영아의 전종격동 흉선종: 증례보고

황인경 • 한승민 • 김효선 • 한정우 • 유철주

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A Huge Anterior Mediastinal Thymoma of an Infant: A Case Report

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A seven months old male infant visited Severance Children's Hospital for evaluation of anterior mediastinal mass. With chest computed tomography (CT) image and biopsy, precursor T-cell lymphoblastic lymphoma was suspected but the ultrasonography guided biopsy specimen was insufficient to confirm the disease. Because there was a life-threatening risk to perform open biopsy to the small infant, we started chemotherapy empirically. The mass decreased, however, the lesion increased again and did not respond to the drugs. Finally we decided to resect the anterior mass with sternostomy and the pathology report finally resulted in thymoma.

Key Words: Anterior mediastinal mass, Thymoma

pISSN 2233-5250 / eISSN 2233-4580
http://dx.doi.org/10.15264/cpho.2015.22.2.167
Clin Pediatr Hematol Oncol 2015;22:167～170

Received on September 15, 2015
Revised on September 28, 2015
Accepted on October 6, 2015

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Introduction

Thymoma is a neoplasm of thymus that originates in the gland's epithelium, and is a very rare tumor, in children and only a few cases have been reported. Thymoma is categorized into 6 types on the basis of its histology (Table 1). In 6 types, type B thymoma is composed of epithelial cells and an abundant lymphocytic population [1]. Management of thymoma includes surgical resection, radiation and chemotherapy. Complete resection is very important in the treatment of thymoma, even for high stage or recurrent thymoma. However some of the thymoma like stage III or IV disease are condidered as unresectable disease, which are treated with chemotherapy [2]. Distinction lymphocyte

Table 1. World Health Organization (WHO) pathologic classification of thymoma

WHO classification	Histologiy
A	Medullary thymoma
AB	Mixed thymoma
B1	Predominantly cortical thymoma
B2	Cortical thymoma
B3	Well-differentiated thymic carcinoma
C	Thymic carcinoma

rich thymoma from T-lymphoblastic lymphoma (T-LBL) is difficult especially with small biopsy [3]. Management of thymoma includes surgical resection, in contrast, treatment of T-LBL is only chemotherapy. So, differential diagnosis between two diseases is very important.

Case Report

A seven month old male who has no specific past history visited a clinic and his lung sound was decreased, So he was checked with chest computed tomography (CT). The patient was refered to our hospital because of anterior mediastinal mass on September 24th, 2014 (Fig. 1 and Fig. 2) and had no symptoms at that time. According to our radiologist's reading on the outside chest CT, an 11 cm sized huge anterior mediastinal mass showed relatively homogenous enhancement without internal fat, calcification or necrosis and lymphoma was suspected (Fig. 2). The mass was pushing heart, the great vessels, left bronchi and other adjacent organs. On initial laboratory results, were white blood cells (WBC) were 15,380/μL, hemoglobin 12.5 g/dL, hematocrit 36.7%, platelet counts 265,000/μL, and no blast cells were checked. In addition, Lactate dehydrogenase was 327 IU/L, alpha fetoprotein was 21.91 ng/mL and total human chorionic gonadotropin was under 0.1 mIU/mL. We reviewed the initial pathology taken from other hospital and there were small lymphoid cells, more likely T lymphoblastic lymphoma (CD3, TdT (+)), but the tissue size was too small to identify T cell receptor signals. We took ultrasound guided biopsy again and the pathology resulted in normal thymic tissue which was non-diagnostic. Even-though the final pathology was normal, considering that initial pathology was T-cell lymphoblastic lymphoma and lymphoma is the most common tumor of anterior mediastinal mass in children, we could not exclude T-cell lymphoblastic lymphoma, so we started induction chemotherapy from October 3rd, 2014 for lymphoblastic lymphoma based on modified Berlin-Frankfurt-Munster (BFM) protocol. We took chest sonography in the middle of induction chemotherapy (December 26th, 2014). The mass was sized 4.5×2.8×5.9 cm showing about 50% decreased. At the end of induction chemotherapy, we took the chest MRI study, and the mass size was 4×6×8 cm, without change. The radiologists thought the remained mass was thymic hyperplasia rather than remained tumor.

