



Case report

Thymolipoma associated with lymphocytosis in a 6-year-old girl: A case report



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ABSTRACT

Thymolipoma is a benign and rare tumor that could be found at any age. Thymolipoma associated with the myasthenia gravis, Graves disease, aplastic anemia, and hypogammaglobulinemia was reported previously, but in this case, thymolipoma is associated with lymphocytosis. A 6-year-old girl was brought to the hospital because of a chronic cough. Her evaluation revealed a 130 × 160 × 160 mm fat-containing soft tissue mass arising from anterior mediastinum with complete left lung collapse and contralateral mediastinal shift. Her past medical history showed that she had been evaluated and treated unsuccessfully due to severe lymphocytosis two years earlier. Her peripheral blood and bone marrow cell morphology were normal; in contrast, blood cell count and CD flow cytometry showed severe lymphocytosis. The patient's tumor was excised entirely without any complications, and lymphocytosis resolved during the follow-up period. Because the T lymphocytes are developed in the thymus, and more than 80% of cells in CD flow cytometry were T lymphocytes, and the lymphocytosis resolved with tumor removal; therefore, the authors suggested that Thymolipoma could be associated with lymphocytosis.

1. Introduction

Thymolipoma is an uncommon cause of anterior mediastinal mass that occurs at any age, but it is a rare condition in children. Therefore, there are not enough case series in children to explain its presentations, complications, and natural history. Thymolipoma could be asymptomatic; however, its mass effects in mediastinum can cause some manifestations. Patients with thymolipoma may have respiratory symptoms such as dyspnea and cough. Thymolipoma has been reported to be associated with conditions such as myasthenia gravis, Graves disease, aplastic anemia, and hypogammaglobulinemia, but in our patient, thymolipoma is associated with severe lymphocytosis that resolved with its excision.

2. Case presentation

A six-year-old girl was brought to Asthma and Allergy Clinic for

several weeks of dry cough without any improvement despite using cold medications, Amoxicillin-clavulanic acid, and azithromycin. Past medical history review showed that she had been evaluated and treated unsuccessfully for lymphocyte dominant leukocytosis without reaching any diagnosis two years earlier. At that time, her physical examination, peripheral blood cell morphology, blood biochemistry, bone marrow biopsy, and abdominal ultrasound had been reported normal. However, peripheral blood CD (cluster of differentiation) flow cytometry had shown that more than 85% of cells were mature T-lymphocytes (Table 1). Nevertheless, there was no chest x-ray report in her medical records, then She had been treated with Hydroxyurea because of lymphocytosis, but because of its ineffectiveness and lack of specific diagnosis, this drug had been discontinued after 18 months. Her Physical examination in our hospital revealed, weight was 14 kg (-3SD), her height was 110 cm (-1SD), heart and lung sounds were absent over the left hemithorax, chest percussion was dull on the left side, and resonance on the right side. The chest inspection showed bulging of the left

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Table 1
Hematology and CD flow cytometry results of the patient.

