Thymomas in Childhood: 11 Cases From a Single Institution

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Aim: Thymomas are rare in children. Our aim was to review clinical and pathologic characteristics and outcome in children with thymomas.

Patients and Methods: Between 1979 and 2011, 11 children with thymomas were diagnosed. Hospital files were reviewed for presenting complaints, clinical, radiologic, and other laboratory data, surgical practices, chemotherapy and radiotherapy outcomes.

Results: Median age was 8 years (range, 1 to 13 y). Male to female ratio was 9/2. Most common initial complaints were dyspnea, cough, chest pain, and fever. Median time from onset of symptoms was 1 month (range, 0.23 to 3 mo). Associated conditions including hyper-IgE syndrome, hypogammaglobulinemia, and systemic lupus erythematosus plus idiopathic thrombocytopenic purpura were present in 3 patients. Chest x-rays and/or thoracic computed tomographies displayed thymic hyperplasia and/or masses in anterior mediastinum accompanied by pleural (n = 2) and pericardial effusions (n = 1), pulmonary metastases (n = 1), and cervical lymph node metastasis (n = 1). Compression or invasion of trachea or vessels was documented in 5 cases. Seven cases underwent initial tumor resection; others experienced open or trucut biopsies. Histopathologically, 5 cases had invasive and 6 had benign thymomas. Benign thymomas did not receive any postoperative treatment; all cases are disease free at a median follow-up of 211 months. Three of 5 cases with invasive thymomas underwent surgery, 4/5 received chemotherapy and external radiotherapy (3600 to 4500 cGy). Two invasive thymomas died of disease. Three cases with invasive thymomas are disease free at a median follow-up of 209 months.

Conclusions: Benign thymomas have excellent prognosis. For invasive thymomas with or without metastasis, radiotherapy, and chemotherapy offers survival advantage. Complete surgical resection may increase chances for cure.

Key Words: thymoma, children, invasive, malignant

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Lymphomas, carcinoid tumors, and germ cell tumors may arise within the thymus; however, only thymomas and thymic carcinomas originate from thymic epithelial components. Thymic neoplasms constitute about 15% of anterior mediastinal masses in children with thymomas being the most common one.[1] Thymoma is a rare tumor stemming from epithelial cells of the thymus.[2,3] It mostly presents in fourth and fifth decades of life,[4] and $<10\%$ of thymomas are diagnosed in patients younger than 20 years of age.[4]

Benign thymomas are mostly asymptomatic in childhood,[5] but malignant thymomas are highly aggressive and they present with dyspnea, cough, superior vena cava syndrome, or other symptoms due to compression/invasion of adjacent vital organs.[6] Patients can present with paraneoplastic syndromes including myasthenia gravis, pure red cell aplasia, systemic lupus erythematosus (SLE), hypertrophic pulmonary osteoarthropathy, hypo/hypergammaglobulinemia, or cellular immunodeficiency.[5,7–17] Chest computed tomography (CT) is the suggested imaging method and it provides information about location, size, contour, and extent of tumor involvement.[4,15,16] Magnetic resonance imaging gives little information beyond obtained with CT.[4,15,16]

Different histopathologic subtypes are defined in the literature.[17–19] Distant metastasis and/or local invasion to surrounding structures suggest malignant potential of thymoma,[5,15,20,21] and these characteristics are well correlated with the World Health Organization (WHO) classification.[16] Surgery is the main treatment approach for stage I thymoma.[18] However, stage II and III thymomas may require chemotherapy and/or radiotherapy in addition to surgery.[18,19,22] There is limited number of patients with thymomas reported in the literature. We aimed to investigate clinical characteristics, treatment results, and outcomes of patients with thymoma.

MATERIALS AND METHODS

We performed a retrospective review of the medical records of 11 children with thymomas who were treated at our institution between 1979 and 2011. All patient files were reviewed for demographic data, signs and symptoms, physical examination findings, diagnostic procedures, tumor characteristics, treatment, and outcome.

Survival and follow-up times were reported in the Table 1. The patients were followed regularly after completion of treatment at intervals depending on their disease characteristics. The patients were seen every 1 to 2 years for long-term follow-up.

