findings of thymic tumors and their mimics.

TEACHING POINTS

See last page

At imaging, the thymus appears in a variety of shapes and sizes, even in the same individual. It gradually involutes with age and may acutely shrink during periods of bodily stress. During the recovery period, it grows back to its original size or even larger, a phenomenon known as thymic rebound hyperplasia. These anatomic variations and dynamic changes appear to be the main source of confusion with pathologic conditions. In turn, these misinterpretations may lead to prolongation or alteration of the chemotherapy regimen or to unnecessary radiation therapy, biopsy, or thymectomy. Familiarity with the embryology, anatomy, and dynamic physiology of the thymus is essential to avoid unnecessary imaging or invasive procedures. Radiologists play a major role in differentiating normal thymic variants, ectopic thymic tissue, and nonneoplastic thymic conditions such as rebound hyperplasia from neoplastic conditions. Knowledge of the imaging findings of thymic tumors and their mimics may help radiologists arrive at the correct diagnosis.

Abbreviation: FDG = fluorodeoxyglucose

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Introduction

The thymus is a lymphatic organ that plays a vital role in the development and maturation of the immune system during childhood, specifically T cells, which are instrumental in regulating cellular immunity, and B cells, which are instrumental in regulating humoral immunity. The thymus is sensitive to any kind of bodily stress, including systemic infection, neoplasms, surgery, and chemotherapy, and responds with rapid atrophy, only to regrow to its original size or even larger. The thymus is disproportionately larger in infants but gradually becomes replaced by fat and involutes throughout maturation. Nevertheless, the thymus maintains its ability to grow back at any time and at any age.

Descriptions of the thymus date back to more than 2000 years ago, yet its functions were not known for centuries. The thymus was once worshipped as the "seat of the soul" by the Greeks, and the thyme plant was burned during the rituals of sacrifice (1–4). For many decades, the thymus was blamed for a variety of childhood ailments. To name a few, "thymic asthma" and "status thymolymphaticus" were based on the assumption that the thymus was responsible for airway obstruction; in a way, it was considered "the seat of Satan" as opposed to the seat of the soul.

Despite the advances made in imaging technology and in understanding the dynamic physiology of the thymus, its variations in size and shape continue to be a source of misinterpretation. Unfortunately, these misinterpretations may result in unnecessary and costly percutaneous or open biopsies, total thymectomies, and irradiation (3,4).

The objectives of this article are *(a)* to familiarize radiologists with the normal radiologic anatomy of the thymus in children and adults, its expected involution with age, its dramatic response to stress, and likewise its regrowth after recovery; *(b)* to illustrate a wide range of neoplastic conditions affecting the thymus; and *(c)* to advocate more conservative management in patients with unexpected thymic enlargement.

Embryology

A knowledge of thymic embryology is essential to understand how the arrest of thymic tissue during its caudal migration may result in ectopic or accessory thymic tissue. During the 6th gestational week, thymic primordia arise from the third and fourth pharyngeal pouches. During the 7th week, the bud-like thymic primordia elongate and become cylindrical, forming thymopharyngeal ducts, and migrate caudally and medially to their final destination in the anterior mediastinum. During the 8th gestational week, the thymic primordia fuse at their lower poles. The thymus is purely epithelial up to this point. However, during the 10th week small lymphoid cells migrate from fetal liver tissue and bone marrow into the primordia, causing thymic lobulation. During the 14th to 16th weeks, the thymus further differentiates into cortical and medullary components.

Figure 1. Ectopic parapharyngeal thymus in a 7-week-old boy with a "mass" in the right mandibular angle. Coronal contrast material–enhanced T1-weighted magnetic resonance (MR) image shows an enhancing parapharyngeal mass (arrow), which is isointense relative to the mediastinal thymus (arrowhead). At needle biopsy, the mass was proved to be ectopic thymic tissue.

Ectopic and accessory thymic tissue may occur anywhere along the path of descent (thymopharyngeal duct) as the result of failure of descent, sequestration, or failure to involute. Ectopic or accessory thymic tissue may be found in the vicinity of the superior vena cava, brachiocephalic vessels, and aorta. Rarely, it may be found in the posterior mediastinum (5) or even in the dermis (6). Ectopic thymic tissue may manifest as a neck mass, which can be mistaken for a pathologic process (7) (Fig 1). Also, as the thymopharyngeal duct undergoes atrophy, thymic remnants may develop into cysts. Because the parathyroid glands similarly arise from the third and fourth pharyngeal pouches, ectopic parathyroid glands, and hence parathyroid adenomas, may appear anywhere near or within the thyroid or thymus (8) (Fig 2).

Teaching Point

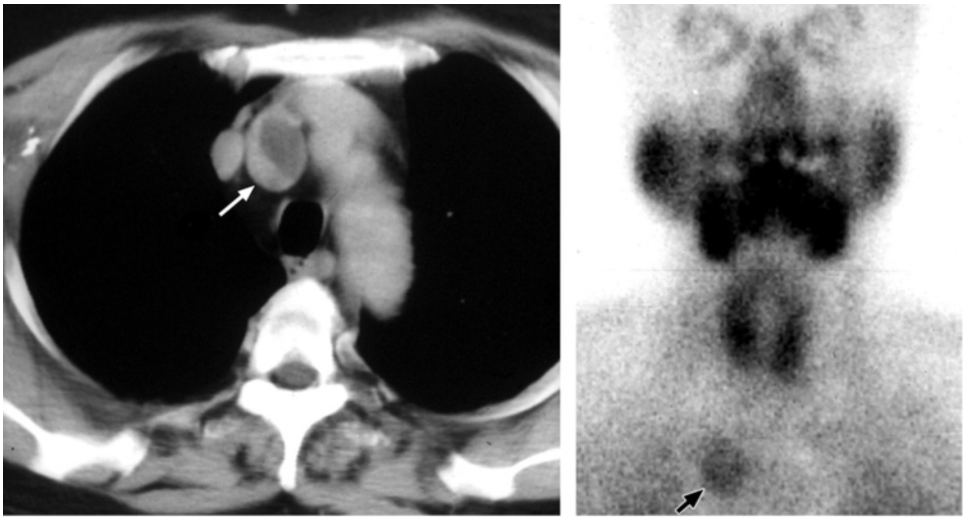

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Figure 2. Intrathymic ectopic parathyroid adenoma in a 66-year-old woman with hypercalcemia and renal stones. **(a)** Contrast-enhanced computed tomographic (CT) scan shows a partially cystic mass (arrow) between the superior vena cava and aorta. **(b)** Coronal technetium 99m–sestamibi scan shows uptake by the mass (arrow). (Reprinted, with permission, from reference 8.)

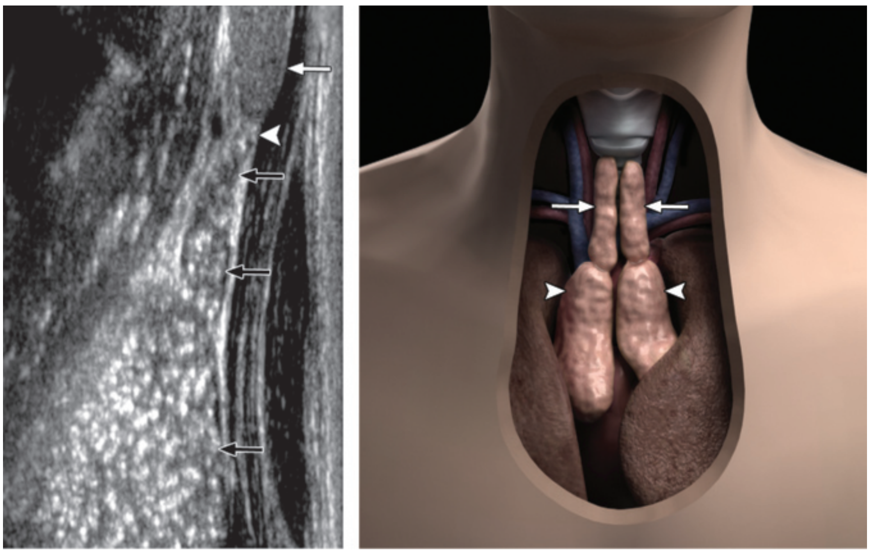

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Figure 3. Normal thymus with a cervical component in a 12-year-old boy. **(a)** Sagittal ultrasonographic (US) image shows the mediastinal and cervical components of the thymus (black arrows) attached to the lower pole of the thyroid (white arrow) via the thyrothymic ligament (arrowhead). Note the "starry sky" appearance of the thymus; this is created by hyperechoic fat against the background of the remaining hypoechoic lymphoid tissue. **(b)** Corresponding anatomic drawing shows the mediastinal (arrowheads) and cervical (arrows) components of the thymus.

