Observational Study

Medicine®

OPEN

Clinical manifestation of pediatric mediastinal tumors, a single center experience

Chieh-Ho Chen, MD[a], Kang-Hsi Wu, MD[b], Yu-Hua Chao, MD[c], De-Fu Weng, MD[b], Jeng-Sheng Chang, MD[d], Chien-Heng Lin, MD[a,e,*]

Abstract

Medical decisions should be well-planned to improve prognosis and reduce complications of mediastinal tumors. In this study, we analyzed the clinical presentations of pediatric mediastinal tumors and their correlation with long-term clinical outcome.

Forty patients under 18 years of age diagnosed with mediastinal tumors at China Medical University Children's Hospital between 2001 and 2016 were enrolled. The patients' sex, age of onset, initial clinical symptoms, and treatment outcomes were analyzed.

75% of the patients with mediastinal tumors in this study were men, and the median age of onset was 13 years old (age range: 0–17 years). The overall mortality rate was 40%. The most common tumors were lymphoma (47.5%), followed by germ cell tumors (12.5%), neuroblastoma (12.5%), and thymoma (7.5%). Neuroblastoma was more prevalent in girls younger than 5 years old. The initial presentations of these patients included breathing difficulty (65%), productive cough (47.5%), pleural effusion (54.5%), superior vena cava (SVC) syndrome (35%), neck mass (35%), airway compression (32.5%), fever (30%), chest pain (27.5%), and pericardial effusion (25%). Lymphomas were more likely to be accompanied by neck mass (52.6% vs19.0%, $P = .04$) and SVC syndrome (52.6% vs 19.0%, $P = .026$), yet also had a better 1-year-survival rate (68.4% vs 52.4%, $P = .02$).

Overall, lymphoma should be suspected when children present with neck mass and SVC syndrome. Neuroblastoma with a posterior mediastinal origin should be suspected among children younger than 5 years old. Tumor-related airway obstruction, pleural effusion, and pericardial effusion were leading cause of cardiopulmonary instability during sedation for invasive procedures, which should be managed cautiously.

Abbreviations: ECMO = extracorporeal membrane oxygenation, LDH = lactate dehydrogenase, PEFR = peak expiratory flow rate, SVC = superior vena cava, VMA = vanillylmandelic acid.

Keywords: airway obstruction, lymphoma, neuroblastoma, pediatrics

1. Introduction

Mediastinum is in the central part of thoracic cavity, and contains many vital organs, such as heart, trachea, thymus, esophagus, etc. The structure of the mediastinum can be divided into 3 compartments, namely, the anterior, middle, and posterior mediastinum, from which various types of tumors may originate.[1,2]

Tumors arising from the mediastinum are rare in children and adolescents, and most such tumors are malignant in nature. For instance, thymomas and lymphomas can arise from the anterior mediastinum. Germ cell tumors mainly arise from the middle mediastinum, while neurogenic tumors often originate from the sympathetic nerve chains or spinal roots of the posterior mediastinum.[3] Tumor markers, such as alpha-fetoprotein, beta-HCG, lactate dehydrogenase (LDH), and urine vanillylmandelic acid (VMA) can be used to identify specific cancer types.[4]

Most of symptoms and signs of mediastinal tumors come up due to mass effect. For example, local compression to trachea may cause severe breathing problems. Dysphagia is resulted from esophageal narrowing. Superior vena cava syndrome is caused by obstructed venous return. Malignant tumors may also cause systemic symptoms such as fever, or tumor lysis syndrome. Sedation can be a dangerous procedure owning to impaired cardiopulmonary function. Detailed assessment before invasive procedure is important to minimize risk of sudden collapse.

To the best of our knowledge, there have been no prior studies involving Asian, pediatric populations focusing on the correlations between the initial clinical presentation of mediastinal tumors and their long-term prognoses. Therefore, we conducted this study to analyze the clinical presentation of pediatric mediastinal tumors at our hospital in order to develop useful predictive prognostic factors.

Editor: Lindsay Calderon.

Ethics approval and consent to participate: This study was approved by the Institutional Review Board (NA/CMUH106-REC1-129) of our hospital committee. Informed consent was obtained from the patients enrolled in this study.

Consent for publication: Not applicable.

