

# Best Cases from the AFIP

## Thymoma<sup>1</sup>

**Editor's Note.**—Everyone who has taken the course in radiologic pathology at the Armed Forces Institute of Pathology (AFIP) remembers bringing two beautifully illustrated cases for accession to the Institute. In recent years, the staff of the Department of Radiologic Pathology has judged the "best cases" by organ system, and recognition is given to the winners on the last day of the class. With each issue of *RadioGraphics*, one of these cases is published, written by the winning resident. Radiologic-pathologic correlation is emphasized, and the causes of the imaging signs of various diseases are illustrated.

*Leopoldo Santana, MD • Amparo Givica, MD • Carmen Camacho, MD*

### History

A 26-year-old man presented to his general physician with long-standing thoracic pain. At the time of the chest discomfort, the patient smoked 20 cigarettes per day. The remaining family and medical history was unremarkable. Physical examination results and laboratory data were normal. An incidental lesion was found adjacent to the cardiac apex on a chest radiograph obtained as an initial test in our department. Further evaluation was required.

### Imaging Findings

Chest radiographs showed a large left anteroinferior mediastinal soft-tissue opacity with smoothly marginated borders against the adjacent lung (Fig 1). This lesion was attached to the cardiac apex, occupying the left cardiophrenic angle and simulating enlargement of the left ventricle in the frontal plane. Echocardiography showed a paracardiac cystic mass with good through transmission adjacent to the left ventricular wall. It did not communicate with the pericardium and contained a solid nodule along its wall (Fig 2). Findings at axial contrast material-enhanced computed tomography (CT) revealed a rounded, well-circumscribed mass measuring 9 × 8.5 cm. It was located in the left cardiophrenic angle and was attached to the left ventricle. The mass had a predominantly cystic component with several nodules of increased attenuation along its inner wall (Figs 3, 4). Calcification was not detected. In addition, remnant thymic tissue was observed in the anterosuperior mediastinum (Fig 5).

**Index terms:** Mediastinum, neoplasms, 67.3154, 67.3155 • Thymus, neoplasms, 67.3154, 67.3155

**RadioGraphics 2002;** 22:S95–S102

<sup>1</sup>From the Department of Radiology, Hospital Universitario Insular de Gran Canaria, Las Palmas de Gran Canaria, Spain. Received April 25, 2002; revision requested May 24 and received July 1; accepted July 9. **Address correspondence to** L.S., C/ Tomas Morales N° 97, 6° D, 35004 Las Palmas de Gran Canaria, Spain (e-mail: leosan43@hotmail.com).

©RSNA, 2002

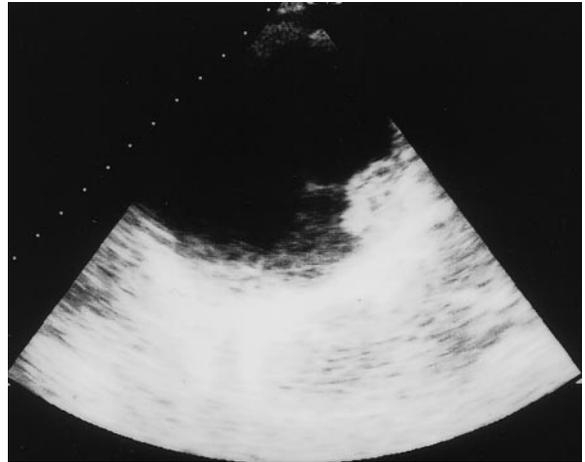


1a.

**Figures 1, 2.** (1a) Posteroanterior chest radiograph shows a well-defined soft-tissue mass with sharp and lobulated borders at the left cardiophrenic angle. It is attached to the left ventricle (silhouette sign), simulating left-sided cardiac enlargement. These findings are compatible with an extraparenchymal lesion. No calcifications or air-fluid levels are seen. (1b) Lateral chest radiograph shows that the soft-tissue mass is extraparenchymal and rounded and is located in the anteroinferior mediastinum (projecting over the cardiac silhouette). No infiltration of the adjacent structures is seen. (2) Echocardiogram shows that the mass is paracardiac and cystic. It has good through transmission, and a nodule is attached to the posterolateral wall.