Date	Diagnostic Testing
2018	WBC = $30.23 \times 10^3/\mu\text{L}$, Neutrophils = 10.1%, Lymphocytes = 85.7%, Monocytes = 1.3%, Basophils = 0.2%, RBC = $4.94 \times 10^6/\mu\text{L}$, HGB = 13.5, HCT = 41, MCV = 83, MCH = 27, MCHC = 33, PLATELETS = $328 \times 10^3/\mu\text{L}$ ESR = 4
2018	Bone marrow flow cytometric immunophenotyping analysis: CD2 = 79.0%, CD3 = 52.9%, CD4 = 34.6%, CD5 = 70.9%, CD7 = 79.3%, CD8 = 42.0%, CD10 = 11.8%, CD13 = 3.9%, CD19 = 17.2%, CD20 = 21.9%, CD33 = 14%, CD34 = 3.4%, CD4/CD8(dual) = 3.1%, CD2/CD19(dual) = 0.9% Peripheral blood flow cytometric immunophenotyping analysis: CD2 = 93.1%, CD3 = 91.3%, CD4 = 44.1%, CD5 = 91.1%, CD7 = 91.4%, CD8 = 41.3%, CD19 = 5.2%, CD20 = 5.3%, CD22 = 5.0%, CD23 = 2.0%, CD34 = 0.3%, CD38 = 72.2%, CD45 = 96.4%, CD117 = 0.5%
2018	BCR-ABL(M-BCR) = Negative, BCR-ABL(m-BCR) = Negative, ETV6-RUNX 1 t (12,21) (p13,q22) = Negative, Inv(16) (p13,q22) = Negative
2020	Six months before tumor removal and under treatment with Hydroxyurea: WBC = $27.41 \times 10^3/\mu\text{L}$, Neutrophils = 4.7%, Lymphocytes = 92.5%, Monocytes = 2%, Eosinophils = 0.7%, RBC = $3.93 \times 10^6/\mu\text{L}$, HGB = 12.6, HCT = 38.1, MCV = 96.9, MCH = 32.1, MCHC = 33.1, PLATELETS = $355 \times 10^3/\mu\text{L}$ After one month of tumor removal: WBC = $6.2 \times 10^3/\mu\text{L}$, Neutrophils = 50%, Lymphocytes = 44%, Monocytes = 5%, Eosinophils = 1%, RBC = $4.86 \times 10^6/\mu\text{L}$, HGB = 12.5, HCT = 38.4, MCV = 79.0, MCH = 25.7, MCHC = 32.55, PLATELETS = $195 \times 10^3/\mu\text{L}$ ESR = 4

Hemithorax. There was no respiratory distress or cyanosis. Respiratory rate was 32 per minute, the heart rate was 93 per minute, blood pressure was 120/80, and her oxygen saturation by pulse oximetry was 92% in room air. The complete blood count result was severe lymphocytosis the same as two years earlier, and peripheral blood immunophenotyping demonstrated that 80% of cells were mature T cells. (Table 1).

The chest x-ray (Fig. 3) unveiled diffuse opacification of the left Hemithorax with the contralateral mediastinal shift. The chest spiral computed tomography with intravenous contrast showed a $130 \times 160 \times$

160 mm heterogeneous fat-containing soft tissue mass arising from anterior mediastinum with complete left lung collapse and contralateral mediastinal shift with no evidence of peripheral organs invasion or adjacent bony chest wall destruction or encasement or involvement of major mediastinal vessels (Fig. 1).

Needle biopsy under ultrasound guide performed, but it was not helpful because of not providing enough tissue for diagnosis; consequently, an open biopsy was recommended. The open biopsy result was a yellow tissue with elastic consistency on its macroscopy, and its microscopy was abundant mature adipose tissue with less amount of mature thymus tissue (10% of total tissue) without any evidence of malignant changes, as a result, based on open biopsy, the diagnosis of thymolipoma was made, and tumor excision was recommended (Fig. 2). Abdominal ultrasound was normal, and there was no splenomegaly,



Fig. 2. High power view of patient's removed mass.