All data generated or analyzed during this study are included in this published article.

No financial support was received for this work.

The authors have no conflicts of interest to disclose.

[a] Division of Pediatric Pulmonology, [b] Division of Pediatric Hematology & Oncology, [c] Department of Pediatrics, Chung Shan Medical University Hospital, [d] Division of Pediatric Cardiology, China Medical University Children's Hospital, North District, Taichung City, [e] Department of Biomedical Imaging and Radiological Science, College of Medicine, China Medical University, Taichung, Taiwan.

[*] Correspondence: Chien-Heng Lin, Division of Pediatric Pulmonology, China Medical University Children's Hospital, No 2, Yuh-Der Road, Taichung 404, Taiwan (e-mail: lch227@ms39.hinet.net).

Medicine (2019) 98:32(e16732)

Received: 20 February 2019 / Received in final form: 8 July 2019 / Accepted: 14 July 2019

http://dx.doi.org/10.1097/MD.0000000000016732

Table 1

Classification of mediastinal tumors in the study group.

Tumor type	Case number (%)	Age of onset (mean yr ± SD)	Sex M (%)	Mortality N (%)
Malignant tumors	N = 38 (95)	10.7 ± 5.8	28 (71)	16 (42.1)
Lymphoma	19 (47.5)	12.0 ± 4.2	15 (79.1)	6 (31.5)
Germ-cell tumor	5 (12.5)	13.0 ± 2.9	5 (100.0)	4 (80.0)
Neuroblastoma	5 (12.5)	1.8 ± 2.0	1 (20.0)	2 (40.0)
Thymoma	3 (7.5)	13.3 ± 2.9	2 (66.7)	2 (66.7)
Others	4 (10.5)	10.8 ± 5.3	3 (75)	4 (100)
Pleuropulmonary blastoma	1 (2.5)	2	0 (0)	0 (0)
Angiosarcoma	1 (2.5)	15	1 (100)	1 (100)
Synovial sarcoma	1 (2.5)	15	1 (100)	1 (100)
Tracheal carcinoma	1 (2.5)	11	1 (100)	0 (0)
Benign tumors	N = 2 (5)	10.5 ± 5.3	2 (100)	0 (0)
Thymic hyperplasia	1 (2.5)	5	1 (100)	0 (0)
Gangioneuroma	1 (2.5)	16	1 (100)	0 (0)
Total	N = 40 (100)	10.7 ± 5.7	30 (75)	16 (40)

2. Methods

We collected data for patients with pathologically proven mediastinal tumors diagnosed from January 2001 to May 2016 at China Medical University Children's Hospital by retrospective chart review. Our institute is the largest children's hospital in central Taiwan with 256 beds in total and annual admission numbers of 70,000 patients per year.

All the private information of these patients was de-identified and kept anonymous. The information collected from their medical charts was reviewed independently by 2 researchers. Data such as patients' sex, age of disease onset, initial clinical symptoms, hospital course, and outcomes such as airway obstruction, pleural effusion, pericardial effusion, superior vena cava (SVC) syndrome, and treatment outcomes were reviewed and collected. The primary outcome was to depict epidemiologic study of pediatric malignant mediastinal tumors in Taiwan. The secondary aim was to determine any correlations between the clinical symptoms and mortality for the various tumor types. We compared the initial clinical presentations of the tumors between the patients who remained alive and those who died. This study was approved by the Institutional Review Board (NA/CMUH106-REC1–129) of our hospital committee. The Pearson chi-square test or Fisher exact test was used as appropriate for categorical variables. Student *t* test was used for parametric variables, while the Mann–Whitney *U* test and Kruskal-Wallis test were used for non-parametric variables. All of the tests were 2-tailed, and a *P* value of $<.05$ was considered statistically significant. All of the data were analyzed using Stata Statistical Software, Release 14 (StataCorp LLC, College Station, TX).