Anatomy

The thymus is located in the anterior mediastinum. It overlies the pericardium, aortic arch, left innominate vein, and trachea. The thymus may extend superiorly to the lower pole of the thyroid (Fig 3) and inferiorly to the diaphragm. The thymus is attached to the thyroid by the thyrothymic ligament (Fig 3) (9,10).

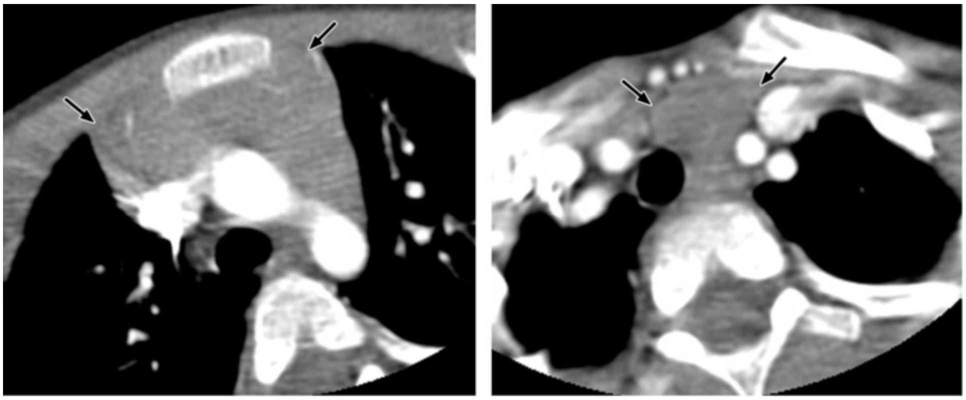

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Figure 4. Cervical component of the thymus in a 3-year-old boy with a strong maternal family history of papillary thyroid carcinoma. The cervical component was misinterpreted as an "exophytic tumor of the thyroid gland." Contrast-enhanced CT scans show a normal mediastinal thymus (arrows in **a**) and its cervical component (arrows in **b**). Follow-up studies 2 years later showed no change, and the patient remained asymptomatic.

A number of studies have described various locations and extensions of the thymus. In an analysis of 50 consecutive thymectomies performed for myasthenia gravis, the thymus was found outside its classic boundaries in the neck in 16 patients (32%) and in the mediastinum in 49 patients (98%). For instance, one or both lobes were found behind the thyroid in 13 patients (26%) (11). Familiarity with these variations is essential in distinguishing thymic tissue from pathologic masses (Figs 1, 4, 5).

Thymic morphology varies greatly even in the same age group. For instance, in young adults, it is typically bilobed and V-shaped, with two small processes extending into the neck (Figs 3–5); however, it can also be unilobed, trilobed, or shaped like an X or inverted V (12).

The size of the thymus varies as well. A recent study of 136 thymic specimens from healthy victims of sudden death concluded that the thymus attains its maximum size during the first few months of life and does not grow any larger beyond puberty (13).

The thymus can weigh from 5 g to 50 g throughout a person's life, with a slight increase in weight during the first decade of life and a gradual decrease thereafter (14). The weight of the thymus as a percentage of total body mass is greatest at or near the time of birth (15).

As children grow older and their immune systems mature, the thymus undergoes physiologic involution. Ultimately, the thymus becomes replaced by fat, yet it maintains its original configuration.

Appearance of Normal Thymus at Imaging

Given the variability in shape and size of the thymus, familiarity with the broad spectrum of imaging appearances of the normal thymus will help radiologists minimize the number of invasive procedures.

Teaching Point

Conventional Radiography

On frontal chest radiographs in infants and young children, the thymus is strikingly large but difficult to discriminate from the cardiac silhouette. The thymus usually has smooth borders and remains visible on radiographs through the age of 3 years. The thymic wave sign, a scalloped or wavy contour of the organ, is created by the impression of the anterior reflection of the ribs (Fig 6). The thymic sail sign, a triangular, slightly convex right lobe of the thymus with a sharply demarcated base caused by the minor fissure (Fig 6), is seen in approximately 5% of children (16).

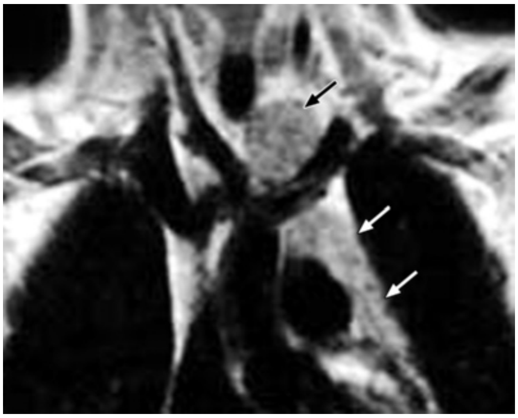

Figure 5. Normal thymus mistaken for a metastasis in an 11-year-old boy. The patient completed preoperative chemotherapy for a metastatic osteosarcoma of the femur in June 1996. He underwent above-the-knee amputation, wedge resection of pulmonary metastases, and postoperative chemotherapy. In October 1996, results of a biopsy of a "mediastinal mass," performed at an outside institution, reportedly showed "malignant cells consistent with metastasis." This result prompted a thymectomy in December 1996, at which a normal thymus was found. Coronal T1-weighted MR image shows a normal thymus with its mediastinal (white arrows) and cervical (black arrow) components.

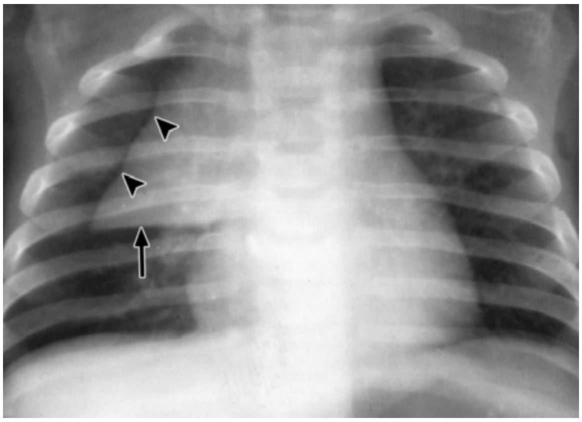

Figure 6. Thymic wave sign and sail sign in a 5-month-old girl with mild respiratory distress. Frontal chest radiograph shows the thymic wave sign (arrowheads), which is created by the impression of the anterior ribs on the normal thymus, and the thymic sail sign (arrow), which is created by the right lobe of the thymus abutting the minor fissure.

Figure 7. Normal echotexture of the cervical component of the thymus in a 7-year-old girl with a right-sided aortic arch. The patient was referred for assessment of a suspected "supraclavicular mass" seen at CT. Sagittal US image of the lower neck shows a normal thymus (arrows), which has heterogeneous hypoechoic echotexture relative to that of the thyroid. *SCV* = subclavian vein.

Ultrasonography

On US images, the thymus in infants may have multiple linear or branching echogenic foci (17). In a study of 56 infants (aged 0–10 months), the echogenicity of the thymus was homogeneous and thus similar to that of the liver and spleen in 42 infants (75%). In 14 infants (25%), the echogenicity was slightly less homogeneous than that of the liver or spleen (18).

In older children, the echo pattern of the thymus appears as a fine mixture of remaining lymphoid tissue and fat. The cervical component of the thymus, which is occasionally detected with US, shows distinct hyperechoic foci that resemble a starry sky (Figs 3, 7). The thymus is very pliable and does not cause compression or displacement of the adjacent structures. This finding can be a particularly important part of a real-time sonographic examination because cardiac pulsations and respiratory motions affect the shape of the thymus. In contrast, solid tumors or diffuse infiltrative processes are less malleable and more rigid.