1b.



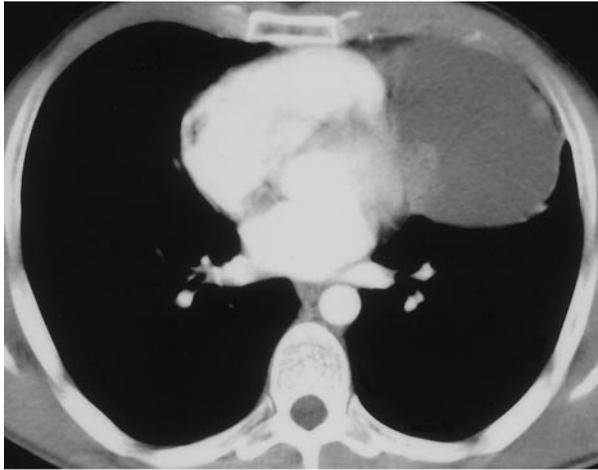
2.

### Pathologic Evaluation

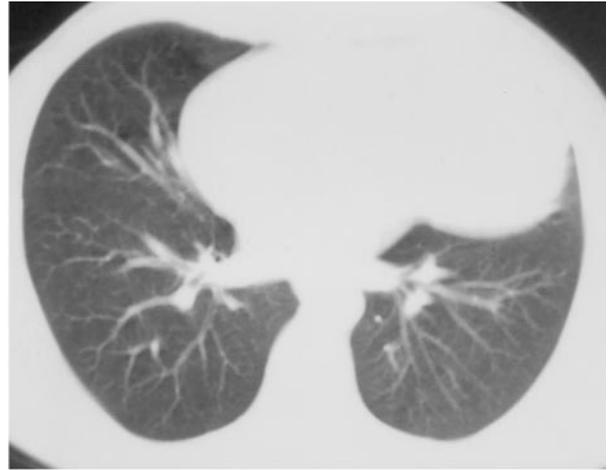
The patient underwent a video-assisted thoracic evaluation, which showed a 15-cm left-sided paracardiac cyst. The lesion seemed to be attached to the pericardium. Biopsy was performed, and the specimen was removed en bloc by median sternotomy 1 month later.

The tumor was oval with a smooth external surface. The size was 9 cm. The cut surface was grayish pink, and almost the entire tumor was cystic with irregular nodules on the inner surface (Fig 6). Histologic analysis of the resected specimen demonstrated a tumor completely encapsulated by a fibrous capsule with calcium deposits. It was composed of a mixture of epithelial cells in

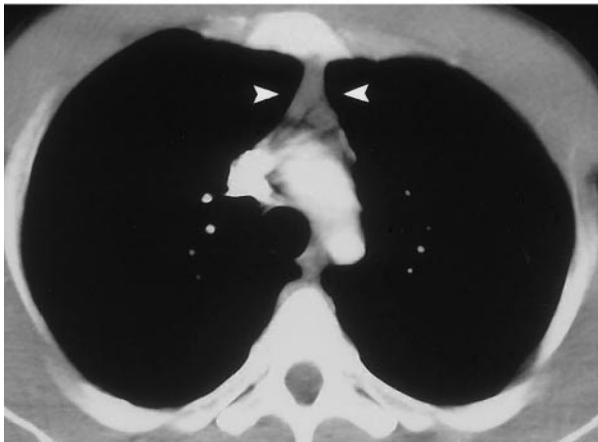
a diffuse lymphocytic background with perivascular spaces (Fig 7). The epithelial cells were large, with vesicular nuclei, small nucleoli, and indistinct cytoplasmic processes. Their epithelial nature was supported by positive cytokeratin immunostaining. The lymphocytes had an active appearance, increased size, and a recognizable chromatin pattern and demonstrated mitosis. On the basis of these histologic findings, the cystic mass was identified as a predominantly lymphocytic thymoma according to the traditional Bernatz classification or as a predominantly cortical thymoma according to the Müller-Hermelink classification.



3.



4.