So we consulted again to the department of thoracic surgery for open biopsy, the surgeon was unwilling to perform the operation because of the patients' young age and aggressiveness of the procedure; the sternostomy should be done to remove the mass. We continued the consolidation chemotherapy with methotrexate and purinetone, however

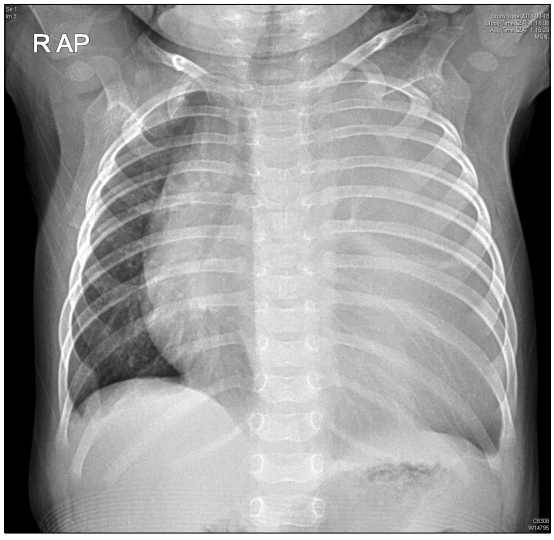

Fig. 1. Chest x-ray taken at the first visit.

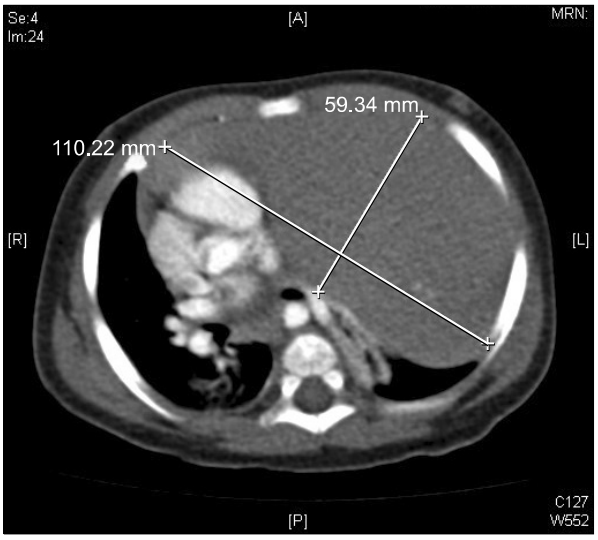

Fig. 2. Chest CT scan shows the huge anterior mediastinal mass (11×5.9 cm sized) pressing the heart and the great vessels to right side.

during follow up, the mass increased again (8.7×6.7×10 cm) on ultrasonography after 2nd consolidation chemotherapy (February 4th, 2015). We changed the regimen to nelarabine chemotherapy for refractory T cell lymphoblastic lymphoma. However, the therapy didn't showed favorable response; stable disease was still noted after the Nelarabine. To be sure of the disease status and to set up the right treatment plan for the patient, there was no time to postpone the operation at that moment. So we consult to the department of chest surgery again for open biopsy. On March 10th 2015, the patient received excision of tumor under mid-sternotomy. Pathology of the mass was reported to be completely excised thymoma, type B1, associated with thymic hyperplasia. The tumor was encapsulated well without adjacent organ invasion (Stage I). Positron emission tomography-computed tomography (PET-CT), chest ultrasonography and chest CT were performed on May, 2015 to evaluate postsurgical status. There was no recurrence of tumor. With chest ultrasonography follow-up on July 31st, 2015, the thymus increased from 3.9 cm to 4.6 cm, but there was no mass lesion (Fig. 3). We are planning to check-up him in the out patients clinic regularly with chest X-ray and ultrasonography.

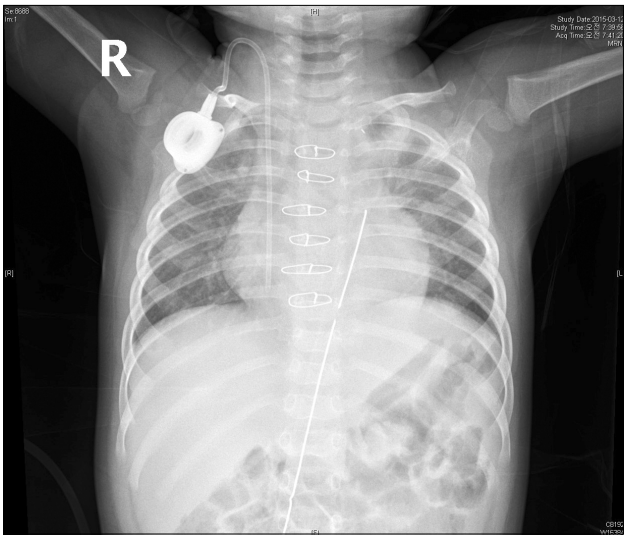

Fig. 3. Chest X-ray taken after the anterior mediastinal mass was resected.