Teaching Point

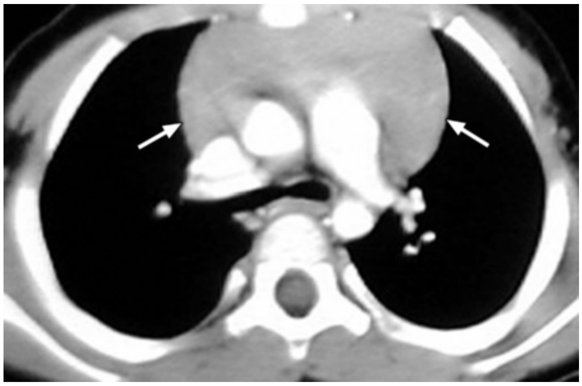

Figure 8. Quadrilateral appearance of the thymus in a healthy 1-year-old boy. Contrast-enhanced CT scan of the chest, obtained at the level of the pulmonary artery, shows a quadrilateral thymus with convex lateral borders (arrows).

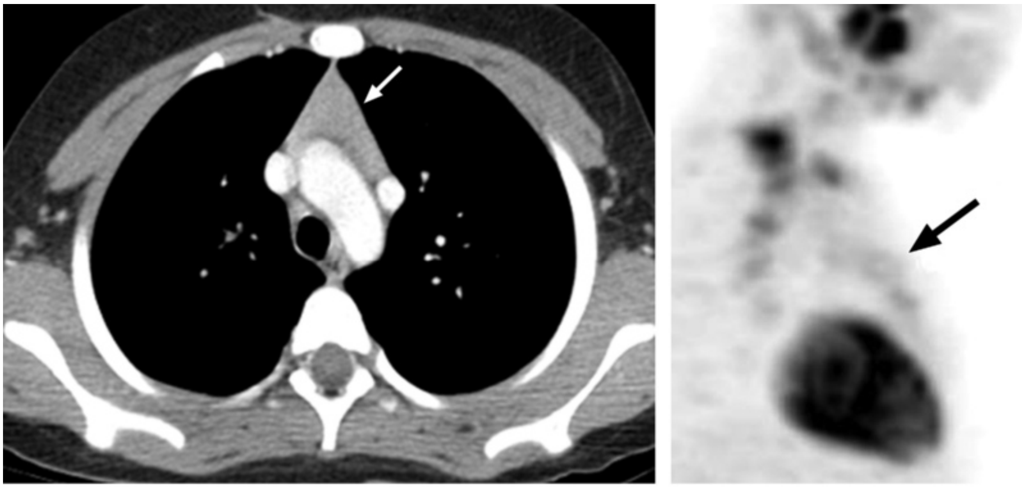

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Figure 9. Normal thymus in a 5-year-old girl with Burkitt lymphoma of the maxilla and central nervous system. The thymus was mistaken for recurrent lymphoma at positron emission tomography (PET)/CT, and needle biopsy was performed, which showed normal thymic tissue. **(a)** Contrast-enhanced CT scan obtained at the level of the aortic arch shows a normal-for-age triangular or arrowhead-shaped thymus (arrow). **(b)** Sagittal PET image shows the thymus (arrow), which does not demonstrate fluorodeoxyglucose (FDG) avidity.

Computed Tomography

Typically, the thymus is visible at CT and fills the perivascular space throughout the first 2 decades of life (Fig 8). In children younger than 5 years, it typically appears quadrilateral with convex borders (Fig 8). As children grow, the thymus gradually becomes triangular (Fig 9a) with straight or concave borders (19).

MR Imaging

At MR imaging, the thymus appears homogeneous, with signal intensity greater than that of muscle on T1-weighted images and signal intensity close to that of fat on T2-weighted images (20).

Positron Emission Tomography

A normal thymus may be barely visible on PET scans (Fig 9b). However, it may show striking FDG avidity in rebound hyperplasia, causing false alarm for recurrent lymphoma.

Thymic Disorders

Thymic Hyperplasia

Histologically, thymic hyperplasia can be divided into two distinct types: true hyperplasia and lymphoid (follicular) hyperplasia.

True Thymic Hyperplasia.—True thymic hyperplasia is characterized by an increase in the size and weight of the thymus with preservation of its organized microscopic features (10,12,21). Although a hyperplastic thymus may retain its normal shape, it more commonly loses its distinct bilobed appearance and instead appears oval (22,23).

Clinically, patients with true thymic hyperplasia can be divided into three groups: those without a related preexisting condition; those recovering

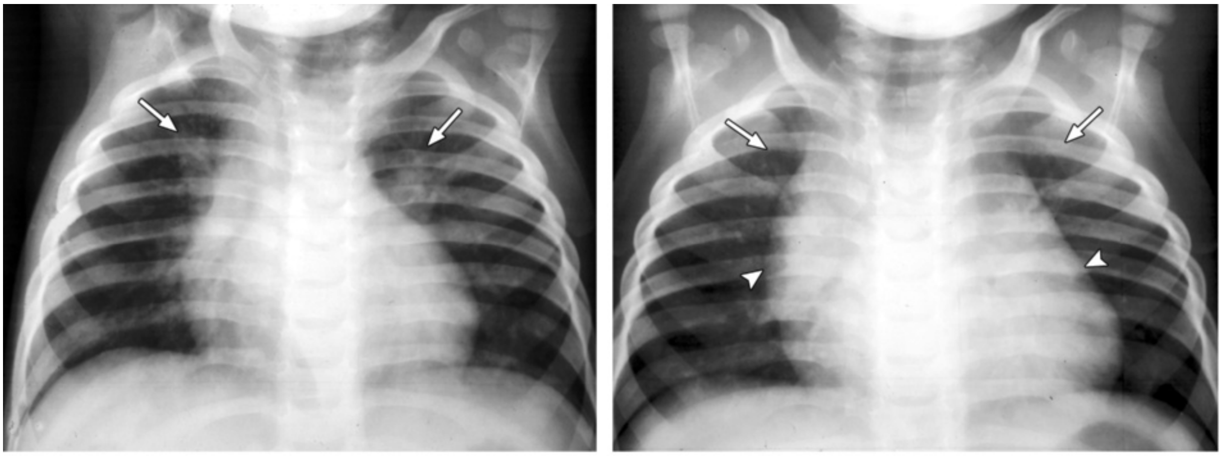

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Figure 10. Thymic rebound hyperplasia in an 18-month-old girl recovering from pneumonia. **(a)** Frontal chest radiograph shows air trapping and bilateral perihilar-peribronchial infiltrates (arrows), findings consistent with viral pneumonia. **(b)** Follow-up radiograph shows thymic rebound hyperplasia (arrowheads) and resolution of the pneumonic infiltrates (arrows).

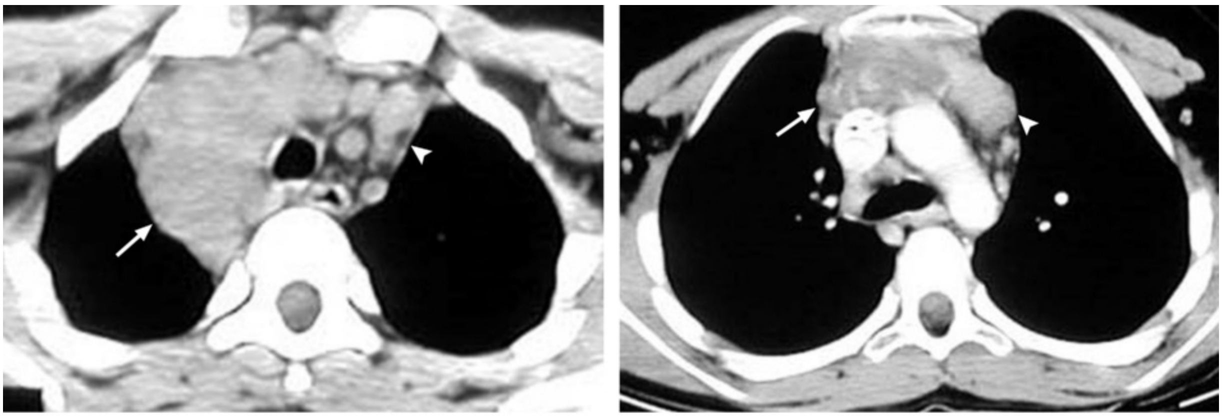

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Figure 11. Thymic rebound hyperplasia in an 11-year-old girl with Hodgkin lymphoma. **(a)** Contrast-enhanced CT scan obtained at diagnosis shows right-sided mediastinal adenopathy (arrow). Arrowhead = thymus. **(b)** CT scan obtained after completion of chemotherapy shows regression of the adenopathy (arrow). There is early thymic rebound hyperplasia (arrowhead). **(c)** CT scan obtained 1 month after chemotherapy shows that the nodal mass has almost resolved (arrow) and the thymic rebound hyperplasia is nearly complete (arrowhead).

from a recent stress event such as pneumonia (Fig 10), corticosteroid therapy, radiation therapy, chemotherapy (Figs 11, 12), surgery, or burns; and those with other disorders such as hyperthyroidism, sarcoidosis, or red blood cell aplasia (21,24).

