Childhood mediastinal masses in infants and children

Türkan Tansel[1], Ertan Onursal[1], Enver Dayıoğlu[1], Murat Başaran[1], Zerrin Sungur[2] Emre Çamcı[2], Dilek Yılmazbayhan[3], Rukiye Eker[4], Türkan Ertuğrul[4]

Departments of [1]Cardiovascular Surgery, [2]Anesthesiology, [3]Pathology, and [4]Pediatrics, Istanbul University Istanbul Faculty of Medicine, İstanbul, Turkey

SUMMARY: Tansel T, Onursal E, Dayıoğlu E, Başaran M, Sungur Z, Çamcı E, Yılmazbayhan D, Eker R, Ertuğrul T. Mediastinal masses in infants and children. Turk J Pediatr 2006; 48: 8-12.

We reviewed all cases of primary pediatric mediastinal masses diagnosed and treated over a 24-year period.

In this study, out of 187 primary mediastinal mass cases diagnosed between 1980 and 2004 in Istanbul University Istanbul Faculty of Medicine, Cardiovascular Surgery Department, 37 pediatric primary mediastinal mass cases were retrospectively evaluated according to age, sex, symptoms, diagnostic procedure, anatomical location, surgical treatment, histopathological evaluation and postoperative adjuvant therapy.

The patients ranged in age from 2 months to 15 years at the time of diagnosis, with a mean age of 8 years. There were 24 benign (64.8%) and 13 malignant (35.2%) tumors. The cases were lymphoma (27%), neurogenic tumors (21.6%), cystic lesions (18.9%), germ cell tumors (13.5%), thymic lesions (10.8%) and cardiac tumors (8.1%). Complete and partial resections of the tumor were the surgical procedures performed in 24 patients (64.8%) and 3 patients (8.1%), respectively. The three patients with a malignant tumor, in whom the entire mass could not be removed, received chemotherapy and radiation after surgery. In 10 patients with lymphoma, surgery was not a part of treatment and they received medical and radiation therapy after the establishment of the definitive diagnosis. All patients survived and were discharged from the hospital. Except for the cases with lyphoma, all patients are now free of recurrent disease. Compared to adults, children had more lymphomas and neurogenic tumors.

Primary pediatric mediastinal malignancies are relatively common in infants and children. Lymphoma, neurogenic tumors and cystic lesions predominated. These differences between the age groups should also be considered when dealing with a mediastinal mass.

Key words: mediastinal masses, children, infants, pediatric tumor.

In infants and children, most intrathoracic tumors are located in or adjacent to the mediastinum[1]. These masses may represent a wide variety of histological morphologies and require many different forms of surgical and nonsurgical treatment[2]. Children, especially those with benign tumors, have very high survival rates after the surgical resection[3]. Herein, we report our series of patients who were diagnosed and treated for a mediastinal tumor, with emphasis on clinical presentation, diagnosis and treatment over a 24-year period.

Material and Methods

A search of the surgical records of Istanbul University, Istanbul Faculty of Medicine, Cardiovascular Surgery Department revealed 187 patients with primary mediastinal cysts and tumors. Out of 187 cases, 37 pediatric patients with a primary mediastinal mass were retrospectively evaluated according to age, sex, symptoms, diagnostic procedure, anatomical location, surgical treatment, histopathological evaluation and postoperative adjuvant therapy.

We classified the tumors by dividing the mediastinum into three areas based on anatomical structures as previously described in the literature[4]: the anterior mediastinum, the middle mediastinum and the posterior mediastinum. Patients with metastatic disease of mediastinum, esophageal diverticula, infection and diaphragmatic hernia into the mediastinum were excluded from the study. Primary tumors of thyroid, parathyroid, esophagus and lung were also excluded.

Results

Thirty-seven patients with pediatric primary mediastinal masses were identified. There were 13 (35.1%) female and 24 (64.9%) male patients in the study. The patients ranged in age from 2 months to 15 years at the time of diagnosis, with a mean of 8 years (Table I). There were 24 benign (64.8%) and 13 malignant (35.2%) tumors. Histologic confirmation was made in all patients.

not a common finding. None of our patients with a posterior mediastinal mass showed a preoperative elevation of vanillylmandelic acid (VMA) levels.