RESULTS

Diagnosis of thymoma was established in 11 of 7500 (0.15%) children with cancer at our department between 1979 and 2011. It constituted 10% of all mediastinal tumors, following neuroblastic and germ cell tumors, when lymphomas were excluded. The median age of all was 8 years (range, 1 to 13 y). Of these patients, 9/11 were males (Table 1). The median time between the onset of symptoms and diagnosis was 1 month (range, 0.23 to 3 mo). The

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TABLE 1. Clinical Characteristics, Treatments, and Outcomes of 11 Children With Thymomas

	Age (year)/ Sex	Accompanying Disease	Type	Chest X-ray	CT	Metastasis	Surgery	Chemotherapy	Radiotherapy	Outcome/ Follow-up Time (mo)
1	5/M	—	Benign	Widened mediastinum	Thymic hyperplasia	–	+	–	–	Alive/166
2	12.5/M	SLE, ITP	Benign	Anterior mediastinal mass	Anterior mediastinal mass with cystic components	–	+	–	–	Alive/169
3	5/M	—	Benign	Widened mediastinum	Anterior mediastinal mass, pulsion of the trachea and the great vessels	–	+	–	–	Alive/163
4	11/F	—	Benign	Pericardial effusion	Anterior mediastinal mass	–	+	–	–	Alive/253
5	8/F	—	Benign	Anterior mediastinal mass	—	–	+	–	–	Alive/367
6	5/M	—	Benign	Anterior mediastinal lobulated mass	—	–	+	–	–	Alive/279
7	4/M	Facial paralysis	Invasive	Anterior mediastinal mass	—	Lymph node	+	COP	Mantle 4000 cGy	DOD/8
8	13/M	Hypogammaglobulinemia	Invasive	Widened mediastinum	Anterior mediastinal mass, bilateral pleural effusion	–	–	COP	3600 cGy	Alive/40
9	13/M	—	Invasive	Widened mediastinum	Anterior mediastinal mass, compression to the trachea	–	+	COP + adriamycine (neoadjuvant)	4500 cGy* (neoadjuvant)	Alive/217
10	12/M	—	Invasive	Diffuse consolidation of the left lung	Anterior mediastinal mass, pericardial effusion, compression on the left main bronchus	Lung	+	COP + adriamycine (neoadjuvant)	4500 cGy† (neoadjuvant)	Alive/209
11	1/M	Hyper IgE syndrome	Invasive	Diffuse consolidation of the left lung	Anterior mediastinal mass, compression on the great vessels	–	–	—	—	DOD/0.8

*Anterior mediastinum and supraclavicular fossa.
†Anterior mediastinum.
COP indicates cyclophosphamide, vincristine, prednisolone; CT, computed tomography; DOD, died of disease; F, female; ITP, idiopathic thrombocytopenic pupura; M, male; SLE, systemic lupus erythematosus.

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median period of follow-up was 209 months (range, 40 to 367 mo).

The most common symptoms at diagnosis were dyspnea (55%), cough (45%), fever (36%), and chest pain (27%). Physical findings at diagnosis were related with respiratory system in 6 patients. One patient had SLE. Accompanying disorders were hyper-IgE syndrome (n = 1), hypogammaglobulinemia (n = 1), and SLE plus idiopathic thrombocytopenic purpura (ITP, n = 1) (Table 1).

Bone marrow aspiration was performed to all but one patients. There was no lymphoblastic or other atypical cellular infiltration. Chest x-ray was done for all patients. It showed mediastinal widening (n = 4), anterior mediastinal mass (n = 4), pericardial effusion (n = 1), and diffuse consolidation of the lung (n = 2). Chest CT was performed in 8 patients, and it showed thymic hyperplasia and/or homogenous masses (n = 4) with cystic changes (n = 1), and compression of the trachea and the great vessels (n = 1) in the group of benign thymomas. However, there were tracheal and/or main bronchial, and great vessel compression (n = 3), pericardial (n = 1), or pleural effusion (n = 1), lung (n = 1) and lymph node metastasis (n = 1) in addition to anterior mediastinal mass (n = 4) in the group of invasive thymomas (Table 1).

Surgical resection was performed in patients with benign thymomas only. However, invasive thymomas defined according to clinical and radiologic findings were treated with different combinations of surgery, chemotherapy, and/or radiotherapy (Table 1). Primary or delayed surgery was performed to 3 invasive thymomas (Table 1). Patients with invasive thymomas were treated with different chemotherapy regimens including COP (cyclophosphamide, vincristine, and prednisolone; n = 2) and COP + adriamycin (n = 2). External radiotherapy was applied to 4 patients with a median dose of 4250 cGy (range, 3600 to 4500 cGy). Histopathologic diagnoses were reported as benign thymoma in 6 (55%), and invasive thymoma in 5 (45%) patients. Demographic and clinical characteristics of the patients are presented in the Table 1.