3. Results

A total of 40 patients were included in our study. Table 1 shows the demographic features of all the cases. The median age of onset was 13 years old (age range: 0–17 years). Males were 3 times more likely to be affected than women, as 30 of the patients were men and only 10 were women. 90% of the mediastinal tumors were malignant in nature (N = 38), with only 2 cases being benign in nature. The most common type of mediastinal tumors in this study were lymphomas (19/40, 47.5%), followed by neuroblastomas (5/40, 12.5%), various types of germ cell tumors and yolk sac tumors (5/40. 12.5%), and thymomas (3/40, 7.5%). Less common diagnoses included pleural pulmonary blastoma (N = 1), angiosarcoma (N = 1), and tracheal carcinoma (N = 1). None of the patients with these rare tumors survived long after their diagnoses. In the children younger than 5 years of age, neuroblastomas were more likely to be identified in girls than in boys, with an odds ratio of 4 to 1. The overall mortality rate for the mediastinal tumors of all types was 40% (N = 16), with lymphomas having a lower mortality rate than the other types of malignancies (31.5% vs 47.6%, $P = .02$).

Common symptoms and signs of mediastinal tumors included breathing difficulty (65%), productive cough (47.5%), pleural effusion (54.5%), SVC syndrome (35%), neck mass (35%), airway compression (32.5%), fever (30%), chest pain (27.5%), and pericardial effusion (25%) (Table 2). Among the lymphoma patients, there was a higher incidence of neck mass and SVC syndrome than among the patients with other types of tumors (52.6% vs 19.0%, $P = .04$). The all-cause mortality rate of the

Table 2

Comparison between lymphoma and non-lymphoma.

	Lymphoma (N = 19)	Non-lymphoma (N = 21)	Total (N = 40)	*P* values
Age of Onset				
Median (Y/o)	13	11.52	12.67	.303
Range (Y/o)	2–17	0–17	0–17	
Sex (Male %)	15 (79.1)	15 (71.4)	30 (75)	.72
Mortality rate	6 (31.5)	10 (47.6)	16 (40)	.02**
Symptoms/Signs				
Fever (BT >38.5°)	6 (31.5)	6 (28.6)	12 (30)	.84
Productive cough	11 (57.9)	8 (38.0)	19 (47.5)	.21
Breathing difficulty	13 (68.4)	13 (61.9)	26 (65)	.67
Stridor	7 (36.8)	6 (28.6)	13 (32.5)	.57
Body weight loss	3 (15.7)	4 (19)	7 (17.5)	.99
Dysphagia	3 (15.7)	1 (4.8)	4 (10)	.34
Chest pain	5 (26.3)	6 (28.6)	11 (27.5)	.99
Hemoptysis	0 (0)	1 (4.8)	1 (2.5)	.34
Neck mass	10 (52.6)	4 (19.0)	14 (35)	.04**
Pericardial effusion	5 (26.3)	5 (23.8)	10 (25)	.99
Pleural effusion	7 (36.8)	10 (47.6)	17 (54.5)	.14
Horner's syndrome	0 (0)	1 (4.8)	1 (2.5)	.34
SVC syndrome	10 (52.6)	4 (19.0)	14 (35)	.04**

SVC = superior vena cava.
** *P* value is less than .05, i.e. statistically significant.

Table 3

Comparison between patients who survived and patients who died.

	Survived (N = 24)	Died (N = 16)	Total (N = 40)	*P* values
Age of Onset				
Median	12.3	13	12.67	.9681
Range	2–15	0–17	0–17 (10.7 ± 5.7)	
Sex (Male %)	16 (66.7)	14 (87.1)	30 (75)	.303
Mortality rate	0 (0)	16 (100)	16 (40)	
Symptoms/Signs				
Fever (BT >38.5°)	7 (29.2)	5 (31.3)	12 (30)	.99
Productive cough	3 (12.5)	4 (25.0)	7 (17.5)	.40
Breathing difficulty	3 (12.5)	1 (6.3)	7 (17.5)	.63
Stridor	6 (28.6)	7 (36.8)	13 (32.5)	.57
Body weight loss	3 (12.5)	4 (25.0)	7 (17.5)	.40
Dysphagia	3 (12.5)	1 (6.3)	4 (10)	.63
Chest pain	7 (29.2)	4 (25.0)	11 (27.5)	.99
Hemoptysis	1 (4.2)	0 (0)	1 (2.5)	.00
Neck mass	7 (29.2)	4 (25)	10 (25)	.71
Pericardial effusion	8 (33.3)	9 (56.3)	17 (54.5)	.15
Pleural effusion	8 (33.3)	9 (56.3)	17 (54.5)	.15
Horner's syndrome	0 (0)	1 (6.3)	1 (2.5)	.21
SVC syndrome	8 (38.0)	6 (37.5)	14 (35)	.76