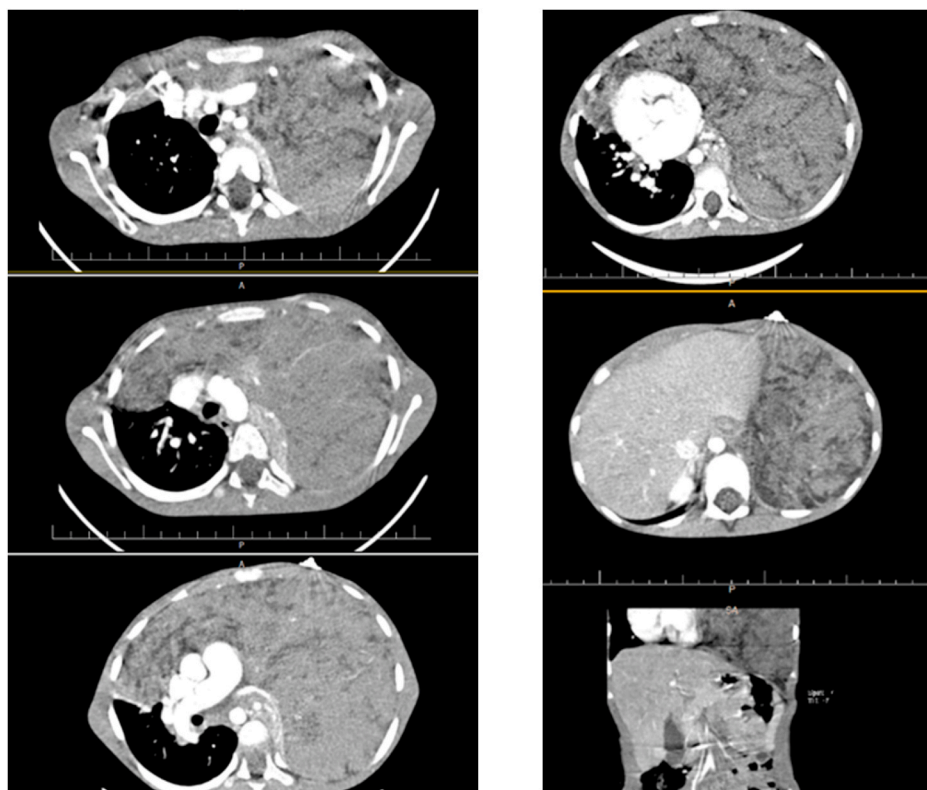


Fig. 1. Chest computed tomography of the patient.

hepatomegaly, or lymph node enlargement.

The tumor was excised entirely via median sternotomy and lateral thoracotomy, and after two days of stay in the pediatric intensive care unit, the child was transferred to the surgical ward, and then the chest tube was removed. After ten days of rehabilitation, the left lung expanded entirely (Fig. 3), and the patient was discharged home without any complications. After a 1-month follow-up, chest x-ray was normal, and the lymphocyte count was normalized. There were not any adverse or unexpected events during treatment and follow-up.

3. Discussion

The absent breath sounds over a hemithorax could be a sign of a fatal condition such as tension pneumothorax, but other less severe diseases such as simple pneumothorax, pleural effusion, and complete one lung atelectasis could have the same presentation. When heart sounds only can be auscultated over the right hemithorax, dextrocardia is a non-serious diagnosis. However, when the heart and breath sounds are absent simultaneously on the left side, more critical conditions that are accompanied by mediastinal shift must come first into mind because of their capability to have fatal consequences. Chest percussion can differentiate tension pneumothorax from the presence of liquid in pleural space or thoracic mass in a patient without heart and breath sounds over a hemithorax. Tension pneumothorax has hyper resonance sound on percussion, but liquid in pleural space and thoracic mass have dull sound on percussion.

The normal lymphocyte count in a person is dependent on her or his age, which is about 5500–7000 per microliter in infancy and is decreased to about 2000–2400 per microliter in adulthood [1]. Lymphocytosis could be caused by a reactive or lymphoproliferative disorder (Table 2).

The main difference between these two groups is that the lymphocyte population is polyclonal in reactive lymphocytosis but is monoclonal in lymphoproliferative disorders. Lymphocytes include B-cell, T-cell, and natural killer (NK) cells that are effector cells in adaptive immunity [2]. Adaptive immunity can be classified into humoral and cell-mediated immunity. The effector function of the B-lymphocytes is humoral immunity, and their primary development site is bone marrow. In contrast, the effector function of the T-lymphocytes is cell-mediated immunity, and their primary development site is in the thymus. The B-lymphocytes express CD 19, CD 22, and FcR, whereas the T-lymphocytes express CD2, CD 4, CD 8, and CD 28 on their surface [3].

The evaluation of the lymphocytosis in children starts with a complete history and physical examination, besides complete blood cell counts with their morphology assessment. Lymphocyte morphology can

Table 2
Causes of lymphocytosis [4].