All benign thymoma cases were alive and under follow-up without disease at a median survival of 211 months (range, 163 to 367 mo). Two of 5 invasive thymoma cases died of disease. The other 3 cases were alive and under follow-up without disease at a median survival of 209 months (range, 40 to 217 mo). A 1-year-old infant (11th case) died due to intrathoracic effects including compression on great vessels and diffuse consolidation of the lung parenchyma leading to the hemodynamic instability 1 month after initial diagnosis without any antineoplastic treatment. A 4-year-old boy (seventh case) underwent initial surgery and received chemotherapy and radiotherapy, but died after recurrence in the cervical lymph nodes at 8 months due to progressive disease. Two cases (ninth, 10th, Table 1) who underwent surgery after receiving chemotherapy + radiotherapy are disease free at 209 and 217 months, respectively. A 13-year-old boy is in remission at 40th month after chemotherapy and radiotherapy and no surgery. Details of the treatment modalities are presented in the Table 1.

DISCUSSION

Thymoma is rare in childhood, with approximately 40 cases reported in the literature to the best of our knowledge.[23–31] Only 11 (0.15%) of almost 7500 childhood tumors diagnosed at our center over 3 decades were thymomas. During the same period, 110 tumor cases[32] originating from the mediastinum were diagnosed at our center, excluding lymphomas, and thymomas ranked third after neurogenic and germ cell tumors with an incidence of 10%. Takeda et al[29] investigated tumor cases originating from mediastinum in children and adults, and reported only 5 thymoma cases in children. Similar to our study, this study also found that thymomas ranked third in frequency after neurogenic and germ cell tumors, with lymphomas excluded. In contrast, Temes et al[3] reported that they did not discover any thymoma cases in children for 22 years.

Thymomas are mostly seen during the fourth and fifth decades of life and no differences have been reported between sexes.[4] No known peak incidence ages have been reported due to low number of cases reported in the literature. However, in our study, the median age was 8 years, with 9 cases (82%) aged 5 years and over. The literature holds rare reports of thymomas in infants, and only 11-month-old,[33] 12-month-old,[34] and 15-month-old[23] cases have been reported. There was only one 12-month-old case in our study. One other significant finding of our study was that 9 of 11 cases (82%) were males. This male predominance needs explanation with further experience.

All cases in our study were symptomatic, most frequently showing dyspnea, cough, and chest pain depending on the development of local mass effects. As a systemic finding, 4 cases had fever. The frequency and severity of complaints during admission were not directly correlated with the presence or absence of invasiveness. The most probable reason for this might be that while noninvasive thymomas cause symptoms through repression due to the structure of the thoracic cage, invasive thymomas cause symptoms by infiltrating adjacent structures. Although most of the thymomas have been reported to be asymptomatic in the literature,[5] all cases in our study were symptomatic. This may more likely be associated with disease characteristics rather than the late admission of patients to our clinic, considering the relatively short median lag time.

Many immune deficiencies and autoimmune diseases may paraneoplastically present with thymomas.[23,33,35] Myasthenia gravis may present with 30% of thymomas in adulthood, whereas it is reported to be < 5% in children.[5,33] Other reported paraneoplastic diseases include pure red cell aplasia, panhypopituitarism, rheumatoid arthritis, Addison disease, dermatomyositis, pemphigus vulgaris, acquired hypogammaglobulinemia, hypertrophic osteoarthropathy, and scleroderma.[5,12,34] Three cases had coexisting diseases in our study and these were hyper-IgE syndrome, hypogammaglobulinemia, and SLE plus ITP. SLE and hypogammaglobulinemia have been reported relatively more frequently in the literature, with no reports of SLE and ITP in the same patient.[7,8] Moreover, information for any association between the hyper Ig-E syndrome and thymoma were not available in the literature.[36] The pathophysiology of immune deficiency and paraneoplastic autoimmune diseases in thymomas remain unknown but there are reports commenting that they may be associated with T and B-cell dysregulation.[8,9] Considering that the main task of the thymus gland is T-cell maturation, occurrence of immune dysfunctions in case of thymoma development is no surprise. However, the pathophysiology of immune dysfunctions remains unclear.