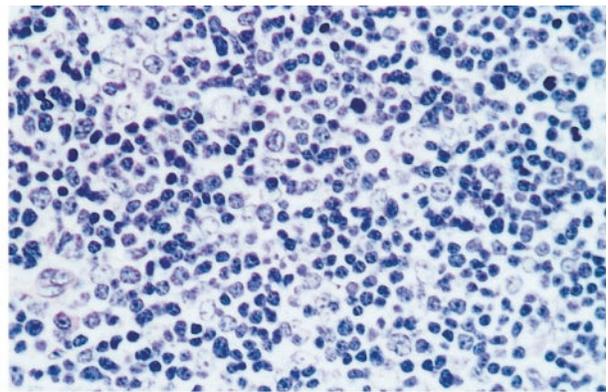


5.

**Figures 3–5.** (3) Contrast-enhanced CT scan shows that the mass is rounded and is located in the anterior-inferior mediastinum (left cardiophrenic angle); it measures  $9 \times 8.5$  cm. The lesion has a predominant cystic component with some peripheral nodular areas that enhance. The left ventricle and the adjacent mediastinal fat are not infiltrated. No peripheral or central calcifications are seen. (4) Contrast-enhanced CT scan shows that the lesion is well defined and compresses the normal pulmonary parenchyma. No infiltration is evident. (5) Contrast-enhanced CT scan shows a soft-tissue mass in the anterosuperior mediastinum (arrowheads), which corresponds to a thymic rest.



6.



7.

**Figures 6, 7.** (6) Photograph of the gross specimen shows the tumor encapsulated by a thick capsule. The inner surface is irregular with excrescences and nodules of tumorous tissue. (7) Photomicrograph (original magnification,  $\times 400$ ; hematoxylin-eosin stain) shows many active, large lymphocytes with a recognizable nuclear chromatin. There are also epithelial cells, which are polygonal with clear nuclei and small nucleoli.

## Discussion

Thymoma is a rare tumor entity. However, it is the most common neoplasm of the anterosuperior mediastinum and the most common primary tumor of the thymus. Seventy percent of thymomas are found in adults in the 5th and 6th decades of life, being rare in children and young adults. There is an approximately equal overall gender ratio. The majority of thymomas are found in the anterior mediastinum. Other locations may be the neck and posterior mediastinum. Most of them range from 5 to 10 cm in size.

The genetic basis of thymoma oncogenesis has been investigated in spontaneous, transgenic, and knock-out animal models. Genes that have been implicated are viral oncogenes (SV 40 large T), D-type cyclins, the cyclin-dependent kinase inhibitor p27, or other less well characterized genes defined by insertional mutagenesis. Only a few cases of aberrant karyotypes have been reported in the literature. These were either complex chromosome aberrations or single unique abnormalities like the translocations t(15;22) (p11;q11) and t(14;20)(q24;p13) or a ring chromosome 6 (1,2).

The histologic classification of thymic epithelial tumors and its relationship with prognosis still remains controversial. Several classifications, based on different pathologic criteria, have been proposed over the past 40 years. The oldest one was proposed by Bernatz et al (3). Thymomas were classified on the basis of the lymphocyte-to-epithelial cell ratio and the shape of epithelial cells into four subtypes: predominantly spindle cell (if more than two-thirds of the epithelial cells are fusiform), predominantly lymphocytic (if more than two-thirds of the cells are lymphocytes), predominantly mixed (if epithelial cells and lymphocytes are present in approximately equal numbers), and predominantly epithelial (if more than two-thirds of the cells are polygonal cells) (4,5). On the basis of this system, some studies have indicated that epithelial and mixed (lymphocytic-epithelial) thymomas are biologically more aggressive than lymphocytic and spindle cell neoplasms. In fact, spindle cell thymomas seem to carry the best prognosis with no tumor-related death; in contrast, lymphocytic and mixed thymomas seem to be associated with an intermediate

prognosis, whereas epithelial tumors seem to have a dismal prognosis (6). It has also been noted that myasthenia gravis and some other disorders are more likely to accompany epithelial and mixed lesions rather than spindle cell thymomas (5). However, many investigators consider that this histologic classification has failed to reveal the relationship between the pathologic types and the clinical behaviors (7,8). For this reason, some other classifications have been developed.