When the body is exposed to stress, the thymus may shrink to as little as 40% of its original volume, depending on the severity and duration of the stress (24). Once the body recovers, the thymus usually grows back to its original size within 9 months; it can grow to be as much as 50% larger, a phenomenon known as thymic rebound hyperplasia (24). Rebound hyperplasia is commonly seen in children (Figs 10–12) but also occurs in adults (25).

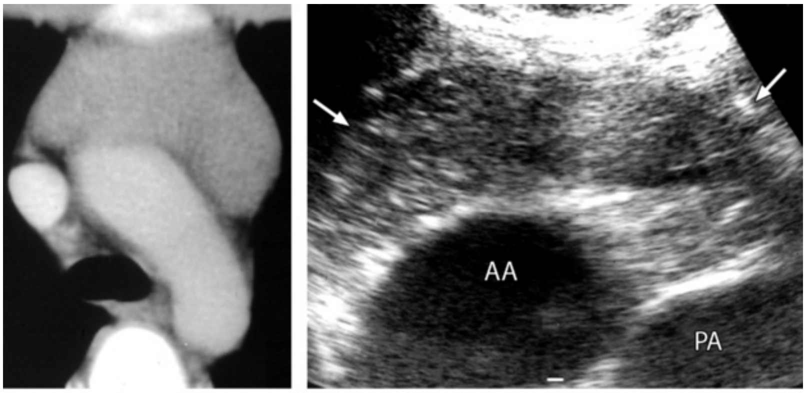

Figure 12. Dramatic thymic rebound hyperplasia in a 14-year-old boy who completed chemotherapy for primary mediastinal T-cell lymphoma 6 months earlier. The mediastinal "mass" was repeatedly misinterpreted as recurrent lymphoma. **(a)** Contrast-enhanced CT scan shows a solid heart-shaped thymus anterior to the aortic arch. **(b)** Suprasternal transverse US image shows a normal thymus (arrows) with smooth borders and echotexture between that of the liver and thyroid. No biopsy was performed. *AA* = aortic arch, *PA* = pulmonary artery.

Among patients who undergo chemotherapy, approximately 10%–25% may develop rebound hyperplasia. This phenomenon usually occurs within 2 years of initiation of chemotherapy. However, there is a reported case of rebound hyperplasia occurring 5 years after completion of chemotherapy (26). A review of the results of serial CT studies of 120 patients with malignant testicular teratomas revealed that 14 patients (11.7%) developed thymic enlargement 3–14 months after initiation of chemotherapy (25).

The diagnostic challenge in patients with a known neoplasm is to distinguish thymic hyperplasia from recurrent or metastatic tumors. Teaching Point Thymic rebound hyperplasia typically shows diffuse enlargement, a fine mixture of fat and lymphoid tissue, a smooth contour, and normal vessels; in contrast, thymic neoplasia is usually associated with a nodular contour and frequently contains necrotic (Fig 13) or calcified foci (25). There are heterogeneous features seen at US, CT, or MR imaging, with contrast enhancement especially a distinguishing feature from hyperplasia.

Thymic Lymphoid Hyperplasia.—Thymic lymphoid hyperplasia is characterized by the presence of a hyperplastic lymphoid germinal center in the thymic medulla that is associated with lymphocytic and plasma cell infiltration. Unlike true hyperplasia, lymphoid hyperplasia may occur with or without thymic enlargement. Thymic lymphoid hyperplasia is commonly associated with autoimmune diseases such as myasthenia gravis, thyrotoxicosis, and connective tissue disease (27) and

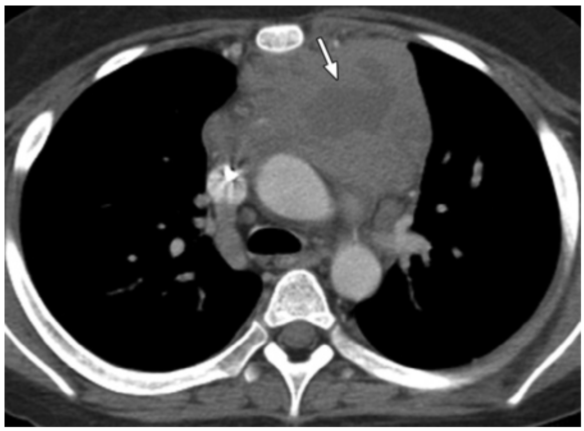

Figure 13. Relapsed acute lymphoblastic leukemia in a 13-year-old boy. Contrast-enhanced CT scan shows multiple enlarged lymph nodes and a large thymic mass with a necrotic center (arrow).

has been reported to occur in the early stages of human immunodeficiency virus infection (28).

Although thymic lymphoid hyperplasia usually appears as a normal thymus at conventional radiography, at CT it may appear normal (45% of cases), enlarged (35%), or as a focal thymic mass (20%) (24).

Thymic Cysts

Congenital thymic cysts originate from embryonic remnants and may be found along the thymopharyngeal duct, which extends from the upper neck to the anterior mediastinum. Congenital thymic cysts occur rarely in the posterior mediastinum or near the diaphragm (29). Acquired thymic cysts have been reported to occur before (Fig 14) and after (Fig 15) chemo-

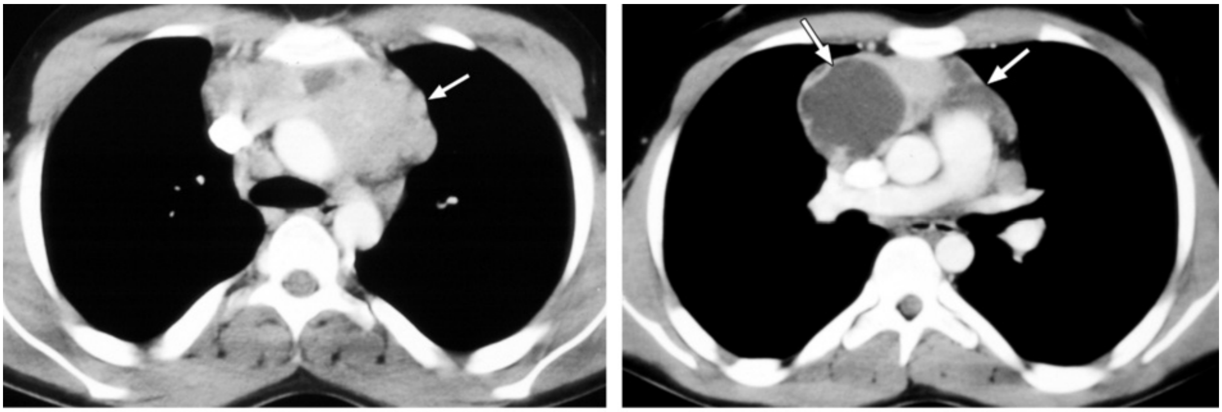

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Figure 14. Cystic changes of the thymus and lymph nodes at diagnosis in a 19-year-old man with Hodgkin lymphoma. Contrast-enhanced CT scans show a solid (arrow in **a**) and cystic (arrows in **b**) thymic mass. By the time the patient completed chemotherapy, the cystic nodes had resolved but the cystic areas in the thymus remained unchanged.