Thymomas are described as malignant or invasive according to microscopic and/or macroscopic local invasion or

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presence of distant metastasis.[31] Although many systems are used in thymoma staging and prognosis evaluation, the WHO histologic classification,[1] the Masaoka staging system,[5] and the TNM classification[2] are the most frequently used. The parameters used in these stagings are histopathologic features of tumor cells, capsule invasion status, adjacent pleura and/or pericardial invasion, organ metastasis, presence of distant metastasis, and surgical resectability.[1,2,27] Both the WHO classification system and the Masaoka staging are postoperative staging systems and preoperative staging is needed to ensure an optimal treatment approach at the clinical setting.[1,2] It is known that WHO type A-B2 tumors and Masaoka stage I-II are more locoregional.[1] As Masaoka stages III and IV exhibit macroscopic invasion of the adjacent organs, pleura, pericardium, and hematogenous and/or lymphatic distant metastasis, these stages can also be clinically evaluated.[1,2,23] In this way, invasion in the trachea, main bronchi, major vessels, pericardium, pleura, and the lungs was diagnosed by chest CT in histopathologically malignant cases in our study. In 1 benign case, there was compression instead of invasion in the trachea and major vessels. There were cystic components in the mass in another case. Therefore, CT findings are very important in cases considered to have thymoma, and one may think of a higher probability of malignancy in the presence of invasion and/or distant metastasis. Irregular mass margins, invasion of mediastinal structures, and/or concurrent pleural invasion have been reported to be the potential indicators of malignancy in the literature.[23] In contrast, the presence of cystic changes in CT was reported to indicate benign thymoma, similar to one of our cases.[28]

Metastatic disease is rare in thymoma and is most frequently seen in the pleura.[5] Distant metastases are quite rare and were found only in 2 cases in our study, namely lung and lymph node metastasis.

Surgery, chemotherapy, and/or radiotherapy are used to treat thymomas. The main treatment in the Masaoka stage I and II cases is surgery and survival is almost 100% in totally resected cases.[5] In our study, all Masaoka stage I and II cases showing no clinical or radiologic invasive features survived, and in addition, none of these cases experienced relapses.

Although the Masaoka staging is the most important prognostic factor in survival, its contribution to optimal treatment planning in a clinical setting is debatable since it is a postsurgical staging system. At our center, surgical resection is preferred after neoadjuvant chemotherapy and/or radiotherapy in cases with invasion to adjacent organs, regional or distant metastasis, and a high possibility of surgical complications. Using this approach, 2 cases were fully cured with surgery after chemotherapy and radiotherapy, and 1 case required no surgery. Timing of surgery should be planned with consideration to the sensitivity of invasive thymomas to radiotherapy[2,5] and chemotherapy.[24,37–40]

Because of the lack of experience with this rare tumor in children, the contribution of radiotherapy to survival and the optimal chemotherapy protocols are not yet clear. Considering that half of childhood thymoma cases reported in the literature are malignant,[23–31] radiotherapy and chemotherapy seem to be vital. In adult patients, although the use of radiotherapy is arguable in totally resected stage II cases, radiotherapy is recommended in more advanced stages.[1,40] In our study, radiotherapy was given to cases who had invasive tumors with positive surgical margins.

It has been well known for some time that thymomas are sensitive to chemotherapy.[1,24,37,38,40,41] Although thymomas are sensitive to many chemotherapy drugs, platinum-based protocols have been reported to be effective in adult studies.[2,5,17,40,41] Loehrer et al[38] reported that combined chemotherapy with cisplatin, doxorubicin, and cyclophosphamide might be effective in adult cases with metastatic and recurrent thymomas. They also reported that this chemotherapy protocol might be effective for limited-stage unresectable thymomas[37] combined with external radiotherapy. It is also reported that platinum-containing regimens are effective in adult patients with recurrent thymomas.[2,5,17,38,41–43] No effective combined chemotherapy regimen is established in childhood cases; however, there are several published case reports in the literature.[24,31,39] In our study, the common drugs used in the chemotherapy protocols were vincristine, cyclophosphamide, and prednisolone similar to lymphomas, with 2 cases received adriamycin. These chemotherapy regimens could be applied due to their high tolerability and no long-term side effects. However, administration of adriamycin must be carefully carried out with respect to cardiotoxicity if there is an indication of mediastinal radiotherapy.

Two invasive thymoma cases died in our study. One case died after lymph node metastasis, and another case died in several days due to extensive locoregional disease without receiving any treatment. Similar cases who died due to rapid mass progression of the disease have been reported in the literature.[30] Urgent diagnosis is critical because of the proximity of the tumor to vital organs. Since the patient was an infant having a low intrathoracic volume, we believe this could explain the rapid deterioration.