mediastinal tumors as 40%. Most of the deceased patients died during long-term follow-up for anti-cancer treatment. Nevertheless, 2 deaths were related to sedation and anesthesia during invasive procedures (a CT-guide biopsy and CVC insertion, respectively); both patients received emergency cardiopulmonary resuscitation but to no avail. Furthermore, in comparing the survivors to the non-survivors, we found that there were no significant differences in initial presentation between the survivors and those who died (Table 3).

4. Discussion

From our limited data, we found that men and adolescents were more frequently affected by mediastinal tumors, especially lymphoma or leukemia tumors, than women and young children. Meanwhile, neuroblastomas should be most highly suspected among children younger than 5 years old. Nevertheless, the age of onset and sexual distribution of mediastinal tumors may vary, however, among different studies. Liu et al[5] from China showed a bimodal age distribution for mediastinal tumors, with increased incidences in patients aged <10 years old and between 60 and 70 years old. That study also showed a higher incidence of respiratory discomfort in pediatric patients as compared with adult patients, probably owning to smaller intrathoracic volumes for tumor compression in children than in adults.[5] Gun et al[6] from Turkey showed that among 120 cases of mediastinal tumors, the patients were predominantly women (59%) and had a median age of around 5.8 years old, which was much younger than the median age of the patients in our study. Moreover, 28% of the mediastinal tumors in the Gun et al[6] study were benign in nature with neurogenic origin. The difference in disease spectrum between that study and the present study could have resulted from the different age distribution of the patients in both studies. In the Gun et al[6] study, the patients had a younger average age and were more likely to have had posterior mediastinal involvement. On the other hand, in our study, the mean disease onset age was higher and the tumors were more likely to be lethal. The effect of ethnicity on disease distribution, particularly among Asians, could be investigated further in the future.

Among the patients in this study, lymphoma tumors were the most common type of mediastinal tumors. However, despite their high incidence rate, the prognosis for lymphoma tumors was better than those for other types of tumors, a finding which could have resulted from the advanced nature of current lymphoma therapy.[7,8] The 7-year event-free survival rate of non-Hodgkin lymphoma reported for the Taiwan Pediatric Oncology Group (TPOG) 2000 protocol exceeded 60%.[8] Meanwhile, a study from Japan by Osumi et al[9] reported that the 5-year survival rate of mediastinal B-cell lymphoma in children and adolescents could even reach up to 80%, which is much better than the 5-year survival rates for many types of pediatric malignancies. Since lymphoma could occasionally be diagnosed from laboratory results such as elevated lactic dehydrogenase (LDH) levels or the presence of blast cells in hemograms, early induction therapy or cytoreduction therapy with corticosteroids could alleviate its symptoms and improve long-term outcomes. Nevertheless, tumor lysis syndrome should be monitored carefully during lymphoma treatment in case of nephrotoxicity and electrolyte imbalance.[10]

It is noteworthy that neuroendocrinal tumors tend to arise from the paravertebral area in the posterior mediastinum, though most of the tumors in our study arose from the anterior mediastinum.[11] Originating from neural crest cells of the adrenal glands and sympathetic chains, neuroblastomas constitute the most common solid malignancy in young children. In the present study, 4 cases of neuroblastoma were identified in children under 5 years of age. This result was quite similar to that of a study from Spain conducted in 2007, which showed a predominance of neuroblastomas (47%), ganglioneuroblastomas (30%), and ganglioneuromas (23%) among 56 patients.[12] Thoracic neuroblastomas have many unique clinical features compared with abdominal neuroblastomas, including Horner syndrome, opsoclonus, empyema, and even Guillain Barre-like syndrome.[13–15] In addition, thoracic neuroblastomas can also occasionally be discovered in adolescence or adulthood.[16,17] Thoracic neuroblastomas have relatively better outcomes than neuroblastomas originating from other areas.[18] Evidence has shown that early surgical intervention to treat localized mediastinal neuroblastomas improves the associated overall survival rate.[19] Since patients with thoracic neuroblastomas tend to be younger than those with other mediastinal tumors, careful clinical evaluations, assessments, and treatments should be performed for these patients.