Discussion

Mediastinal tumors and cyst in children and young adult are rare. Among all of the rare mediastinal masses, 35% to 55% present in the anterior mediastinum, and 85% originate from thymic, lymphomatous, and germ cell tissues. When anterior mediatinal mass is found in children about half of them are known to be lymphoma (45%), while followed by teratoma (24%), and thymoma (16%)[4]. Lymphoma is the most common anterior mediastinal tumor and more than 60% of the lymphoma are Hodgkin lymphoma [5]. The treatment of lymphoma and teratoma is based on chemotherapy, however surgical resection is essential management for thymoma. Recently, chemotherapy of invasive thymoma has been tried in adult. In adults, complete remission rate reported after the chemotherapy was 47% and partial response rate was 44% [6]. But there are only a few trial of chemotherapy for invasive thymoma in children. In one report of retrospective study of 36 pediatic thymoma and thymic carcinoma patients from the European Cooperative Study Group for Pediatric Rare Tumors, 3 patients of 16 thymoma patients received chemotherapy without surgery and only one patient with WHO type B1 thymoma showed partial response and, thymomas progressed in the other 2 patients [7].

In our case, patient was seven months old, and his growth and development was normal. He didn't show symptoms related to tumor and he has been growing normally without any other symptoms.

Like our patient, the majority of anterior mediastinal masses are diagnosed incidentally (about 50% of cases) and the prognosis of patient with symptoms are worse than patients without symptoms. If the symptoms present to the patients with anterior mass, they are usually more severe than patients with other region mass of mediastinum because the anterior mass can compress respiratory and cardiovascular systems. The most common pressure points of an anterior mediastinal mass on the respiratory system are trachea or carina. In comparison with respiratory symptoms, cardiovascular symptoms are less common. In cardiovascular symptoms, pericardial involvement and superi-

or vena cava (SVC) syndrome are included. SVC syndrome occurs in 1.5% of children and is an emergent symptom when tumor is involved.

If possible, thymoma and thymic carcinoma should be resected. In contrast, mass excision is not necessary for most of lymphoma, benign teratoma and thymic hyperplasia. However diagnosis is often difficult without open biopsy as shown in our case, so surgical biopsy was preferred in anterior mass of adults. According to Kent MS, et al, 27.8% of thymectomies were not needed for therapy and the most of them were thymic hyperplasia (13.3%) and lymphoma (3.8%)[8]. The yield of a transthoracic needle biopsy is low, and there is some risk of seeding on the pleural space with needle biopsy, so thymectomy is often undertaken on the clinical or radiographic suspicion of thymoma. However the incidence of thymoma is extremely low in children and the risk of morbidity and mortality in children's sternostomy is higher, open surgery in children is less preferred than in adults [8]. So, often we need to make diagnosis of the anterior mass of infant without open biopsy if the mass is not obvious thymoma. Hence imaging study is importnant in the diagnosis of antorior mediastinal mass, and wecan use chest X-ray, chest CT, MRI, and sometimes ultrasonography [9]. If lobular, homogeneous or slightly heterogeneous lesion is observed in CT images, thymoma should be considered first. In cases of lymphoma, multiple markedly enlarged or matted lymphnodes are shown on images. With large heterogeneous mass with lung metastasis, non-seminomatous germ cell tumor should be considered. Sometimes, clinical characteristics can be informative for the diagnosis, for example, a rapid onset of symptoms is suggestive of lymphoblastic lymphoma, intermediate onset Hodgkin lymphoma or mediastinal large cell lymphoma and a chronic onset tumors can sugest teratoma [10]. However image and cinical manifestations, and even biopsy results are sometimes insufficient for diagnosis such as our case, so there has been many needs for a to find new diagnostic marker. In one study, for distinguishing T-LBL separated from lymphocyte abundant thymoma, which could be confused pathologically, Jegalian AG et al. configured out that NOTCH1 intracellular domain could be diagnostic marker [3]. In conclusion, when pediatric patient has anterior mediastinal mass, lymphoma and germ cell tumor should be considered first. However we have to remember that the anterior mediastinal mass is rarely thymoma. Especially, differential diagnosis between the diseases are often difficult problem, so when the patient with anterior mediastinal mass do not present any symptoms or signs implying lymphoma or germ cell tumors, we need to consider thymoma.

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