

Case Report

Massive Thymic Hyperplasia Mimicking Lymphoma: A Case Report and Review of Literature

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Purpose: A case of massive thymic hyperplasia presenting as a large anterior mediastinal mass is reported. **Patient:** A 4-year-old Thai boy presented with an acute febrile illness and respiratory symptoms and later transferred to our institute when an anterior mediastinal mass with right upper lung infiltration was detected in chest roentgenogram. **Results:** A computed tomography scan of the chest revealed a large homogenous anterior mediastinal mass. All laboratory studies for the patient including routine hematology, chemistry studies as well as biological tumor marker studies such as alpha-fetoprotein, beta-human chorionic gonadotropin and lactic dehydrogenase were within normal limits. A bone marrow aspiration showed no evidence of malignancy. The diagnosis was made by an open incision biopsy, which showed normal thymic tissue. The patient was discharged without any medication and asked to follow-up three weeks later. On his return, his thymic image showed a spontaneous resolution in size. **Conclusions:** Massive thymic hyperplasia is a rare cause of mediastinal mass during the first two decades of life, however, should be considered in the differential diagnosis especially if there is no evidence of mass compression or any positivity of tumor markers.

Key Words: ● Massive thymic hyperplasia ● Anterior mediastinal mass

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Massive thymic hyperplasia is a rare condition during the first two decades of life but

must be considered in the differential diagnosis of an anterior mediastinal mass.¹ The majority of mediastinal masses in this age group are malignant, mostly Hodgkins and Non-Hodgkins lymphoma.² Less than 5% of mediastinal masses are of thymic origin. We report

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here a child who presented with a large anterior mediastinal mass resulting from massive thymic hyperplasia with spontaneous resolution.

Case report

A 4-year-old boy first presented with an acute febrile illness and respiratory symptoms. Physical examination was normal except for mild dyspnea, medium crepitation and slight wheeze in both lungs. He was treated for pneumonia and wheezing associated respiratory tract infection (WARI) and later transferred to our institute when an anterosuperior mediastinal mass with right upper lung infiltration and atelectasis was detected in chest roentgenogram. (Fig. 1) Subsequently, a computed tomography scan of the chest (Fig 2) revealed presence of homogenous anterior mediastinal mass occupying almost the whole upper third of both hemithorax.

The patient had had a multiple episodes of WARI since one year of age. Previous chest roentgenograms were normal. All laboratory studies for the patient, including routine hematology, chemistry studies as well as biological tumor marker studies such as alpha- fetoprotein, beta-human chorionic gonadotropin and lactic dehydrogenase were within normal limits (Table 1).

A Bone marrow aspiration showed no evidence of malignancy. The patient was

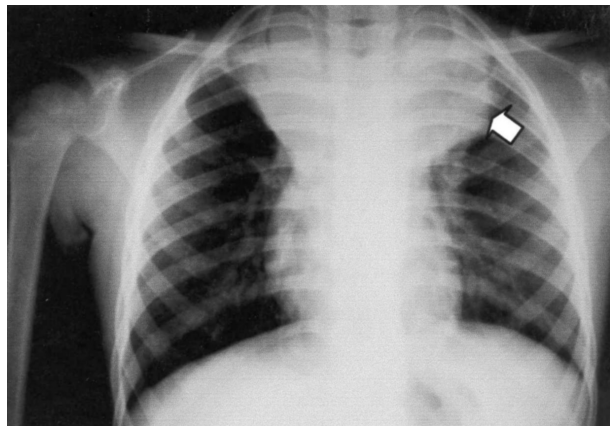


Fig 1 The AP chest radiograph showed a large mediastinal mass (white arrow) which looked like a tumor. Minimal infiltration in the upper lobe of right lung was observed. Note that the trachea was not compressed by the mass.