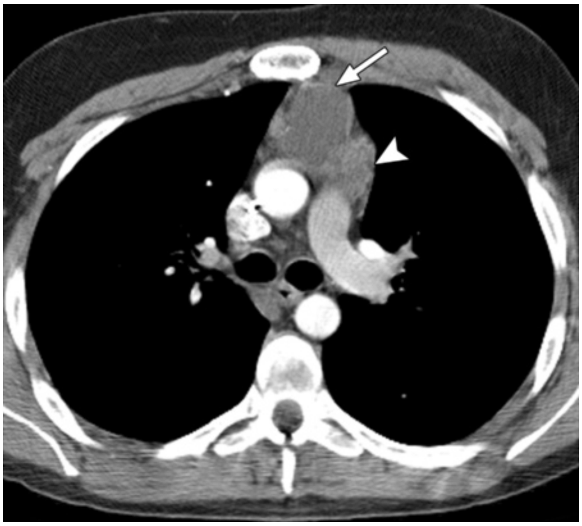


Figure 15. Cystic change of the thymus in a 28-year-old man with Hodgkin lymphoma treated 3 years earlier. Contrast-enhanced CT scan shows a thymic cyst (arrow) and thymic rebound hyperplasia (arrowhead).

therapy for non-Hodgkin or Hodgkin lymphoma, after thoracotomy, and in about 40% of patients with thymomas (30). Cystic changes can be seen in a variety of thymic tumors, including thymic epithelial tumors, Hodgkin and non-Hodgkin lymphomas, germ cell tumors, and thymic carcinomas (10,12,24). Multilocular thymic cysts in children with human immunodeficiency virus infection were reported when the retroviral medications were not as available as they are today (31).

On radiographs, thymic cysts usually appear as homogeneous circumscribed masses that may have calcified rims (12). Their opacity is usually in the range of water, although this may vary depending on the presence of blood products or fat. At CT, thymic cysts are unremarkable, have thin walls and no solid component, and show no contrast enhancement (24).

Thymic Tumors

Tumors of the thymus are classified into epithelial tumors including thymoma and thymic carcinoma, lymphomas including Hodgkin and non-Hodgkin lymphomas, Langerhans cell histiocytosis, thymolipoma, carcinoid tumor, germ cell tumors, sarcoma, and metastatic tumors. In adults, thymoma is the most frequent primary tumor of the thymus; lymphoma is the second most common, followed by germ cell neoplasm. In children, lymphoma is the most common primary tumor of the thymus; germ cell neoplasm is the second most common (32,33). Thymomas are rarely seen in children.

Thymoma.—Thymomas are benign or low-grade malignant tumors arising from the thymic epithelium and are characterized by the presence of a variable number of immature, nonneoplastic T cells (21).

Thymomas represent 20% of all mediastinal neoplasms in adults; they are the most common anterior mediastinal primary neoplasm in adults but account for less than 5% of mediastinal tumors in children (33). The peak prevalence of thymoma is during the fifth and sixth decades of life. Thymomas have no sex predilection. About one-half of thymomas are found in the upper and middle thirds of the mediastinum, and the remainder are found in the lower third (21).

Patients with thymoma are frequently asymptomatic; however, 20%–30% of patients have pressure-induced symptoms such as cough, chest pain, dyspnea, dysphagia, hoarseness, or superior vena cava syndrome. One-third to one-half of thymoma patients develop myasthenia gravis (21,24). Patients with thymoma may also develop pure red blood cell aplasia, hypogammaglobulinemia,

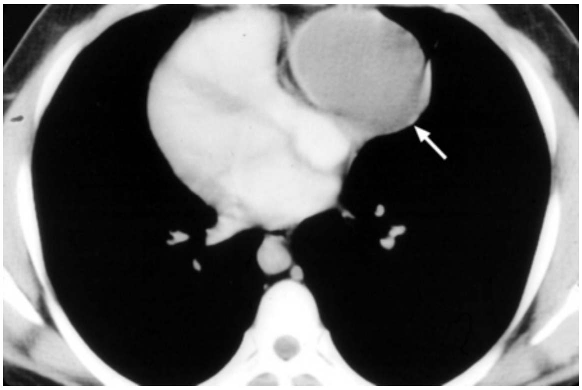


Figure 16. Thymoma in a 27-year-old woman. Contrast-enhanced CT scan obtained at the level of the left ventricle shows a solid enhancing thymic mass (arrow). Note the indentation of the left ventricle by the mass, an appearance unlike that of thymic rebound hyperplasia. The mass was proved to be a thymoma at biopsy.

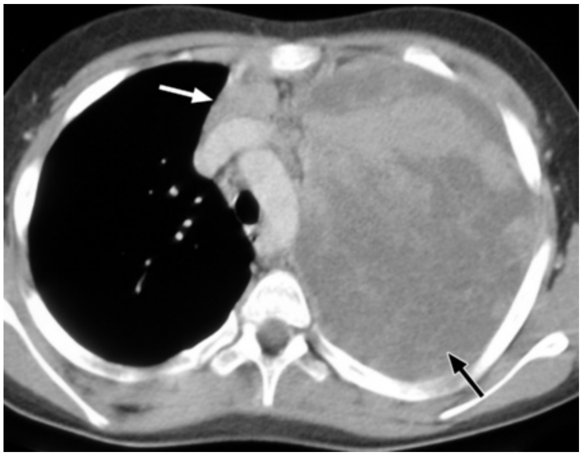


Figure 17. Invasive thymoma in a 13-year-old boy. Contrast-enhanced CT scan obtained at the level of the aortic arch shows a large heterogeneously enhancing solid tumor (black arrow), which arises from the thymus (white arrow) and grows along the pleura.

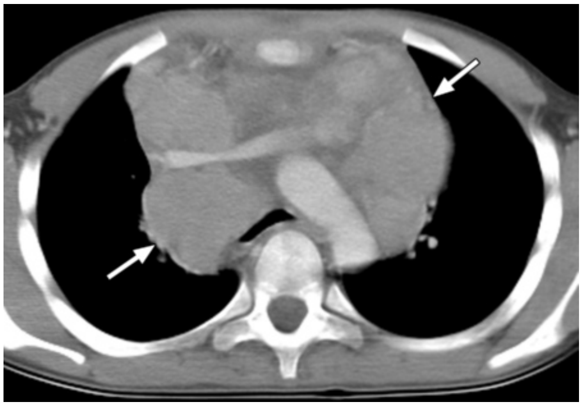


Figure 18. Thymic carcinoma (nasopharyngeal-like) in a 12-year-old boy with intermittent fever and shortness of breath. Contrast-enhanced CT scan obtained at the level of the aortic arch shows a large thymic mass with a nodular contour (arrows) encasing the innominate vein.

connective tissue disease, autoimmune disease, or inflammatory bowel disease (21,24).

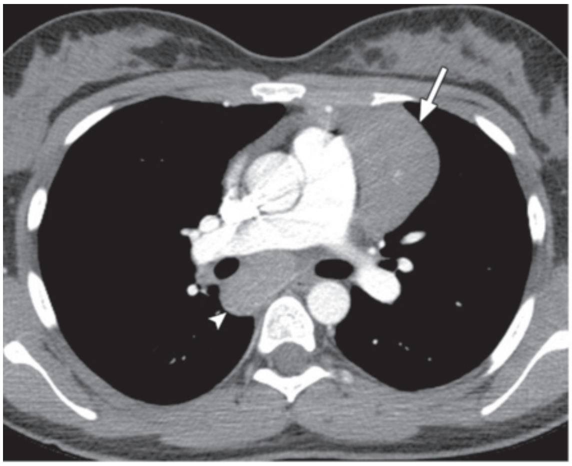
At radiography, thymomas typically appear as sharply marginated retrosternal areas of increased opacity with smooth or lobulated borders. Thymomas may project to either side of the mediastinum and obscure the heart border.

On CT scans, thymomas usually appear as homogeneous solid masses with soft-tissue attenuation and well-demarcated borders (Fig 16). Thymomas may be oval, round, or lobulated and usually do not conform to the shape of the thymus. Large thymomas may show areas of cystic or necrotic degeneration. Calcification may be present in the capsule or throughout the mass. Well-defined fat planes between the thymoma and adjacent structures generally indicate absence of extensive local invasion. However, minimal invasion may escape detection at imaging. Certain findings, such as encasement of mediastinal structures, infiltration of fat planes, and an irregular interface between the mass and lung parenchyma, are highly suggestive of invasion. Pleural thickening, nodularity, or effusion generally indicates pleural invasion by the thymoma (Fig 17).