The location, initial presentation, age of disease onset, and pathological types of tumors may also highly affect patients' clinical outcomes. Commonly, patients with mediastinal tumors present with obvious respiratory or circulatory symptoms and signs such as cough, shortness of breath, hemoptysis, and chest pain. Thus, the early detection of such tumors and the prevention of possible life-threatening events constitute a key challenge for clinical practitioners. Such tumors can even be lethal if they overly compress large airways or blood vessels (such as the superior vena cava or internal jugular artery), leading to ventilation/perfusion mismatch and resulting in decompensated cardiopulmonary circulations. Pericardial or pleural effusion may further impair patients' respiratory capacity. Moreover, sedation can be dangerous in patients with impending respiratory or circulatory failure, which requires advanced life-support. Therefore, for patients with severe airway compromise, securing

airway integrity should be the priority of management.[20] Symptomatic mediastinal tumors are often detectable through a chest x-ray or chest CT scan. Echocardiography and pulmonary ultrasounds can further be used for the evaluation of cardiac and pleural involvement.[1,21]

In our study, the patients with mediastinal lymphomas were notably more likely to have SVC syndrome, which may be easily discovered by healthcare providers upon physical examination, such as facial and neck edema, neck vein engorgement, and even blurred visions.[22] The blood flow of the SVC is reduced in patients with SVC syndrome due to external compression of the vein by the tumor mass, enlarged lymph nodes, or intravascular thromboembolism. The central venous pressure may be elevated and accompanied by the development of collateral venous circulations (varices). Swelling of the affected side of the face, upper extremities, and respiratory tract mucosa may become prominent if the condition progresses. The treatment of SVC syndrome is focused on reducing the severity of venous obstruction. Glucocorticoids may be useful in the cytoreduction of lymphomas and thymomas, while radiotherapy may be used for solid tumors.[23] An intravascular stent and surgical bypass are occasionally used for refractory cases.[22] In our study, most of the lymphoma patients with SVC syndrome received systemic corticosteroids for cytoreduction to release their venous compression.

Since most pediatric mediastinal tumors are malignant in nature, and since their long-term outcomes are not predictable based on their initial presentations, establishing a definitive diagnosis of mediastinal tumors is crucial for the planning of their future treatment. In most cancers, diagnosis and staging should be made based on the histopathological results. Nonetheless, the risk and benefit of obtaining the necessary tissue via a procedure with general anesthesia require careful measurement. Airway problems are prevalent in the majority of such patients, and these problems can sometimes be lethal. A chest CT scan with contrast is a highly sensitive tool for identifying the locations of mediastinal lesions and their thoracic involvements, especially the degree of large airway and great vessel compression, and should be performed prior to any invasive procedure.[21,24] A CT-guided fine-needle biopsy performed by an interventional radiologist is commonly used to obtain tumor tissue. The success rate of this procedure has been reported to be approximately 30%.[25] MRI is another excellent tool for assessment of mediastinal lesions owning to its clear soft tissue image resolution and direct multiplanar imaging.[26]

Sedation may be dangerous due to the risk of cardiopulmonary compromise caused by the compression of both large airways and the pulmonary vessels by the tumor mass, resulting in a V/Q mismatch of pulmonary blood flows.[27] Moreover, during deep sedation, the respiratory rate and tidal volume may be decreased due to reduced respiratory muscle tone, while the airflow of the bronchi may be obstructed thanks to increased airway compressibility.[28] Furthermore, bleeding and pneumothorax are other potential complications of lung biopsy, while pleural effusion, pericardial effusion, and tumor embolism may further hinder cardiopulmonary function. A high level of tracheal or bronchial stenosis caused by the tumor mass is associated with poor outcomes.[29] Among the patients enrolled in our study, there was one who experienced sudden hypotension and desaturation during a CT-guided biopsy. Immediate cardiopulmonary resuscitation was performed but in vain, requiring extracorporeal membrane oxygenation (ECMO) for stabilization. Unfortunately, the patient did not survive. A study from Japan showed that for 12 patients with mediastinal tumors, the median time of symptom onset to diagnosis was 8.5 days, yet warning signs leading to admission were noted on average only 2 days prior to admission, and 5 of the patients underwent cardiopulmonary resuscitation. The author concluded by noting the importance of the early awareness and recognition of airway symptoms by medical providers in patients with mediastinal tumors.[28]