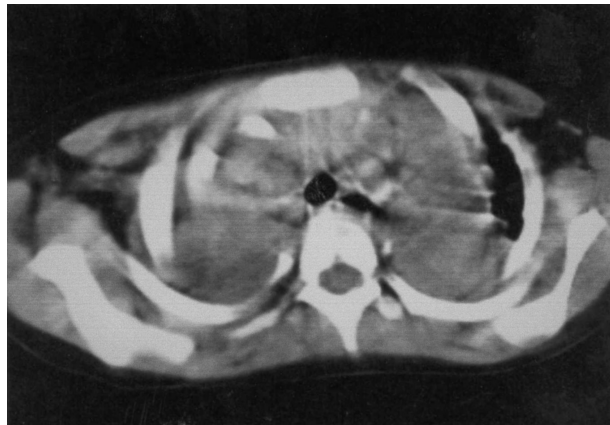


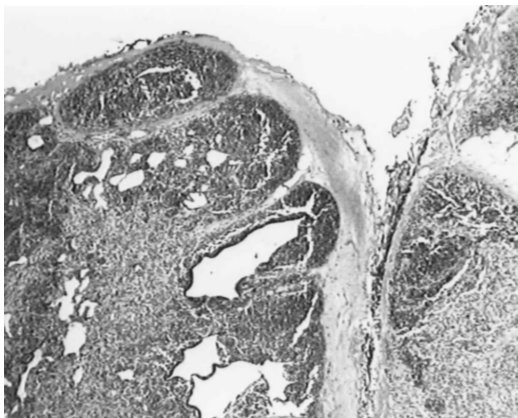
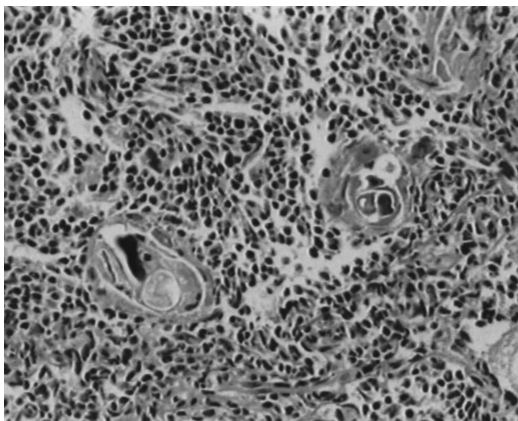
Fig 2 Computed tomography of the chest revealed the homogeneity of the large anterior mediastinal mass. Its margin was well defined and cannot be distinguished from the normal thymus.

consulted for surgical evaluation. An open biopsy specimen showed normal thymic architecture.

Pathological findings: Grossly, the specimen from incisional biopsy appeared as 3 pieces of grayish brown and rubbery tissue ranging from 1-1.5 cm. Microscopically, sections demonstrated lobules of thymus

Table 1 Laboratory investigations

CBC	Hb 10.1 g/dL Hct 34.8% WBC 8,000/ μ L (L 39% N 38% M 4% AL 12%) plt 380,000/ μ L
Electrolyte	Na 140 mM/L K 3.9 mM/L Cl 104 mM/L Co ₂ 20 mM/L Ca 9.1 mg/dL PO ₄ 3.6 mg/dL Uric acid 1.5 mg/dL Mg 0.83 mM/L
BUN/Cr	4/0.5 mg/dL
Alpha fetoprotein	1.2 (N 0-10 IU/mL)
Beta HCG	<3 (N < 5 mIU/mL)
LDH	605 (N 203-537 U/L)

**Fig 3** Pathological sections demonstrated lobules of thymus gland.**Fig 4** Pathological sections revealed numerous Hassall's corpuscles

gland characterized by lobules of mixed lymphoid cells and thymic epithelial cell (Fig 3). Hassall's corpuscles were frequently noted (Fig 4). Immunostaining for CD3 and Tdt was done and confirmed that the lymphoid cells were T-lymphoblastic cells normally existing in thymic cortex. Thymic epithelial cells were positive for keratin as usual. The findings were consistent with normal thymus gland. Together with radiographic image of huge mediastinal mass, it was considered that the mass represented massive thymic hyperplasia.