Reactive	Infections	
		Viral: Any infection with Epstein-Barr virus, any infection with Cytomegalovirus, Mononucleosis syndrome (adenovirus type 12, herpes virus-6), HIV-1 infection (during early seroconversions associated with CMV) (chronic, associated with post-splenectomy state), HTLV-1 associated benign T cell lymphocytosis, mumps, varicella, influenza, hepatitis, rubella, roseola, Infectious lymphocytosis (coxsackievirus B2, enteroviruses including poliovirus, others)
		Bacterial: Pertussis, (Occasional) cat scratch fever, tuberculosis, brucellosis, syphilis
		Protozoal: Toxoplasmosis
		Parasitic: Babesiosis
		Drug-induced, Serum sickness
		Post-trauma, Post-splenectomy, Cigarette smokers
	Hypersensitivity Stress	
	Autoimmune	Lymphocytosis of large granular lymphocytes, Rheumatoid arthritis, Malignant thymoma
	Endocrine	Hyperthyroidism
lymphoproliferative	B-cell neoplasms	Small lymphocytic lymphoma, Lymphoplasmacytic lymphoma, Follicular lymphoma, Burkitt's lymphoma, Diffuse large B-cell lymphoma, Mantle cell lymphoma, Hairy cell leukemia, Precursor B lymphoblastic leukemia/lymphoma
	T-cell neoplasms	T-cell large granular lymphocyte leukemia, T-cell prolymphocytic leukemia, Peripheral T-cell lymphoma, Anaplastic large cell lymphoma, T/null cell, Adult T-cell lymphoma/leukemia, Precursor T lymphoblastic leukemia/lymphoma
	Natural killer cell neoplasms	Natural killer cell large granular lymphocyte leukemia

help to differentiate the causes of lymphocytosis. Atypical lymphocytes that are large lymphocytes with basophilic cytoplasm with a large nucleus could be seen in infectious diseases caused by Epstein-Barr virus, cytomegalovirus, coxsackievirus B2, HIV, HTLV-1, mumps, varicella,

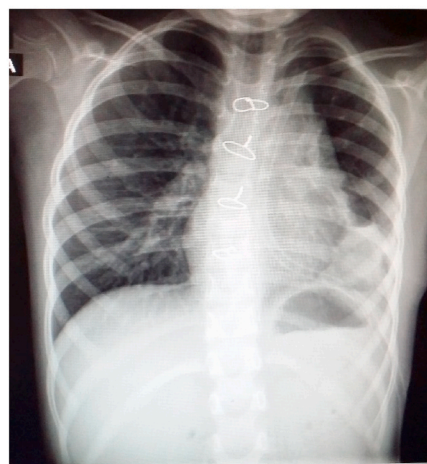
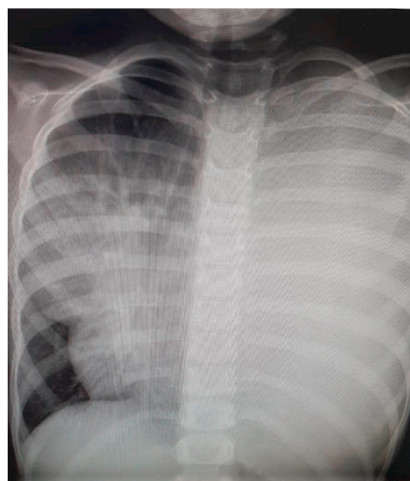


Fig. 3. Chest x-ray of the patient before (left) and after (right) tumor excision.

influenza viruses, and also in hepatitis, rubella, and roseola. Lymphocyte morphology, CD flow cytometry, gene rearrangement analysis could also be helpful in the diagnosis of lymphocytosis due to lymphoproliferative disease [4].