In conclusion, thymomas are rare during childhood, and benign thymomas have excellent prognosis. Complete surgical resection increases the chances of cure. For invasive thymomas with or without metastasis, radiotherapy and/or chemotherapy in addition to surgical resection offer the chance of survival. The optimum chemotherapy regimen is not yet clear in children, and multicentered studies are needed in this field.

REFERENCES

1. Gielda BT, Peng R, Coleman JL, et al. Treatment of early stage thymic tumors: surgery and radiation therapy. *Curr Treat Options Oncol*. 2008;9:259–268.
2. Kondo K. Optimal therapy for thymoma. *J Med Invest*. 2008; 55:17–28.
3. Temes R, Allen N, Chavez T, et al. Primary mediastinal malignancies in children: report of 22 patients and comparison to 197 adults. *Oncologist*. 2000;5:179–184.
4. Pappo AS, Rodriguez-Galindo C, Furman WL. Management of infrequent cancers of childhood. In: Pizzo PA, Poplack DG, eds. *Principles and Practice of Pediatric Oncology*. 6th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins Health; 2011:1103–1104.
5. Dhall G, Ginsburg HB, Bodenstein L, et al. Thymoma in children: report of two cases and review of literature. *J Pediatr Hematol Oncol*. 2004;26:681–685.
6. Spigland N, Di Lorenzo M, Youssef S, et al. Malignant thymoma in children: a 20-year review. *J Pediatr Surg*. 1990; 25:1143–1146.
7. Taheri D, Suzangar HR, Sherkat R, et al. Thymoma associated with hypergammaglobulinemia: a case report. *Iranian J Pathol*. 2009;4:44–47.