Many methods have been proposed for maintaining airway patency and cardiopulmonary function in patients with mediastinal tumors undergoing sedation and invasive procedures. The initiation of preventive VA-ECMO before de-bulking surgery or open lung biopsy should also be considered in critical cases even without intubation.[25,30] For patients proven by imaging study to have a severe degree of airway obstruction, Shamberg et al[31] have suggested using a pulmonary function test to provide an additional preoperative evaluation of flow restriction. Peak expiratory flow rate (PEFR) may be limited in patients with airway obstruction. A multidisciplinary approach by surgeons, anesthesiologists, and intensivists should be planned initially to reduce the risk of emergency resuscitation, and the medical team should have clear communications and informed consent with the patient's family prior to the invasive intervention to avoid legal issues afterwards.

The greatest drawback to our study was the limited number of cases from a single hospital. Due to the low incidence of mediastinal tumors in general populations, there were only 40 cases of mediastinal tumors at the hospital over a period of 15 years. Nevertheless, to the best of our knowledge, this study is still the largest case series review of pediatric mediastinal tumors in Taiwan. We found that the survival rate of lymphoma tumors was higher than those for other types of mediastinal tumors, possibly due to the more effective chemotherapy protocol used to treat lymphoma. Meanwhile, it is important to assess and manage the airway during invasive procedures or sedation in these patients. Further multicenter large-scale studies should be performed to investigate the epidemiology of pediatric mediastinal tumors in Asians and possible prevention methods for the long-term complications of mediastinal tumors.

5. Conclusion

Lymphoma has better prognoses than other types of malignant tumors; however, patients with lymphoma are more likely to have SVC syndrome and neck mass. Neuroblastoma should be most highly suspected among children younger than 5 years old. Deep sedation in patients with mediastinal tumors may be life-threatening due to high risk of acute airway obstruction, so its use should be assessed and managed carefully through cooperative teamwork.

Author contributions

Conceptualization: Chieh-Ho Chen, Chien-Heng Lin.
Formal analysis: De-Fu Weng.
Investigation: Kang-Hsi Wu, Yu-Hua Chao.
Methodology: Kang-Hsi Wu, Yu-Hua Chao.
Writing – original draft: Chieh-Ho Chen, Chien-Heng Lin.
Writing – review & editing: Chieh-Ho Chen, Kang-Hsi Wu, Jeng-Sheng Chang.

References

[1] Thacker PG, Mahani MG, Heider A, et al. Imaging evaluation of mediastinal masses in children and adults: practical diagnostic approach based on a new classification system. J Thorac Imaging 2015;30:247–67.

[2] McCarville MB. Malignant pulmonary and mediastinal tumors in children: differential diagnoses. Cancer Imaging 2010;10:S35–41.

[3] Takeda SI, 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.

[4] Sandoval JA, Malkas LH, Hickey RJ. Clinical significance of serum biomarkers in pediatric solid mediastinal and abdominal tumors. Int J Mol Sci 2012;13:1126–53.

[5] Liu T, Lika'a Fasih Y, Xie X, et al. Mediastinal lesions across the age spectrum: a clinicopathological comparison between pediatric and adult patients. Oncotarget 2017;8:59845–53.

[6] Gun F, Erginel B, Ünüvar A, et al. Mediastinal masses in children: experience with 120 cases. Pediatr Hematol Oncol 2012;29:141–7.

[7] Guo J, Zhu YP, Gao J, et al. Clinical and prognostic analysis of 43 children with mature B-cell non-Hodgkin's lymphoma/acute lymphoblastic leukemia. Zhongguo Shi Yan Xue Ye Xue Za Zhi 2016;24:72–9.

[8] Yang CP, Hung JJ, Jaing TH, et al. Treatment results of the TPOG-NHL92 protocols for childhood non-Hodgkin's lymphomas in Taiwan: a report from the Taiwan Pediatric Oncology Group (TPOG). Acta Paediatr Taiwan 2000;41:193–204.

