HYPERPLASIA OF THYMIC GLAND

Y M Lee, M T Koh, A Omar, A Majid

ABSTRACT

Hyperplasia of the thymus is the most common anterior mediastinal mass in infants. It is however exceedingly difficult to evaluate by the weight of the gland as it continues to grow after birth until puberty and thereafter undergoes progressive atrophy. It normally maintains most of the radiographic characteristics of the normal thymus. Massive thymic hyperplasia, a rare variant of true thymic hyperplasia is extremely rare during the first two decades of life and clinically can cause mediastinal compression or acute and recurrent pulmonary infection. Two such cases are reported and the clinico-pathology is briefly described and discussed.

Keywords: *massive thymic hyperplasia*

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INTRODUCTION

Hyperplasia of the thymus is the most common anterior mediastinal mass found in infants. Its variant, massive thymic hyperplasia (MTH) however is extremely rare during the first two decades of life and must be considered in the differential diagnosis of anterior mediastinal tumour. We report two such cases which were encountered in 1993 and 1994 respectively.

CASE REPORTS

Case 1

A three-month-old baby girl first presented with febrile illness and upper respiratory symptoms which failed to resolve with conservative medical treatment. Subsequent radiological examination of the chest including computed tomographic (CT) scan (Fig 1) revealed presence of a homogenous anterosuperior mediastinal mass occupying almost the whole upper third of the left hemithorax. Peripheral blood smear revealed a lymphocytosis of 79% of 16.2 x 10^9/L. Examination of a biopsy of the mass taken through a left mediastinotomy showed small lymphoid cells arranged in a diffused pattern with occasional follicle and presence of rare ill-formed Hassall's corpuscles. No further action was taken and the patient remained well and radiologically the thymic image remained unchanged at a follow-up one year after the surgery.

Case 2

An eleven-month-old male infant weighing 8 kg first presented with a 10-day history of febrile illness and upper respiratory symptoms. Preliminary chest radiography (Fig 2) and subsequent CT scan of the thorax (Fig 3) revealed almost complete occupation of left hemithorax by a homogeneous anterior mediastinal mass resulting in shifting of mediastinum to the right.

Department of Surgery
University of Malaya
Lembah Pantai
59100 Kuala Lumpur
Malaysia

Y M Lee, FRCS (Eng)
Lecturer

A Majid, FRCS (Edin)
Professor and Head of Department

Department of Paediatries
University of Malaya

M T Koh, MRCPaed (UK)
Lecturer

A Omar, MRCPaed (UK)
Associate Professor

Correspondence to: Dr Y M Lee

Fig 1 – CT scan revealing presence of a homogenous anterosuperior mediastinal mass occupying the upper third of the left hemithorax.

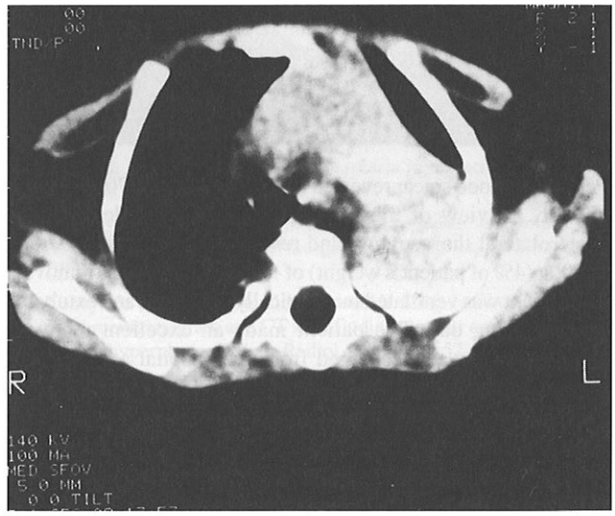


Fig 2 – Chest X-ray showing complete occupation of the left hemithorax by the mediastinal mass and shifting of the mediastinum to the right.