The mediastinal localization of the tumors is given in Table II. For the whole series, 10 patients (27%) had tumors in the anterior mediastinum. In our study, common tumors in this anatomical location included thymic pathologies, germ cell tumors and lymphomas. Of these tumors, thymic pathologies and germ cell tumors were the most common masses, representing more than two-thirds (8/10) of cases. Lymphoma was the least common tumor of this location, representing 20% (2/10) of cases. There were 19 tumors (51.3%) in the middle mediastinum. These consisted primarily of lymphomas and cardiac tumors. In the posterior mediastinum, there were eight tumors (21.6%). The most common neoplasms of the posterior mediastinum were neurogenic tumors.

Table I. Mediastinal Masses in Infants and Children

Histology (n)	0–1 year	2–5 years	6–10 years	11–15 years
Lymphoma	–	–	2	8
Neurogenic tumors	–	5	2	1
Cystic lesions	–	3	1	3
Thymic pathologies	2	–	–	2
Germ cell tumors	4	1	–	–
Cardiac myxoma	–	–	1	1
Cardiac epithelioid	1			
Hemangioendothelioma	–	–	–	

Table II. Mediastinal Localization of the Tumors

Histology	Anterior	Middle	Posterior
Lymphoma	2	8	–
Neurogenic tumors	–	–	8
Cystic lesions	–	7	–
Thymic pathologies	4	–	–
Germ cell tumors	4	1	–
Cardiac myxoma	–	2	–
Cardiac epithelioid hemangioendothelioma	–	1	–

There were 28 (75.7%) symptomatic patients in our series. Common symptoms in patients with these tumors included respiratory symptoms (cough, stridor, dyspnea) in 18 patients (60.7%), fatigue and fever in seven patients (25%), myasthenic symptoms in one patient (3.6%), neurological complications in one patient (3.6%), and peripheric emboli in one patient (3.6%). Hepatosplenomegaly was

The distribution of histological diagnoses in the study is shown in Table III. Lymphomas were the most common tumors and represented 27% of our patients (10/37). They generally presented in the teen years and were located in the middle mediastinum. Lymphomas were Hodgkin's diease in 60% (6/10) and non-Hodgkin's lymphoma in the remaining (40%) (4/10). Neurogenic tumors represented 21.6%

Table III. Histopathological Diagnosis of the Tumors

Diagnosis	Number (n)	Histopathology (n)
Lymphoma	10	– Hodgkin's disease (6) – Lymphoblastic lymphoma (4)
Neurogenic tumors	8	– Ganglioneuroma (6) – Neuroblastoma (1) – Meningocele (1)
Cystic lesions	7	– Bronchogenic cyst (3) – Pericardial cyst (1) – Cystic hygromas (1) – Cardiac cyst hydatid (2)
Thymic pathologies	4	– Thymoma (2) – Thymic cyst (1) – Thymic hyperplasia (1)
Germ cell tumors	5	– Teratoma (4) – Endodermal sinus tumor (1)
Cardiac	3	– Myxoma (2) – Epithelioid hemangioendothelioma (1)

of our total group and were the second most common mediastinal tumor. They were usually located in the posterior mediastinum. None of the patients with a posterior mediastinal mass in the series showed a pre- or post-operative elevation of VMA levels. Despite their close proximity to the vertebral foramen, no patient had symptoms or signs of spinal cord compression. Ganglioneuroma was present in 75% (6/8) and neuroblastoma in (12.5%) (1/8). The remaining patient with an anterior meningocele had been operated successfully in our Neurosurgery Department. There were seven cystic lesions of the mediastinum, representing 18.9% of the patient population. These cysts included cystic hygroma, cardiac cyst hydatid, and pericardial and bronchogenic cysts. Germ cell tumors occurred in 13.5% of the population (5/37); four of them were teratoma and one was an endodermal sinus tumor. The thymic pathologies were seldom and represented 10.8% of the total group (4/37). One patient had thymic cyst, and the mass was discovered as an incidental finding on X-ray film. All thymic lesions were resected without complication. There were also three patients with a cardiac tumor (8.1%) (3/37). These tumors included atrial myxoma (2/3) and epithelioid hemangioendothelioma (1/3).

Transthoracic echocardiography was used in the diagnostic evaluation of these patients.

During the same period, 150 adult cases with primary mediastinal masses were identified. The most common lesions encountered in the adult population were thymic lesions (36.9%), retrosternal goiter (20.6%) and lymphomas (10.9%).

The surgical approach to our patients included lateral thoracotomy in 14 patients (37.8%) and median sternotomy in 13 patients (35.1%). Video-assisted thoracoscopic surgery, anterior mediastinostomy and cervical mediastinoscopy were the procedures used in 10 patients (27.0%) to establish a definitive diagnosis, and the histopathological analysis revealed lymphoma. Surgery was not a part of treatment in these patients; they received medical and radiation therapy after discharge.