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8. Sicherer SH, Cabana MD, Perlman EJ, et al. Thymoma and cellular immune deficiency in an adolescent. *Pediatr Allergy Immunol*. 1998;9:49–52.
9. Agarwal S, Cunningham-Rundles C. Thymoma and immunodeficiency (Good syndrome): a report of 2 unusual cases and review of the literature. *Ann Allergy Asthma Immunol*. 2007; 98:185–190.
10. Aghaji MA, Uzuegbunam C. Invasive thymoma and myasthenia gravis in a three-and-a-half-year-old boy: case report and literature review. *Cent Afr J Med*. 1990;36:263–266.
11. Furman WL, Buckley PJ, Green AA, et al. Thymoma and myasthenia gravis in a 4-year-old child. Case report and review of the literature. *Cancer*. 1985;56:2703–2706.
12. Gharbi A, Benjelloun A, Ouzidane L, et al. Hypertrophic osteoarthropathy associated with malignant thymoma in a child. *J Radiol*. 1997;78:303–304.
13. Di Cataldo A, Villari L, Milone P, et al. Thymic carcinoma, systemic lupus erythematosus, and hypertrophic pulmonary osteoarthropathy in an 11-year-old boy: a novel association. *Pediatr Hematol Oncol*. 2000;17:701–706.
14. Evoli A. Acquired myasthenia gravis in childhood. *Curr Opin Neurol*. 2010;23:536–540.
15. Tomiyama N, Müller NL, Ellis SJ, et al. Invasive and noninvasive thymoma: distinctive CT features. *J Comput Assist Tomogr*. 2001;25:388–393.
16. Inoue A, Tomiyama N, Fujimoto K, et al. MR imaging of thymic epithelial tumors: correlation with World Health Organization classification. *Radiat Med*. 2006;24:171–181.
17. Thomas CR, Wright CD, Loehrer PJ. Thymoma: state of the art. *J Clin Oncol*. 1999;17:2280–2289.
18. Rothstein DH, Voss SD, Isakoff M, et al. Thymoma in a child: case report and review of the literature. *Pediatr Surg Int*. 2005;21:548–551.
19. Quintanilla-Martinez L, Wilkins EW, Choi N, et al. Thymoma. Histologic subclassification is an independent prognostic factor. *Cancer*. 1994;74:606–617.
20. Stachowicz-Stencel T, Bien E, Balcerska A, et al. Thymoma and thymic carcinoma—review of literature and clinical characteristics based on the Polish Paediatric Solid Tumours Study Group experience. *Med Wieku Rozwoj*. 2007;11:313–318.
21. Wang Y, Sun Y, Zhang J, et al. Diagnosis, treatment and prognosis of thymoma: an analysis of 116 cases. *Chin Med J (Engl)*. 2003;116:1187–1190.
22. Kondo K, Monden Y. Therapy for thymic epithelial tumors: a clinical study of 1,320 patients from Japan. *Ann Thorac Surg*. 2003;76:878–884; discussion 84-5.
23. Boylan E, Wyers M, Jaffar R. A rare case of thymoma in a 15-month-old girl. *Pediatr Radiol*. 2011;41:1469–1471.
24. Chabchoub Ben Abdallah R, Maalej B, Abdelmoulla S, et al. Thymoma in children: a report of one case. *Arch Pediatr*. 2011;18:745–749.
25. Lam WW, Chan FL, Lau YL, et al. Paediatric thymoma: unusual occurrence in two siblings. *Pediatr Radiol*. 1993;23: 124–126.
26. Pacilli P, Vigano P, Cogno M, et al. Thymoma in childhood. Clinical case. *G Chir*. 2000;21:375–378.
27. Vaideeswar P, Padmanabhan A, Deshpande JR, et al. Thymoma: a pathological study of 50 cases. *J Postgrad Med*. 2004;50:94–97.
28. Honda S, Morikawa T, Sasaki F, et al. Cystic thymoma in a child: a rare case and review of the literature. *Pediatr Surg Int*. 2007;23:1015–1017.
29. Takeda S, Miyoshi S, Akashi A, et al. Clinical spectrum of primary mediastinal tumors: a comparison of adult and pediatric populations at a single Japanese institution. *J Surg Oncol*. 2003;83:24–30.
30. Dehner LP, Martin SA, Sumner HW. Thymus related tumors and tumor-like lesions in childhood with rapid clinical progression and death. *Hum Pathol*. 1977;8:53–66.
31. Kaplinsky C, Mor C, Cohen IJ, et al. Childhood malignant thymoma: clinical, therapeutic, and immunohistochemical considerations. *Pediatr Hematol Oncol*. 1992;9:261–268.
32. Demir HA, Yalçın B, Çiftçi A, et al. Primary chest tumors in children. *Pediatr Blood Cancer*. 2005;45:473.
33. Ghosh JB, Roy M, Peters T. Thymoma associated with myasthenia gravis in infancy. *Indian J Pediatr*. 2009;76:1057–1058.
34. Liang X, Lovell MA, Capocelli KE, et al. Thymoma in children: report of 2 cases and review of the literature. *Pediatr Dev Pathol*. 2010;13:202–208.
35. Chen YD, Feng QF, Lu HZ, et al. Role of adjuvant radiotherapy for stage II thymoma after complete tumor resection. *Int J Radiat Oncol Biol Phys*. 2010;78:1400–1406.
36. Rezaei N, Hedayat M, Aghamohammadi A, et al. Primary immunodeficiency diseases associated with increased susceptibility to viral infections and malignancies. *J Allergy Clin Immunol*. 2011;127:e2.
37. Loehrer PJ, Chen M, Kim K, et al. Cisplatin, doxorubicin, and cyclophosphamide plus thoracic radiation therapy for limited-stage unresectable thymoma: an intergroup trial. *J Clin Oncol*. 1997;15:3093–3099.
38. Loehrer PJ, Kim K, Aisner SC, et al. Cisplatin plus doxorubicin plus cyclophosphamide in metastatic or recurrent thymoma: final results of an intergroup trial. The Eastern Cooperative Oncology Group, Southwest Oncology Group, and Southeastern Cancer Study Group. *J Clin Oncol*. 1994;12: 1164–1168.
39. Niehues T, Harms D, Jurgens H, et al. Treatment of pediatric malignant thymoma: long-term remission in a 14-year-old boy with EBV-associated thymic carcinoma by aggressive, combined modality treatment. *Med Pediatr Oncol*. 1996;26: 419–424.
40. Evans TL, Lynch TJ. Role of chemotherapy in the management of advanced thymic tumors. *Semin Thorac Cardiovasc Surg*. 2005;17:41–50.
41. Schmitt J, Loehrer PJ. The role of chemotherapy in advanced thymoma. *J Thorac Oncol*. 2010;5:S357–S360.
42. Cowen D, Hannoun-Levi JM, Resbeut M, et al. Natural history and treatment of malignant thymoma. *Oncology (Williston Park)*. 1998;12:1001–1005.
43. Lara PN, Bonomi PD, Faber LP. Retreatment of recurrent invasive thymoma with platinum, doxorubicin, and cyclophosphamide. *Chest*. 1996;110:1115–1117.

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