Marino and Müller-Hermelink (9) and Müller-Hermelink et al (10,11) proposed one of the most widely accepted classifications, based on histologic resemblance to the cortex or medulla of the normal thymus. According to that criterion, thymomas were classified into six categories (from well-differentiated to poorly differentiated tumors): medullary thymomas, mixed thymomas, predominantly cortical (organoid) thymomas, cortical thymomas, well-differentiated thymic carcinoma, and high-grade thymic carcinoma. Some trials revealed that medullary and mixed thymomas were benign tumors with no risk of recurrence, even when capsular invasion was present. Predominantly cortical and cortical thymomas showed intermediate invasiveness and a low, but significant, risk of late relapse, even with minimal invasion. Well-differentiated thymic carcinoma was always invasive and had a significantly increased risk of relapse and death, even for stage II patients (12). Compared with the previous results, this system would have prognostic significance, independent of tumor stage. Increased association with myasthenia gravis has also been reported with predominantly cortical thymomas, cortical thymomas, and well-differentiated thymic carcinoma (11). However, there have been criticisms of this classification because of the confusing nomenclature and the lack of consensus (13).

To produce universal agreement, in 1999 the International Committee of the World Health Organization established a new system based on the morphology of the epithelial cells as well as the lymphocyte-to-epithelial cell ratio. Six categories of thymomas divided into two subtypes were defined: unique thymic tumors (types A, AB, B1, B2, and B3) and malignant thymomas (type C) (4). In summary, the World Health Organization classification tries to reflect both the clinical and the functional features of thymic epithelial tumors (13).

On the other hand, correlation between histologic subtypes and radiographic appearance has not been demonstrated by any study and no histologic subtypes of thymoma seem to be more strongly associated with additional neoplasms (14).

Other authors believe that histologic categorization alone is insufficient to adequately predict biologic behavior and serve as a guide for therapy of patients with primary thymic epithelial neoplasms (15). In contrast, investigators have no doubts about the crucial role that the degree of invasion of surrounding tissues (staging) and the extent of the surgical procedure (complete or partial resection) play as prognostic factors. Finally, one study suggests that analysis of DNA may correlate the ploidy status with the invasiveness or stage of the tumor. Patients with diploid thymomas would have a significantly better prognosis than those with aneuploid types (16).

Twenty percent to 50% of thymomas are asymptomatic. The frequency of thoracic symptoms is related to compression or invasion of adjacent mediastinal structures. Compression of the trachea, recurrent laryngeal nerve, or esophagus may produce cough, dyspnea, chest pain, respiratory infection, hoarseness, or dysphagia. Invasion of the adjacent cardiovascular structures may produce superior vena cava syndrome. Rarely, sudden cardiac death, which is thought to be secondary to right atrial compression by the tumor, may occur (17).

Thymomas can also be related to associated autoimmune and paraneoplastic phenomena, such as pure red cell aplasia (50% of patients with red cell aplasia will have thymoma and 5% of patients with thymoma will have red cell aplasia), hypogammaglobulinemia (10% of patients with thymoma will have hypogammaglobulinemia and 5% of patients with hypogammaglobulinemia will have thymoma), endocrine disorders, cutaneous disorders, and connective tissue disorders. Evidence linking thymoma with other second malignancies (of the rectum, thyroid, breast, and lung) has been provided by the clinical literature (14). Distant metastases are uncommon at initial presentation. However, when present, the most metastatic site is the pleura, with involvement of the kidney, bone, liver, and brain infrequently seen (18).

There is a clear link between thymoma and myasthenia gravis. Myasthenia gravis is an

acquired disorder that is associated with an antibody-mediated autoimmune response against nicotinic acetylcholine receptors. This neurologic disorder is characterized by weakness and fatigability of skeletal muscles and may manifest clinically as generalized or ocular disease. Thymic abnormalities are found in approximately 90% of patients with myasthenia gravis. The most common associated thymic abnormality is follicular thymic hyperplasia, seen in approximately 65% of patients with myasthenia gravis (17). Thymoma is seen in approximately 10%–15% of patients with this disease (17). One-third of patients with thymoma have myasthenia gravis (17). These conditions are not necessarily synchronous. Myasthenia gravis may be diagnosed before or after discovery of a thymoma, or it may appear after surgery.