Thymolipoma is a benign tumor that the patient's problems resolve completely with its removal. This tumor consists of mature thymic and adipose cells. Therefore, Some Authors believe that thymolipoma is a hamartoma; however, others believe it is an adipose tissue tumor. Thymolipoma is associated with an HMGA2 gene translocation in locus 12q15, which could be found in two-thirds of all other lipomas; accordingly, this association supports the assumption that thymolipoma could be an adipose tissue tumor [5]. However, lipoma as an adipose tissue tumor is not associated with autoimmune disease (e.g., Myasthenia gravis) or T cell lymphocytosis. In contrast, thymomas are associated with autoimmune disorders such as myasthenia gravis and are sometimes associated with T cell lymphocytosis [6–8]. Therefore in our case, thymolipoma has characteristics of thymoma. The incidence of thymolipoma is about 0.12 in 100,000 of the population; consequently, it is recognized as a rare tumor. This tumor could occur at any age, but it is often seen in the third and fourth decades. Thymolipoma affects both sexes equally, and it is the cause of thymic tumors in 2–9% of cases. Thymolipoma usually is found accidentally in a chest x-ray that is taken for other reasons, but sometimes it presents because of its mass effects, which could present as chest pain, hoarseness, cyanosis, and cough. Thymolipoma can be associated with myasthenia gravis, graves disease, aplastic anemia, and hypogammaglobulinemia [9–11]. Chest computed tomography shows Thymolipoma as a mediastinal mass with plenty of fat, which has low attenuation with negative Hounsfield unit value. Thymolipoma grows steadily yet retains the thymus configuration and could weigh between 10 and 6000 g. Its microscopy comprises the mature thymus and adipose cells [12]. Thymolipoma differential diagnosis includes lipoma, differentiated liposarcoma, thymic hyperplasia [13], and thymoma. Hale described thymolipoma for the first time in 1949 [14]. Moran et al. have reported a case series of 33 patients with thymolipoma. In their study, age ranged from 2 to 64 (mean, 33) years, and there was no sex preference, and more than half of all patients were asymptomatic, but the less common manifestations were upper respiratory symptoms, chest pain, myasthenia gravis, and neck mass [12]. Shirkhoda et al. described thymolipoma in a 14-year-old girl with diffuse opacification of the hemithorax in chest x-ray, large adipose tissue mass in chest CT, and MRI in 1987. They asserted that MRI could detect adipose tissue in thymolipoma with its high signal intensity on T1 weighted imaging and loss of its signal in fat-suppressed imaging [15]. Beaton et al. reported a case of thymolipoma in a patient with graves disease in 1966 [16]. Rachel et al. have investigated the pathogenesis of thymolipoma by cytogenetic analysis of one case of thymolipoma in a 27-year-old healthy woman. They have found translocation on chromosomes 12q15. Therefore they have suggested that thymolipoma is a neoplasm of thymic fat [5]. Otto et al. examined 72 thymic tumors and found five (7.5%) thymolipoma cases. Among those who had thymolipoma, one patient had erythrocytic hypoplasia in addition to hypogammaglobulinemia, and one other patient had myasthenia gravis [17]. Matsuyama et al. reported a case of thymolipoma in a 46-year-old man with a chest x-ray similar to cardiomegaly, but further investigation by chest CT revealed mediastinal mass near the left ventricular wall. After thoracotomy and the tumor excision, the diagnosis of thymolipoma was made [18].

4. Conclusions

Our patient had lymphocytosis for two years by normal lymphocyte morphology, healthy bone marrow, and 80% mature T-lymphocyte in CD flow cytometry, which her lymphocytosis resolved thoroughly after thymolipoma removal. Therefore, the authors suggested that thymolipoma in this patient is associated with lymphocytosis. This case shows that thymolipoma other than myasthenia gravis, Graves' disease,

aplastic anemia, and hypogammaglobulinemia that all of them have been reported previously may be associated with lymphocytosis. The authors declare that there is no conflict of interest, and parents' written consent for sharing their child's medical records is obtained. The authors did not receive any funding.

Declaration of competing interest

The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.rmcr.2020.101312>.

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