Total and subtotal resections of the tumor were the surgical procedures performed in 24 patients (64.8%) and 3 patients (8.1%), respectively. Twenty–four (64.8%) patients received no adjuvant treatment after the complete surgical resection. The remaining three patients (8.1%) received a combination therapy including surgical resection, chemotherapy and radiation therapy. Except for the cases with lyphoma, all patients are alive without evidence of recurrent disease.

Discussion

The most important factors in the management of an infant or child with a mediastinal mass are the nature of the disease, age, presenting symptoms and location of the mass on X-ray. The symptomatology of a primary mediastinal tumor may vary from patient to patient and usually depends on its anatomic location, size

and nature. In our experience, a significant proportion of patients were symptomatic (75.7%) when first seen, with respiratory problems being the most common symptoms, consistent with other reports in the literature[5]. Physical signs related to mediastinal tumors have not been well defined and our patients were usually free of gross abnormality.

All patients in this study underwent complete physical examination, biochemical analysis and chest radiography as an initial investigation. Developments in the diagnostic modalities have changed the approach of this initial workup[6]. In our study, the introduction of computed tomography (CT) in 1986 is noted by a increased percentage of patients studied by CT. The patients with a mass located in the posterior mediastinum were also evaluated by magnetic resonance imaging (MRI). In such patients, we also measured the level of urinary VMA during the initial diagnostic evaluation. We did not perform a transthoracic fine needle aspiration biopsy; however, video-assisted thoracoscopic surgery, anterior mediastinostomy and/or cervical mediastinoscopy were the procedures used in some patients to reach a definitive diagnosis.

Our most common tumor was also lymphoma, which is consistent with literature[7-8]. Hodgkin's disease occurred in 33-56% of pediatric lymphomas[9]. Our patients with Hodgkin's disease represented 60% of patients and received only chemotherapy and/or radiation therapy. Many studies have reported that neurogenic malignancies are the second most common pediatric mediastinal tumors[3,10-11]. Although neuroblastoma has been reported to be the most common neurogenic tumor in the pediatric population and occurs in children two years of age or younger[3,8], ganglioneuroma was more common in our study. Neurogenic tumors, primarily neuroblastomas and pheochromocytomas, may produce large amounts of catecholamines and there is an intermittent increased urinary excretion of epinephrine, norepinephrine and their metabolic products. Measurement of urinary VMA is a useful screening test; normal levels on three 24-hour collections of this metabolite exclude the diagnosis. Excretion of these compounds may also be elevated in coma, dehydration, or extreme stress states. Interference from epinephrine-like drugs, antihypertensives (methyldopa) and other drugs (tetracycline, quinine) must also be considered in the evaluation of abnormal results. The ages of our patients with neurogenic tumors were usually higher than previously reported series; this and the detection of normal urinary VMA levels in our patients can be explained by the higher incidence of ganglioneuroma in our population.

In our study, there were five germ cell tumors representing 13.5% of our patients. The incidence of germ cell tumors in this series was higher than previously reported[3,5]. Of interest was a 10-month-old boy in whom hemothorax was initially detected during workup for respiratory symptoms. Subsequent evaluation of this patient revealed an endodermal sinus tumor located in the anterior mediastinum, and his symptoms were due to the rupture of the tumor into the pleural cavity. The patient underwent a successful complete resection procedure. The rupture of germ cell tumor into pleural or pericardial cavity is a rarely reported event in the literature[12].

In the pediatric age group, the frequency of benign thymic pathologies including thymic cysts and hyperplasia is usually more than in our population[13-14]. The four patients with thymic pathologies were successfully treated surgically through a median sternotomy. Cystic hygromas are congenital malformations resulting from a failure of the primary lymphatic sacs to establish drainage into the venous system. There was only one patient who was treated for mediastinal cystic hygroma during the study period. The tumor had no extension outside the mediastinum and was totally resected through a left lateral thoracotomy.

Many previous studies have reported that 25-49% of primary mediastinal tumors are malignant[15-17]. In our series, the incidence of malignancy was 35.2%. The patients having a tumor with benign histopathology (24/37) underwent a complete surgical resection and were discharged from the hospital in a good clinical condition. They are still alive without evidence of recurrent disease. The three patients with a malignant tumor, in whom the entire mass was not removed, received chemotherapy and radiation after surgery. In 10 patients with lymphoma, surgery was not a part of treatment and they received medical and radiation therapy after discharge.