The most frequent radiographic appearance of thymoma is a soft-tissue mass in the anterior mediastinum, ranging from small to large and resulting in smoothly marginated, often lobulated borders against the adjacent lung. Possible locations are adjacent to the junction of the great vessels and the pericardium, less commonly the cardiophrenic angle or the adjacent cardiac border, and rarely the neck or other mediastinal compartments (17). On lateral projections, thymoma may be visible as a rounded soft-tissue opacity in the retrosternal clear space or in another anterior mediastinal location (17). Areas of calcification may be detected on plain radiographs (17,18). The pattern of calcification is commonly linear, thin, and peripheral, corresponding to calcium deposits in the tumor capsule (17). Invasive thymomas may demonstrate an irregular interface with the adjacent lung, suggesting invasion, but this may not always be seen on plain radiographs (17). Rarely, thymoma may manifest as predominantly pleural disease, which is usually unilateral and demonstrates nonspecific radiographic patterns such as pleural thickening, pleural masses, or diffuse, nodular, circumferential pleural thickening that encases the ipsilateral lung. In fact, the latter presentation may mimic the appearance of diffuse malignant mesothelioma or metastatic adenocarcinoma (17).

CT is the modality of choice because it is more sensitive than chest radiography in detection of small thymomas (25% of thymomas are not seen

on chest radiographs) (19) and also in demonstration of tumor infiltration of the surrounding mediastinal fat, vascular structures, and adjacent lung (invasive thymoma). Furthermore, CT is an excellent modality for evaluation of pleural and extrapleural seeding by the tumor. On CT scans, thymomas are generally seen as homogeneous, oval, rounded or lobulated soft-tissue masses. In most cases, the contour of the mass is smooth and well defined, and it usually grows asymmetrically to one side of the anterior mediastinum. The mass may be partially or completely outlined by fat or may completely replace the anterior mediastinal fat. However, the absence of fat planes between the mass and mediastinal structures does not necessarily denote invasion (17). Irregular borders between the mass and the adjacent lung suggest invasion (17). After intravenous administration of contrast material, the tumor enhances homogeneously; however, areas of decreased attenuation may be present and correspond to cystic changes or foci of hemorrhage and necrosis. Nodules may arise from the inner wall of a cystic thymoma (ultrasonography [US] is particularly useful in this case). Calcification, even if subtle, can be easily detected with CT (17).

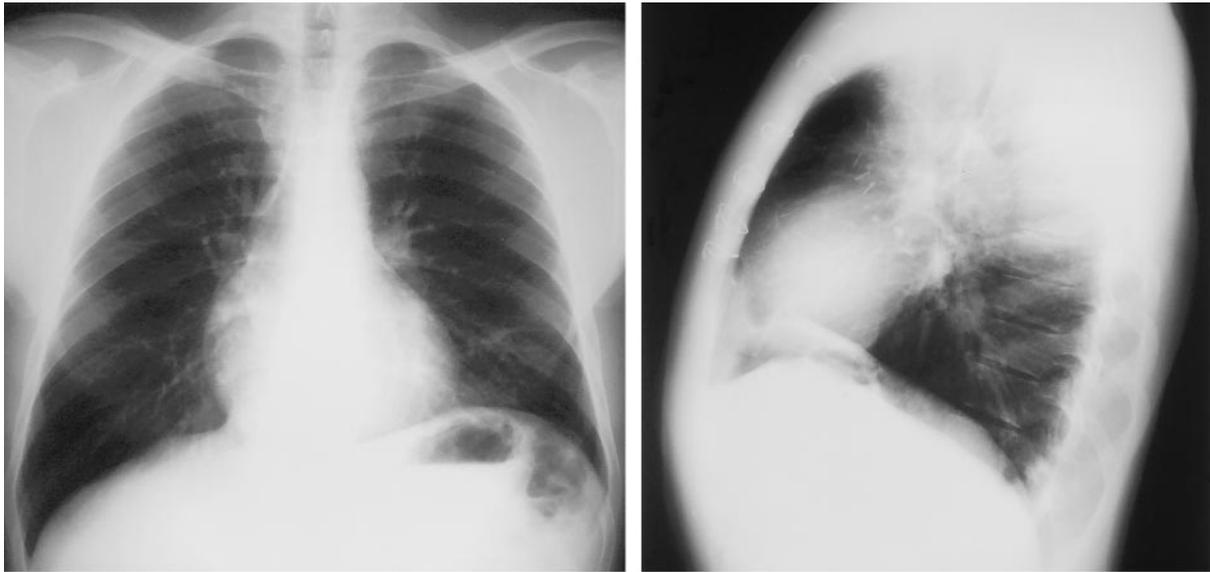
Chen and colleagues (20) demonstrated that CT has a sensitivity of 91% and a specificity of 97% for diagnosis of a thymic mass. The main difficulty for radiologists is to differentiate between hyperplasia and thymoma. Lymphoid follicular hyperplasia is a histologic diagnosis that generally does not produce growth of the thymic gland or may manifest as diffuse enlargement or a focal mass at CT (21), which does not permit radiographic differentiation from thymoma. This becomes more complicated because younger patients (<25 years of age) may have residual thymic tissue. However, thymomas are very infrequent in this group. With increasing age, the thymus undergoes fatty involution, which makes diagnosis of thymoma easier in patients over 40 years of age. Preoperative differentiation between thymoma and hyperplasia or between recurrent thymoma versus scar tissue can be facilitated by somatostatin receptor scintigraphy with the somatostatin analog indium-111 (DTP-D-Phe 1)-octreotide (22). Furthermore, thallium-201 scintigraphy allows distinction between normal thymus, lymphoid follicular hyperplasia, and thymoma in patients with myasthenia gravis. Normal thymus shows no increase in thallium uptake on either early or delayed images, whereas lymphoid follicular hyperplasia shows moderate thallium up-