At MR imaging, thymomas commonly appear as homogeneous or heterogeneous masses with low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. MR imaging can be used to help identify vascular invasion (24). Chemical shift MR imaging, which makes use of the difference in chemical shift ratio, can be valuable in differentiating thymic hyperplasia from thymomas and other thymic tumors (34).

Thymic Carcinoma.—Thymic carcinomas account for about 20% of thymic epithelial tumors. Thymic carcinomas behave more aggressively than invasive thymomas and are more likely to metastasize to distant sites. Although only about 5% of patients with invasive thymomas have distant metastases at diagnosis, 50%–65% of patients with thymic carcinomas have distant metastases at diagnosis (24). Unlike thymomas, in which neoplastic cells show morphologic and immunohistochemical features characteristic of thymic epithelial cells, the epithelial cells of thymic carcinomas show overt atypia (35). Also, thymic carcinomas usually lack a well-defined capsule, whereas up to two-thirds of thymomas are encapsulated.

Thymic carcinoma is uncommon in adults and even rarer among children. The mean age of patients with thymic carcinomas is 50 years (24). Thymic carcinomas freely invade adjacent structures and often cause compressive symptoms. Unlike



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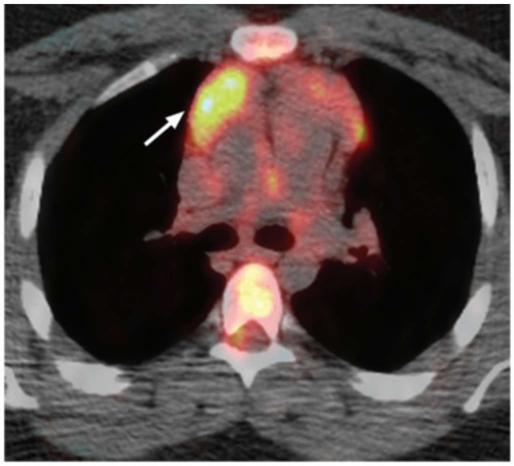

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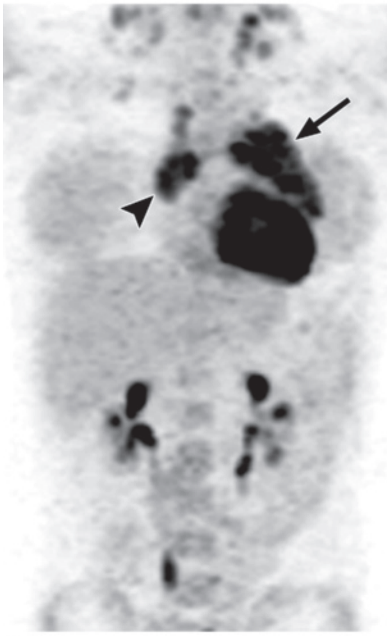

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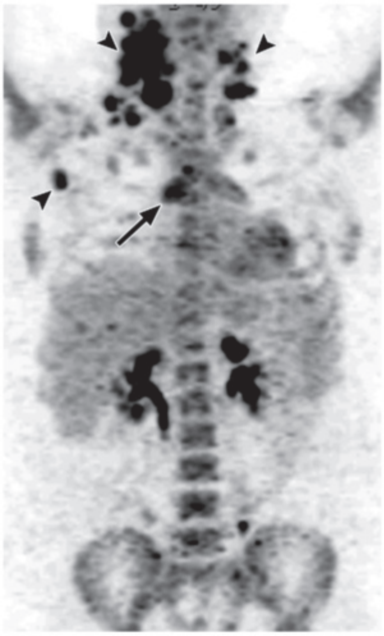

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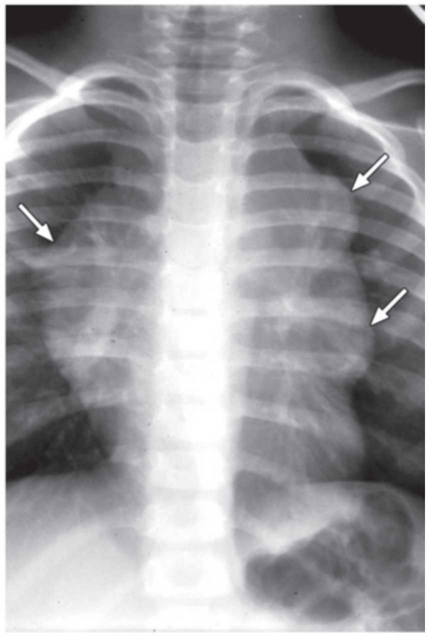


21.

Figures 19–21. **(19)** Concurrent thymic and lymph node involvement by Hodgkin lymphoma in a 51-year-old woman. **(a)** Contrast-enhanced CT scan shows involvement of the left lobe of the thymus (arrow) and subcarinal lymph nodes (arrowhead). **(b)** Coronal PET image shows asymmetric FDG avidity of the left thymic lobe (arrow) and subcarinal lymph nodes (arrowhead). **(20)** Thymic involvement by Hodgkin lymphoma in an 18-year-old man. Axial PET/CT **(a)** and coronal PET **(b)** images show cervical and axillary adenopathy (arrowheads in **b**) and asymmetric FDG uptake by the thymus (arrow). **(21)** Acute T-cell lymphoblastic leukemia of the thymus in a 4-year-old boy. Frontal chest radiograph shows a large thymic mass with nodular borders (arrows); the mass is not affected by the anterior second to fourth ribs. Compare this appearance with the wave sign of the normal thymus (Fig 6).

thymomas, thymic carcinomas rarely cause paraneoplastic syndromes such as myasthenia gravis.

On CT scans, thymic carcinomas typically appear as large, multilobulated masses (Fig 18) that may contain areas of low attenuation or calcification. It is difficult to distinguish thymic carcinomas from thymomas solely on the basis of imaging findings. Nevertheless, some features such as distant metastasis or mediastinal lymphadenopathy suggest thymic carcinoma. At MR imaging, thymic carcinomas show high signal intensity on both T1- and T2-weighted images. Hemorrhage or necrosis can cause heterogeneous signal intensity (24).

In general, before considering a diagnosis of thymic carcinoma, radiologists should consider more common possibilities such as metastatic carcinomas (12).

Lymphomas.—Involvement of the thymus by lymphomas (Figs 19, 20) and leukemias (Fig 21) usually occurs in the setting of widespread systemic disease, although isolated thymic involvement is not uncommon.

Lymphoma is the most common cause of an anterior mediastinal mass in children and the second most common cause of an anterior mediastinal mass in adults. The average age of a patient with mediastinal lymphoma is approximately 30 years.

Hodgkin lymphoma may manifest with isolated thymic involvement, isolated nodal involvement, or a combination of both (9,24). A review of the CT findings in 43 patients with newly diagnosed Hodgkin lymphoma revealed that 24 patients (56%) had thymic enlargement; six patients (14%) had isolated thymic involvement, whereas 18 (42%) had disease involving the thymus and mediastinal lymph nodes (36). In patients with Hodgkin lymphoma involving the thymus, the thymus is enlarged, sharply demarcated, and occasionally enclosed within a thick capsule (21). Thymic involvement is much less common in patients with non-Hodgkin lymphoma (24).

Differentiating primary thymic lymphomas from thymomas solely on the basis of imaging findings can be difficult. However, thymic lymphomas typically occur in a younger age group than do thymomas and tend to be more aggressive and more responsive to therapy (21).

Homogeneous enlargement of the thymus in the presence of mediastinal or hilar lymphadenopathy usually suggests lymphoma. Cystic changes in the thymus with or without calcification are seen at CT in about 20% of patients before they receive therapy (Figs 14, 15) (24,36).

At MR imaging, thymic lymphomas typically have low signal intensity on T1-weighted images and variable signal intensity on T2-weighted images (24). After completion of therapy, thymic lymphomas have diminished signal intensity on both T1- and T2-weighted images, presumably because of fibrosis, whereas recurrent lymphomas usually show persistent high signal intensity on T2-weighted images.