The patient was discharged without any medications. Three weeks later, the patient remained well and radiologically the thymic image showed a spontaneous resolution in size. (Fig 5)

Discussion

Normal thymus gland weighs 10 to 35 grams at birth and reaches a maximum weight of 50 grams between the ages of 11 and 16 years.³ Hyperplasia of the thymus is the most common anterior mediastinal mass in infants but is much less common than lymphoma and teratoma in

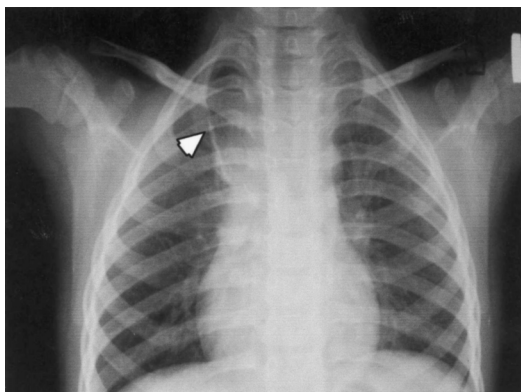


Fig 5 The mediastinal mass which was noted in figure 1 was spontaneously and almost totally disappeared. Minimal residual right upper lobe atelectasis (arrow head) was demonstrated.

the older children. Massive thymic hyperplasia is a rare idiopathic variant of true thymic hyperplasia⁴, in which the gland achieves massive proportions exceeding those usually seen in the normal thymic hyperplastic response to development or after severe systemic stress. Massive thymic hyperplasia has not been reported in several of the large series of mediastinal tumors published in recent years.^{5,6} Up to now, there were only 36 recorded cases in the world literature and all the reported patients were less than 16 years of age with 75% below the age of 10 years.^{7,8}

The diagnosis of massive thymic hyperplasia is made only after demonstrating that the weight of the hyperplastic gland exceeds the maximum thymic weight in children and adolescents. Nevertheless, it is difficult to evaluate thymic hyperplasia by the weight of gland.⁴ Hyperplastic thymic usually weighs 200 to 500 grams range. The largest gland reported

weighed 1,260 grams.⁷ This condition occurs in immunologically normal children⁹ as in our case; however it has been described in patients after thermal burn¹⁰, with hypothyroidism¹¹, hyperthyroidism¹² or after mediastinal radiation or systemic chemotherapy for various malignancies.^{13,14} Most cases are idiopathic, but the underlying pathophysiologic mechanism may be due to the stress.

Clinically, massive thymic hyperplasia is characterized by the followings : asymptomatic enlargement of the anterior mediastinum (38% of cases), symptomatic mass causing respiratory distress, dysphagia, airway obstruction (29% of cases) and acute or recurrent pulmonary infection (35% of cases) which is the presenting symptom in this case. Laboratorily, preoperative peripheral lymphocytosis (29% of cases), with counts decline to normal after thymectomy⁷ is characteristic finding, but this was not present in this case.

Histologically, massive thymic hyperplasia is defined as thymic gland enlargement without alteration of normal histology and must be differentiated from another form of thymic hyperplasia; lymphoid follicular hyperplasia; which is characterized by presence of lymphoid follicles with germinal centers. This condition is frequently found in patient with myasthenia gravis and autoimmune diseases.⁴ In addition, though the immunohistological appearance of massive thymic hyperplasia is similar to that of normal thymus¹⁵, the cytoenzymatic studies have demonstrated a quantitative reduction in ma-

ture T cells in both cortical and medullary areas.¹⁶ Anyhow, cellular analysis showed no evidence of clonal growth of this tumor by examining thymocyte and stromal growth characteristics in vitro and in response to cytokine stimulation.⁹