take on only delayed images and thymoma shows significant (moderate to strong) thallium uptake on both early and delayed images (23). In addition, technetium-99m tetrofosmin planar and single photon emission CT images might be useful for detection of malignant thymoma by showing substantial activity in the primary tumor and metastatic lesions (24).

Magnetic resonance imaging does not add clinically important information to the results of CT in examination of the thymus (23). However, multiplanar imaging may be useful in cases in which the CT appearance is equivocal and is an excellent noninvasive method of evaluating possible vascular involvement by thymoma without the need for intravenous contrast medium (17, 25). Thymomas are isointense relative to skeletal muscle on T1-weighted images and have increased signal intensity (approaching that of fat) on T2-weighted images (17). Cystic areas are seen as low signal intensity on T1-weighted images and high signal intensity on T2-weighted images.

The differential diagnosis may include lymphoma (an ill-defined lobulated mass with associated regional or distant lymphadenopathy). Flow cytometry is useful in distinguishing lymphoma from thymoma (18), neuroendocrine tumors, lymphangioma and hemangioma (cystic lymphangiomas have cystic or solid areas), thymolipoma (CT shows dense fat with homogeneous areas without compression or invasion of adjacent structures), lymphoid follicular hyperplasia (most hyperplastic glands are usually normal in size and have the same signal intensity as normal glands), benign germ cell tumors (sharply defined masses with cystic areas and mixed areas of calcification and fat) (18), and nonseminomatous germ cell tumors (large poorly defined masses with zones of hemorrhage and necrosis) (18). The majority of these patients have elevated serum levels of tumor markers ( $\beta$ -human chorionic gonadotropin or  $\alpha$ -fetoprotein), which are diagnostic of these tumors. In our case, because the mass was located in the cardiophrenic angle, pericardial cyst was included in the list of differential diagnoses (this congenital malformation does not demonstrate solid nodules at CT or US and is more frequent on the right side).

Staging of thymoma is based on the presence or absence of an intact tumor capsule (17). The staging system proposed by Masaoka et al (26) has been widely adopted. Stage is an independent predictor of recurrence and long-term survival (18). The Masaoka system is postsurgical because invasion of the capsule is reliably diagnosed only



**a.** **b.**  
**Figure 8.** Frontal (**a**) and lateral (**b**) postoperative radiographs show complete resolution of the mass.

by pathologic examination (18). In this staging system, stage I thymomas do not demonstrate capsular invasion. Stage II lesions show microscopic invasion of the capsule, mediastinal fat, or surrounding pleura. Stage III tumors invade surrounding organs and structures such as the lung, pericardium, superior vena cava, and aorta. Stage IVa involves pleural or pericardial dissemination. Stage IVb involves lymphogenous or hematogenous metastases.