Differentiating recurrent lymphoma from thymic rebound hyperplasia with imaging can be challenging. In patients with thymic rebound hyperplasia, the thymic enlargement is usually symmetrical; the contour is smooth and nonlobulated and conforms to the shape of neighboring structures (ie, the anterior ribs and heart). In contrast, recurrent thymic lymphomas are generally asymmetric and nodular and show heterogeneous signal intensity on MR images (9). Also, it is imperative to interpret the imaging findings in the setting of clinical data. Unlike patients with relapsed lymphoma, patients with thymic rebound hyperplasia are usually asymptomatic.

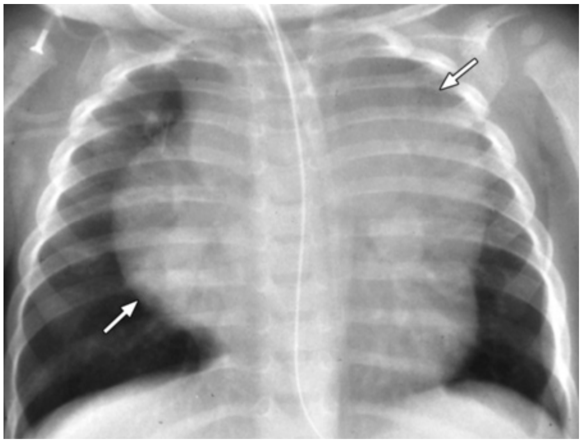
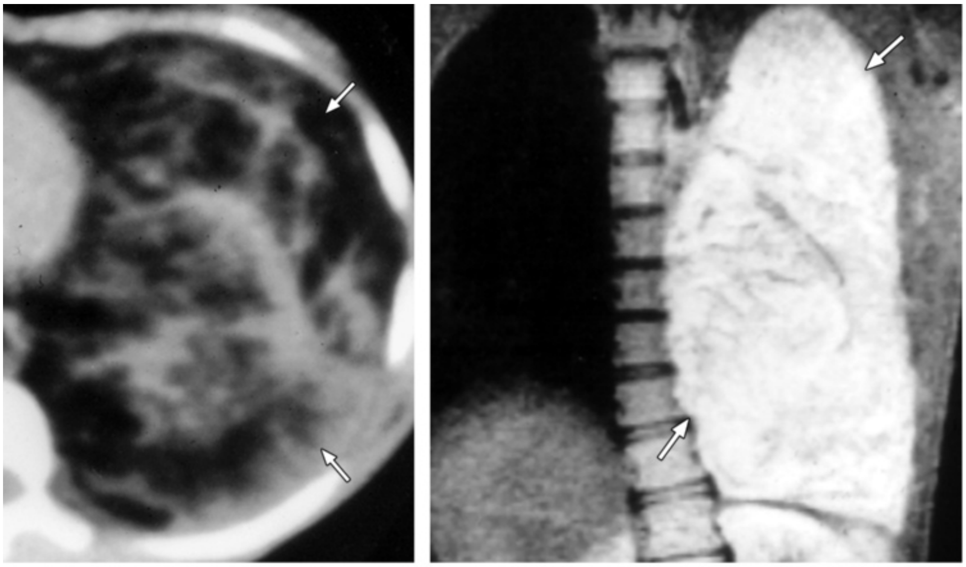


Figure 22. Thymic involvement in systemic Langerhans cell histiocytosis in a 5-month-old girl. Frontal chest radiograph obtained at diagnosis shows a large lobular mass (arrows), which is inseparable from the cardiac silhouette and is not affected by the anterior ribs. The mass completely resolved after chemotherapy but recurred in the thymus 11 months later. Shortly after initiation of chemotherapy, a large necrotic cavity developed with bilateral communicating gas-fluid levels. The patient was last seen in 2001 and was free of disease.

Teaching Point

Thymic and nodal disease in Hodgkin lymphoma resolves after appropriate therapy in the majority of patients. A residual area of soft-tissue density at imaging generally indicates fibrosis, while a new "mass" suggests rebound hyperplasia (37). If CT and MR imaging results fail to resolve the diagnostic dilemma, further evaluation with US can help distinguish hyperplasia from tumor (Fig 12).

Langerhans Cell Histiocytosis.—Langerhans cell histiocytosis frequently involves the thymus in the form of an anterior mediastinal mass and may be visible at imaging (Fig 22). In a study that used chest radiography and CT, seven of 14 patients with Langerhans cell histiocytosis had multisystem involvement, and five of those seven patients had thymic involvement (38). The thymus was enlarged in all five patients and showed cystic changes in four patients; it had a nodular or lobulated outline in two patients and multiple calcifications in one patient. These characteristics regressed or resolved in all patients after chemotherapy.



a. b.

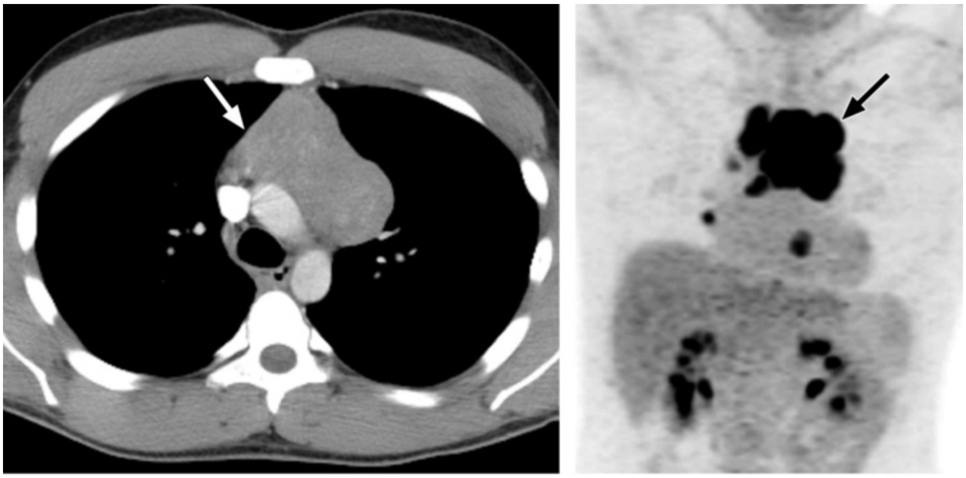
Figure 23. Thymolipoma in a 14-year-old girl with a 2-week history of cough and fever. **(a)** Contrast-enhanced CT scan shows a large, mostly fatty mass (arrows) in the left hemithorax. The mass causes minimal (if any) displacement of the heart. **(b)** Coronal T1-weighted MR image shows the mass (arrows), which has fibrous septa and replaces and assumes the shape of the collapsed lung. After resection of the mass, the left lung fully expanded.

Thymolipoma.—Thymolipomas are rare, benign, well-encapsulated thymic tumors that account for about 5% of thymic neoplasms. Thymolipomas can occur at any age (mean age, 21 years) and have no sex predilection (21). Patients with thymolipomas are usually asymptomatic but may present with compression-related symptoms. Thymolipomas are often large, with a mean diameter of 20 cm, and most weigh more than 500 g (21,24). Their pliability allows thymolipomas to conform to adjacent structures, extend to the cardiophrenic and costophrenic angles, or even occupy almost an entire hemithorax (Fig 23) (9,21,24). Although about 50% of thymolipomas cause mass effect, they do not invade neighboring structures (24).

Results of imaging studies are nearly diagnostic in thymolipomas. At conventional radiography, thymolipomas are usually less opaque than adjacent mediastinal structures. Thymolipomas may mimic cardiomegaly, excessive epicardial fat, diaphragmatic elevation, lobar collapse, or a pericardial cyst or effusion (9,21). At CT, thymolipomas predominantly show fat attenuation interspersed with fibrous septa and normal thymic tissue (Fig 23) (9,12,39). At MR imaging, thymolipomas show high signal intensity on T1- and T2-weighted images (Fig 23) along with strands of lower signal intensity, which indicate fibrous septa. CT and MR imaging should reveal a connection between the thymus and the tumor (9,24).

Thymic Carcinoid.—Thymic carcinoids are rare, well-differentiated neuroendocrine tumors (12). They occur over a wide age range (mean age, 43 years) and occur three times as frequently in men as in women (40,41). Patients with thymic carcinoids often present with endocrine disorders such as Cushing syndrome (25%–40% of patients) or multiple endocrine neoplasia types I and II (about 20% of patients) (24). Most thymic carcinoids are low-grade malignant tumors and tend to recur locally after resection. About 50% of thymic carcinoid tumors are invasive at the time of diagnosis (12,21,24).