Radiographically, the appearance of the normal thymus gland in a large series reviewed by Tausend and Stein has not shown prominence on either side in approximately 50% of thymus; but in the remaining 50%, right-sided prominence was more common than left. Interestingly, the often described "sail sign" was seen in less than 5% of their cases with the prominent right or left lobe. Indentation of the tissue by the anterior ribs is a characteristic of normal thymic tissue and is a helpful sign.¹⁷ In this case, the chest roentgenogram showed no prominent on either side, the sail sign and indentation of the tissue by the anterior rib were not present. Computed tomography scan is helpful for localization and for defining relationships to other structures. There are no pathognomonic computed tomography scan features attributed to massive thymic hyperplasia, and the hyperplastic thymus remains the features of normal thymus on computed tomographic scan irrespective of size.^{18,19} Computed tomographic scan is as accurate as magnetic resonance imaging in cases of homogeneous mass; but in cases of inhomogeneous mass, magnetic resonance imaging is more useful in demonstrating the abnormalities such as infiltrating lesion thus help differentiating the condition.²⁰

In the past, management is directed at establishing a histological diagnosis surgically because there is no reliable non-invasive method to differentiate massive thymic hyperplasia from the other causes of anterior mediastinal mass, particularly lymphoma and thymoma. In most reports in the literature, patients underwent surgical excision of the mass.⁷ It is our opinion that cases of anterior mediastinal mass of which imaging suggests homogeneous mass without evidence of tracheal compression or deviation of mediastinal structure, should be managed conservatively if tumor marker showed negative findings. Investigations with an incisional biopsy to confirm pathologic diagnosis is relevant if there is progression in the size of mass.

In this case we found the rapid spontaneous resolution of mass in three weeks after diagnosis, which is different from the literature that reported the glands to undergo atrophy very slowly with little or no change in size after months or years.^{7,19,21} No explanation can be made for this interesting observation. In case of massive thymic hyperplasia, conservative management with close follow-up may be the appropriate strategy.

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บทคัดย่อ: รายงานผู้ป่วยเด็กชายไทยอายุ 4 ปี มาด้วยไข้ ไอ หอบ การตรวจร่างกายมีอาการเหนื่อย crepitation และ wheeze ที่ปอดทั้งสองข้าง ได้รับการรักษาแบบปอดบวม และ wheezing associated respiratory tract infection (WARI) อาการไม่ดีขึ้น การตรวจฟิล์มเอกซเรย์ปอดและคอมพิวเตอร์ทรวงอก พบก้อนขนาดใหญ่ในทรวงอกทางด้านหน้า การตรวจทางห้องปฏิบัติการทั้ง complete blood count อิเล็กโทรไลต์และเมตาบอลิก รวมทั้ง tumor markers พบว่าผลอยู่ในเกณฑ์ปกติ การตรวจไขกระดูกก็พบว่าปกติเช่นกัน ได้ทำการผ่าตัดเพื่อนำชิ้นเนื้อนั้นมาวินิจฉัยโรค พบว่าเข้าได้กับต่อมไธม์สปกติ จึงสรุปว่า ผู้ป่วยรายนี้เป็น thymic hyperplasia ที่มีขนาดใหญ่ ได้ให้การรักษาแบบประคับประคอง 3 สัปดาห์ต่อมา ผู้ป่วยเด็กสบายดี และการตรวจฟิล์มเอกซเรย์ปอดซ้ำพบว่าขนาดก้อนยุบลงจนเป็นปกติดี ดังนั้น ผู้ป่วยเด็กที่มาด้วยก้อนในทรวงอก หากพบวก้อนไม่มีการกดเบียดอวัยวะใกล้เคียง และการตรวจ tumor markers ให้ผลลบ ควรคำนึงถึงภาวะนี้ด้วย

Key Words: ● Massive thymic hyperplasia ● Anterior mediastinal mass

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ดอกสร้อยพลอยคน

คนเอ๋ยคนจ๋า

คนที่มา	ทำที่	มีดวงเหงา
ปัจจัยสี่	มีใช้	ไม่บรรเทา
ยังมีเจ้า	ขาดของ	ที่ต้องการ
คนเก่าเก่า	เขวว่า	น่าสับสน
หากหาได้	ตกลง	ถึงข้าวสาร
แต่ว่าคน	เหลือขอ	ทรมาณ
อยากขึ้นบาน	อื่นใด	ปล่อยไปเอย

หลวงตาม้าขาว