The method of choice for treating thymomas is complete surgical resection, which almost always consists of a median sternotomy (16). The surgical procedure may involve removal of the tumor itself or complete excision of the tumor and adjacent uninvolved thymus gland (17). Extended thymectomy (en bloc removal of the thymus and neighboring adipose tissues) has been used to prevent recurrences (thymoma seems to have multiple origins) (5,6) and in the treatment of myasthenia gravis with or without associated thymoma. Patients with myasthenia gravis should be in excellent physiologic condition before undergoing surgery (18). Some studies have reported that myasthenia gravis demonstrates a better response to thymectomy when lymphoid follicular hyperplasia rather than thymoma is found at microscopic examination (27).

In stage I (encapsulated thymomas), authors recommend complete removal alone (18) without radiation therapy or any other adjuvant treatment because local recurrence is exceptional after complete excision (6). After surgery, radiation therapy is recommended to reduce the risk of recurrences (27) in patients with invasive thymomas irrespective of surgical extent (complete or incomplete

excision); doses of 40–60 Gy are used. In stage II (invasive disease), radiation therapy should be strongly considered in all patients with completely resected thymomas when tumor extension beyond the capsule is documented at pathologic analysis (18). In stages III and IVa (locally advanced disease or unresectable disease), radical postoperative radiation therapy may control residual disease and provide long-term disease-free survival in a subset of patients after incomplete resections (18). Tc-99m sestamibi scintigraphy is an effective method of predicting the response after radiation therapy (28).

Patients with invasive thymomas who develop metastases and all patients with stage IV disease are potential candidates for chemotherapy (18). In these cases, some authors have suggested a multimodality approach consisting of induction chemotherapy, surgical resection, postoperative radiation therapy, and consolidation chemotherapy to attain a prolonged disease-free survival (29). This strategy may cure locally advanced unresectable malignant thymomas (29).

Chemotherapy in which cisplatin is the cornerstone has an overall response rate of 40%–90% (30). Other new therapeutic strategies such as nonradioactive somatostatin and somatostatin analogs have been used in malignant thymomas, particularly for some of those refractory to conventional adjuvant therapies. Both partial and complete remissions have been reported (4).

In our case, the patient underwent surgery, which resulted in complete removal of the mass (Fig 8). Neither postoperative radiation therapy

nor chemotherapy was necessary because the tumor was encapsulated (stage I). Two years after the surgery, the patient has not experienced recurrences or associated autoimmune disease.