Although thymic carcinoids lack fibrous compartmentalization and cystic changes (frequent findings in thymomas), they commonly exhibit irregular areas of necrosis or hemorrhage. Thymic carcinoids may also contain fine calcifications (10,21). Their appearance on radiographs and CT scans is nonspecific (Fig 24). Furthermore, a mediastinal mass may not be evident at CT,



a. b.

Figure 24. Thymic carcinoid tumor in a 22-year-old man with a 3-month history of a persistent dry cough. **(a)** Contrast-enhanced CT scan shows a heterogeneously enhancing thymic mass (arrow). **(b)** PET image shows intense FDG uptake by the mass (arrow). Note the nodular contour of the mass in both **a** and **b**; contrast that appearance with the homogeneous texture and smooth contour in cases of thymic rebound hyperplasia (Figs 10, 12).

even in the presence of endocrine abnormalities. Thymic carcinoids are more aggressive than thymomas and cause more superior vena cava obstruction (24).

Thymic Germ Cell Tumors.—Germ cell tumors usually arise along the midline, from the pineal region to the sacrococcygeal region. Both pure and mixed germ cell tumors can develop within or near the thymus. The anterior mediastinum is the most common site of extragonadal germ cell tumors (10,21). More than 80% of mediastinal germ cell tumors are benign, the most common being benign teratoma (24).

Germ cell tumors account for 1%–15% of mediastinal tumors in adults and about 25% of mediastinal tumors in children (12). Although benign germ cell tumors have no sex predilection, malignant germ cell tumors tend to occur in men, with a peak prevalence in the third decade of life (12,24).

Mature teratomas are frequently found incidentally at conventional radiography. Although most mature teratomas are asymptomatic, the larger ones may cause compressive symptoms and even erode through the tracheobronchial tree. In contrast, patients with malignant germ cell tumors are usually symptomatic (12,21).

Chest radiography of teratomas typically reveals large, round, lobulated masses. Since teratomas contain derivatives of all three germinal layers, the presence of teeth, bone, or calcification (seen in 20% of cases) is diagnostic (12,21,24). In patients with malignant germ cell tumors, pleural effusion may be present (21).

Figure 25. Teratoma of the thymus in a 27-year-old man. Coronal T1-weighted MR image shows a mediastinal mass (arrow) arising from the left lobe of the thymus (arrowhead). The mass was hyperintense on both T1- and T2-weighted images, a finding indicative of the fat content of a teratoma.

On CT images, teratomas typically appear as a combination of fluid or fat cysts, soft tissue, calcification, and bone or teeth (Fig 25). About 90% of mature teratomas contain fluid and about 75% contain fat. A fat-fluid level within the

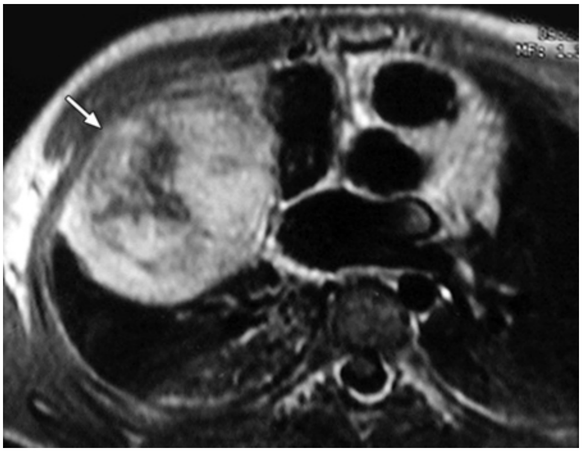


Figure 26. Thymic sarcoma in an asymptomatic 9-year-old girl. The tumor was serendipitously discovered with US. Axial contrast-enhanced nongated T1-weighted MR image shows a heterogeneously enhancing mass (arrow) that arises from the right lobe of the thymus, approaches the diaphragm, and indents the right atrium. After failure of chemotherapy, the tumor was surgically resected, but the patient eventually died of metastatic disease. (Reprinted, with permission, from reference 42.)

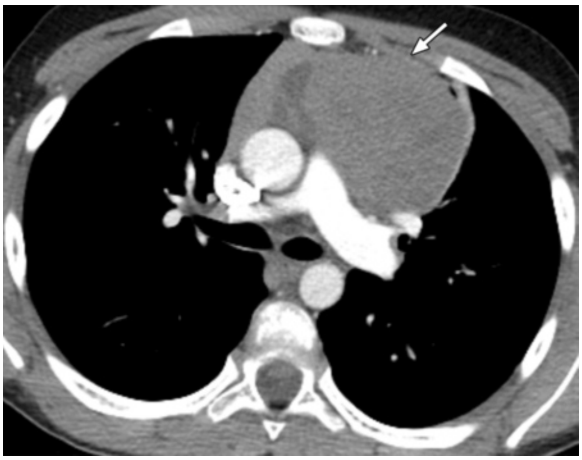


Figure 27. Metastatic disease to the thymus in a 10-year-old boy 2 years after diagnosis of alveolar rhabdomyosarcoma of the thigh. Contrast-enhanced CT scan shows a solid mass (arrow) that virtually replaces the thymus.

mass is diagnostic of teratoma but is seen in only about 10% of cases. Teratomas are usually clearly demarcated and surrounded by a capsule, which may show rim enhancement. Benign teratomas are typically smooth, clearly defined, and cystic; 90% of them contain fat. In contrast, malignant teratomas are nodular and poorly defined and have more solid components than do benign teratomas; only 40% of malignant teratomas contain fat. Compression of adjacent structures, a thick enhancing capsule, and areas of necrosis or hemorrhage are other features of malignant teratomas (21,24).

The appearance of teratomas on MR images depends on the various components of the lesion. Teratomas frequently contain fat, which has high signal intensity on T1-weighted images. Cystic areas in teratomas have low signal intensity on T1-weighted images and high signal intensity on T2-weighted images (24).

Thymic Sarcoma.—Sarcomas of the thymus are extremely rare, and imaging findings have been reported in only a few cases. Thymic sarcomas have a nonspecific appearance at cross-sectional imaging (Fig 26) and carry a grave outcome (42).

Secondary Tumors of the Thymus.—A wide range of primary tumors can involve the thymus. Lung carcinoma can invade the thymus by direct extension, while cancers of the head and neck, abdomen, and pelvis can involve the thymus via lymphatic pathways (Fig 27) (21).

Conclusions

Discovery of a mediastinal mass is usually alarming. Radiologists play a major role in differentiating normal variants, ectopic thymic tissue, and nonneoplastic conditions such as rebound hyperplasia from neoplastic conditions. A thorough knowledge of the embryology and anatomy of the thymus, normal variations and ectopic locations of the thymus, and its dynamic changes is essential to prevent performance of unnecessary invasive procedures.

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RadioGraphics

Clinical and Radiologic Review of the Normal and Abnormal Thymus: Pearls and Pitfalls

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Page 414
Ectopic thymic tissue may manifest as a neck mass, which can be mistaken for a pathologic process (7) (Fig 1).

Page 416
Given the variability in shape and size of the thymus, familiarity with the broad spectrum of imaging appearances of the normal thymus will help radiologists minimize the number of invasive procedures.

Page 417
The thymus is very pliable and does not cause compression or displacement of the adjacent structures. This finding can be a particularly important part of a real-time sonographic examination because cardiac pulsations and respiratory motions affect the shape of the thymus. In contrast, solid tumors or diffuse infiltrative processes are less malleable and more rigid.

Page 420
Thymic rebound hyperplasia typically shows diffuse enlargement, a fine mixture of fat and lymphoid tissue, a smooth contour, and normal vessels; in contrast, thymic neoplasia is usually associated with a nodular contour and frequently contains necrotic (Fig 13) or calcified foci (25).

Page 424
Thymic and nodal disease in Hodgkin lymphoma resolves after appropriate therapy in the majority of patients. A residual area of soft-tissue density at imaging generally indicates fibrosis, while a new “mass” suggests rebound hyperplasia (37).