[9] Osumi T, Tanaka F, Mori T, et al. Primary mediastinal large B-cell lymphoma in Japanese children and adolescents. Int J Hematol 2017;105:440–4.

[10] Elinoff JM, Salit RB, Ackerman HC. The tumor lysis syndrome. N Engl J Med 2011;365:571–2. author reply 573-4.

[11] Mushtaq N, Alam MM, Aslam S, et al. Malignant mediastinal mass in children: a single institutional experience from a developing country. J Pak Med Assoc 2014;64:386–9.

[12] Fraga JC, Aydogdu B, Aufieri R, et al. Surgical treatment for pediatric mediastinal neurogenic tumors. Ann Thorac Surg 2010;90:413–8.

[13] Das RR, Sami A, Seth R, et al. Thoracic neuroblastoma presenting as recurrent empyema. Natl Med J India 2014;27:84–5.

[14] Sung KW, Yoo KH, Koo HH, et al. Neuroblastoma originating from extra-abdominal sites: association with favorable clinical and biological features. J Korean Med Sci 2009;24:461–7.

[15] Sade R, Polat G, Tan H, et al. Thoracic neuroblastoma presenting with Guillain-Barre-like symptoms. Spine J 2015;15:1884–5.

[16] Wiesel O, Bhattacharyya S, Vaitkevicius H, et al. Ataxia induced by a thymic neuroblastoma in the elderly patient. World J Surg Oncol 2015;13:178.

[17] Ödek Ç, Kendirli T, Pekpak E, et al. An unusual case of neuroblastoma: a 17-year-old adolescent presented with bilateral diffuse lung metastasis at initial diagnosis. Turk J Pediatr 2016;58:86–9.

[18] Häberle B, Hero B, Berthold F, et al. Characteristics and outcome of thoracic neuroblastoma. Eur J Pediatr Surg 2002;12:145–50.

[19] Kang CH, Kim YT, Jeon SH, et al. Surgical treatment of malignant mediastinal neurogenic tumors in children. Eur J Cardiothorac Surg 2007;31:725–30.

[20] Stricker PA, Gurnaney HG, Litman RS. Anesthetic management of children with an anterior mediastinal mass. J Clin Anesth 2010;22:159–63.

[21] Newman B. Thoracic neoplasms in children. Radiol Clin N Am 2011;49:633–64.

[22] Wilson LD, Detterbeck FC, Yahalom J. Superior vena cava syndrome with malignant causes. N Engl J Med 2007;356:1862–9.

[23] Ostler PJ, Clarke DP, Watkinson AF, et al. Superior vena cava obstruction: a modern management strategy. Clin Oncol 1997; 9:83–9.

[24] Kirks DR, Fram EK, Vock P, et al. Tracheal compression by mediastinal masses in children: CT evaluation. AJR Am J Roentgenol 1983;141:647–51.

[25] Acker SN, Linton J, Tan GM, et al. A multidisciplinary approach to the management of anterior mediastinal masses in children. J Pediatr Surg 2015;50:875–8.

[26] Ödev K, Arıbaş BK, Nayman A, et al. Imaging of cystic and cyst-like lesions of the mediastinum with pathologic correlation. J Clin Imaging Sci 2012;2:33.

[27] Huang YL, Yang MC, Huang CH, et al. Rescue of cardiopulmonary collapse in anterior mediastinal tumor: case presentation and review of literature. Pediatr Emerg Care 2010;26:296–8.

[28] Ben-Ari J, Schonfeld T, Harlev E, et al. Life-threatening airway obstruction secondary to mass in children-a preventable event? Pediatr Emerg Care 2005;21:427–30.

[29] Piro AJ, Weiss DR, Hellman S. Mediastinal Hodgkin's disease: a possible danger for intubation anesthesia: intubation danger in Hodgkin's disease. Int J Radiat Oncol Biol Phys 1976;1:415–9.

[30] Wickiser JE, Thompson M, Leavey PJ, et al. Extracorporeal membrane oxygenation (ECMO) initiation without intubation in two children with mediastinal malignancy. Pediatr Blood Cancer 2007;49:751–4.

[31] Shamberger RC, Holzman RS, Griscom NT, et al. Prospective evaluation by computed tomography and pulmonary function tests of children with mediastinal masses. Surgery 1995;118:468–71.