**Acknowledgment:** We thank J. L. Afonso Martin, MD, for providing gross pathologic and histologic images.

## References

1. Nakajima H, Nakajima HO, Soonpaa MH. Heritable lympho-epithelial thymoma resulting from a transgene insertional mutation. *Oncogene* 2000; 19:32–38.
2. Sonobe H, Takeuchi T, Ohtsuki Y. A thymoma with clonal complex chromosome abnormalities (letter). *Cancer Genet Cytogenet* 1999; 110:72–74.
3. Bernatz PE, Harrison EG, Clagett OT. Thymoma: a clinicopathologic study. *J Thorac Cardiovasc Surg* 1961; 42:424–433.
4. Müller-Hermelink HK, Marx A. Thymoma. *Curr Opin Oncol* 2000; 12:426–433.
5. Walker A, Mills S, Fechner R. Thymomas and thymic carcinomas. *Semin Diagn Pathol* 1990; 7:250–265.
6. Gripp S, Hilgers K, Wurm R, Schmitt G. Thymoma: prognostic factors and treatment outcomes. *Cancer* 1998; 83:1495–1503.
7. Okumura M, Miyoshi S, Takeuchi Y, et al. Results of surgical treatment of thymoma with special reference to the involved organs. *J Thorac Cardiovasc Surg* 1999; 117:605–613.
8. Regnard JF, Magdeleinat P, Dromer C, et al. Prognostic factors and long-term results after thymoma resection: a series of 307 patients. *J Thorac Cardiovasc Surg* 1996; 112:376–384.
9. Marino M, Müller-Hermelink HK. Thymoma and thymic carcinoma: relation of thymoma epithelial cells to the cortical and medullary differentiation of the thymus. *Virchows Arch A Pathol Anat Histopathol* 1985; 407:119–149.
10. Müller-Hermelink HK, Marino M, Palestro G, et al. Immunohistologic evidences of cortical and medullary differentiation in thymoma. *Virchows Arch A Pathol Anat Histopathol* 1985; 408:143–161.
11. Müller-Hermelink HK, Marino M, Palestro G, et al. Pathology of thymic epithelial tumors. *Curr Top Pathol* 1986; 75:207–268.
12. Quintanilla-Martinez L, Wilkins EW Jr, Choi N, Efid J, Hug E, Harris NL. Thymoma: histologic subclassification is an independent prognostic factor. *Cancer* 1994; 74:606–617.
13. Okumura M, Miyoshi S, Fujii Y, Takeuchi Y, Shiono H. Clinical and functional significance of WHO classification on human thymic epithelial neoplasm: a study of 146 consecutive tumors. *Am J Surg Pathol* 2001; 25:103–110.
14. Welsh JS, Wilkins KB, Green R. Association between thymoma and second neoplasms. *JAMA* 2000; 283:1142–1143.
15. Suster S, Moran CA. Thymoma, atypical thymoma, and thymic carcinoma: a novel conceptual approach to the classification of thymic epithelial neoplasms. *Am J Clin Pathol* 1999; 111:826–833.
16. Gawrychowski J, Rokicki M, Gabriel A. Thymoma: the usefulness of some prognostic factors for diagnosis and surgical treatment. *Eur J Surg Oncol* 2000; 26:203–208.
17. Rosado-de-Christenson ML, Galobardes J, Morán CA. Thymoma: radiologic-pathologic correlation. *RadioGraphics* 1992; 12:151–168.
18. Thomas CR, Wright CD, Loehrer PJ. Thymoma: state of the art. *J Clin Oncol* 1999; 17:2280–2289.
19. Morgenthaler TI, Brown LR, Colby TV. Thymoma. *Mayo Clin Proc* 1993; 68:1110–1123.
20. Chen J, Weisbrod GL, Herman SJ. Computed tomography and pathologic correlations of thymic lesions. *J Thorac Imaging* 1988; 3:61–65.
21. Nicolaou S, Müller NL, Li D. Thymus in myasthenia gravis: comparison of CT and pathologic findings and clinical outcome after thymectomy. *Radiology* 1996; 201:471–474.
22. Marienhagen J, Schalke B, Aebert H. Somatostatin receptor scintigraphy in thymoma: imaging method and clinical application. *Pathol Res Pract* 1999; 195:575–581.
23. Higuchi T, Taki J, Kinuya S, et al. Thymic lesions in patients with myasthenia gravis: characterization with thallium 201 scintigraphy. *Radiology* 2001; 221:201–206.
24. Hashimoto T, Takahashi K, Goto M. Tc-99m tetrofosmin uptake of malignant thymoma in primary tumor and metastatic lesions. *Clin Nucl Med* 2001; 26:562–564.
25. Naidich JB, Zerhouni EA. Computed tomography and magnetic resonance of the thorax. New York, NY: Raven, 1991.
26. Masaoka A, Monden Y, Nakahara K. Follow-up study of thymomas with special reference to their clinical stages. *Cancer* 1981; 48:2485–2492.
27. Budde JM, Cullen DM, Anthony AG, Mansour KA, Miller JI Jr. Predictors of outcome in thymectomy for myasthenia gravis. *Ann Thorac Surg* 2001; 72:197–202.
28. Koukouraki S, Prassopoulos P, Koukourakis M, Velidaki A, Karkavitsas N. Tc-99m sestamibi scintigraphy: an effective method to predict the response of thymoma after radiotherapy. *Clin Nucl Med* 2000; 25:727–728.
29. Shin DM, Walsh GL. A multidisciplinary approach to therapy for unresectable malignant thymoma. *Ann Intern Med* 1998; 129:100–104.
30. Hejna M, Haberal I, Raderer M. Nonsurgical management of malignant thymoma. *Cancer* 1999; 85:1871–1884.