The surgical approach to these tumors has changed significantly over time. In the past, death was usually related either to the mass effect of the tumor or the complications of general anesthesia, but with refinements in surgical technique and anesthetic management, the mortality rate significantly decreased following surgical intervention. The significant increase in median sternotomy possibly reflects the increased experience of cardiothoracic surgeons with this incision. The use of video-assisted thoracoscopic surgery, cervical mediastinal exploration and anterior mediastonomy as the surgical and/or diagnostic procedure has greatly increased as well.

In our study, the relative frequency of mediastinal masses in children was higher than in previous series. Thirty-seven of 187 patients with primary mediastinal masses were children (19.8% versus 80.2%). In addition, compared to adult patients, there were significantly more lymphomas (27% versus 10.9%) and neurogenic tumors (26% versus 0.5%) in the pediatric group. Although the most common lesions in adults are thymic lesions, thymic pathologies were uncommon in the pediatric age group (10.8% versus 36.9%).

In conclusion, primary pediatric mediastinal malignancies are relatively common in infants and children. Lymphoma, neurogenic tumors and cystic lesions predominated. With improved surgical techniques and therapeutic regimens, the primary pediatric mediastinal tumors can be treated with acceptable morbidity and mortality rates. The differences between the age groups should also be considered when dealing with a mediastinal mass.

REFERENCES

1. King RM, Telander RL, Smithson WA, Banks PM, Han MT. Primary mediastinal tumors in children. J Pediatr Surg 1982; 17: 512-520.
2. Pokorny WJ, Sherman JO. Mediastinal masses in infants and children. J Thorac Cardiovasc Surg 1974; 68: 869-875.
3. Grosfeld JL, Skinner MA, Rescorla FJ, West KW, Scherer LR. Mediastinal tumors in children: experience with 196 cases. Ann Surg Oncol 1994; 1: 121-127.
4. Burkell CC, Cross JM, Kent HP, Nanson EM. Mass lesions of the mediastinum. Curr Probl Surg 1969; 7: 2-57.
5. Azarow KS, Pearl RH, Zurcher R, Edwards FH, Cohen AJ. Primary mediastinal masses. A comparison of adult and pediatric populations. J Thorac Cardiovasc Surg 1993; 106: 67-72.
6. Davis RD, Oldham NH, Sabiston DC. Primary cysts and neoplasms of the mediastinum: recent changes in clinical presentation, methods of diagnosis, management and results. Ann Thorac Surg 1987; 44: 229-237.
7. Grosfeld JL. Primary tumors of the chest wall and mediastinum in children. Semin Thorac Cardiovasc Surg 1994; 6: 235-239.
8. Simpson I, Campbell PE. Mediastinal masses in childhood: a review from a paediatric pathologist's point of view. Prog Ped Surg 1991; 27: 92-126.
9. White L, Siegel SE, Quah TC. Non-Hodgkin's lymphomas in children. Patterns of disease and classification. Crit Rev Oncol Hematol 1992; 13: 55-71.
10. Sairanen H, Leijala M, Louhimo I. Primary mediastinal tumors in children. Eur J Cardiothorac Surg 1987; 1: 148-151.
11. Temes R, Allen N, Chavez T, Crowell R, Key C, Wernly J. Primary mediastinal malignancies in children: report of 22 patients and comparison to 197 adults. Oncologist 2000; 5: 179-184.
12. Lack EE, Weinstein HJ, Welch KJ. Mediastinal germ cell tumors in childhood. J Thorac Cardiovasc Surg 1985; 89: 826-835.
13. Cohen AJ, Thompson LN, Edwards FH, Bellamy RF. Primary cysts and tumors of the mediastinum. Ann Thorac Surg 1991; 51: 378-384.
14. Mullen B, Richardson JD. Primary anterior mediastinal tumors in children and adults. Ann Thorac Surg 1986; 42: 338-345.
15. Wongsangiem M, Tangthangtham A. Primary tumors of the mediastinum: 190 cases analysis (1975-1995). J Med Assoc Thai 1996; 79: 689-697.
16. Goldberg M, Burkes R. Current management of mediastinal tumors. Oncology 1994; 8: 99-111.
17. Hoffman O, Gillespie D, Aughenbaugh G, et al. Primary mediastinal neoplasms (other than thymoma). Mayo Clin Proc 1993; 68: 880-891.