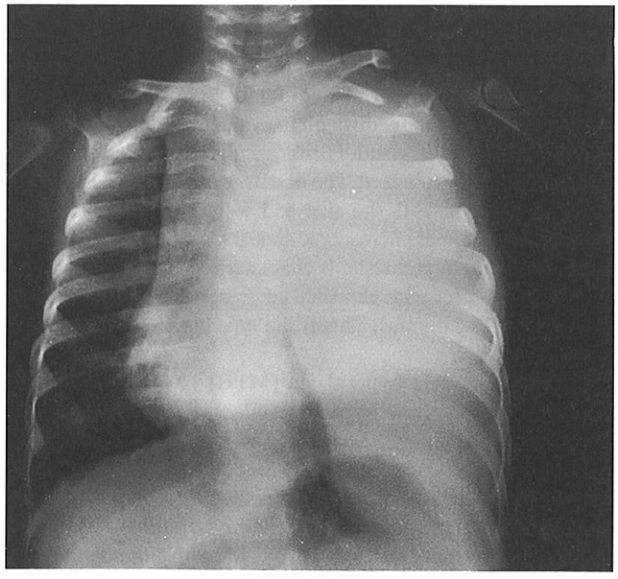
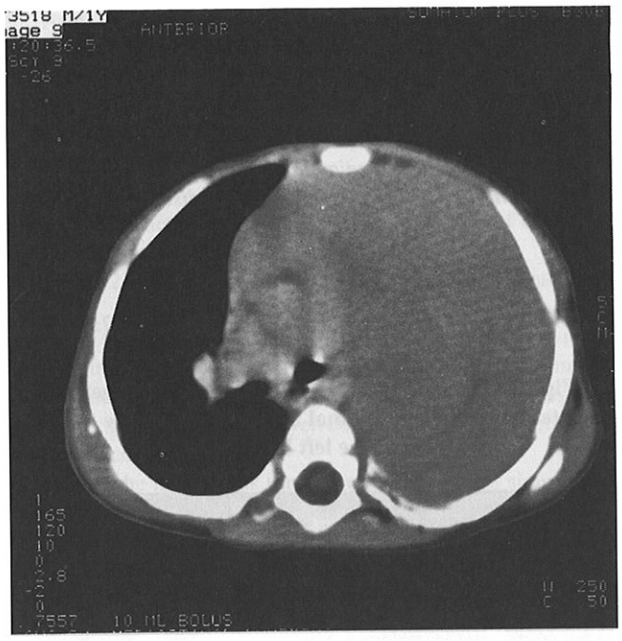


Fig 3 – CT scan showing complete occupation of the left hemithorax by the mediastinal mass and hypoplasia of the left lung.



Peripheral blood smear revealed a lymphocytosis of 70% of 37.80 x 10^9/L. In view of this finding, our patient underwent left posterolateral thoracotomy and resection of the lesion. A total of 500g (4% of patient's weight) of 'tumour' tissue was removed. The patient was ventilated mechanically overnight and extubated the following day. The patient made an excellent recovery thereafter and was discharged from the hospital a week later. Repeated chest radiography following surgery showed gradual re-expansion of the left lung and shifting of the mediastinum to the centre of the chest. Histopathological examination showed thymic tissue which was composed of numerous hyperplastic lymphoid follicles with the corresponding epithelial component and Hassall's corpuscles. The tissue was generally congested and no evidence of neoplasia was seen. The interpretation was consistent with diagnosis of massive thymic hyperplasia.

DISCUSSION

The thymus is embryologically derived from the third and fourth pairs of pharyngeal pouches. At birth, it weighs 10 to 35 gm and continues to grow in size until puberty, when it achieves a maximum weight of 10 to 50 gm[1]. It undergoes progressive atrophy after that, to no more than 5 to 15 gm in the elderly. The rate of changes is extremely variable, and therefore it is difficult to determine the weight of the thymus appropriate for age[2]. Hence, it is exceedingly difficult to evaluate thymic hyperplasia by the weight of the gland. Histologically, two types of thymic hyperplasia are recognised. The first, true hyperplasia, is defined as an increase in both the size and weight of the gland with retention of a normal microscopic appearance for age. The second type, lymphoid hyperplasia, is characterised by the presence of lymphoid follicles with germinal centres, regardless of the size or weight of the thymus. This is the type classically associated with myasthenia gravis.

Massive thymic hyperplasia (MTH) is a rare idiopathic variant of true thymic hyperplasia[2]. Besides the two cases described in this report, 33 cases had been previously reported[3]. It achieves massive proportions far exceeding those usually seen in the normal thymic hyperplastic response to development or after severe systemic stress. As there are no generally accepted criteria for defining "massive", the following guidelines are suggested for the definition of MTH[3]: (1) It should be greater than the heart shadow on posteroanterior chest radiograph. (2) The thymus should weigh several times the expected weight for the age of the patient. (3) It should represent more than 2% of the body mass. As in thymic hyperplasia, generalised hyperplasia with preservation of the normal thymic architecture is present in MTH and it occurs in the absence of known provocative systemic stress[2,4]. In this aspect, it is different from lymphoid follicular hyperplasia of myasthenia gravis, from thymoma, and from thymic lymphoma by the absence of germinal centres, the absence of neoplastic cells, and the preservation of normal thymic histology. In addition, although the immunohistological appearance of MTH is similar to that of normal thymus[4], cytoenzymatic studies have shown a quantitative reduction in mature T cells in both cortical and medullary areas[5].

Hyperplastic thymus still normally maintains most of the radiographic characteristics of the normal thymus[6]. There is often a change in shape between supine and upright radiographs. Fluoroscopic examination usually demonstrates an apparent increase and decrease in size with expiration and inspiration. With the exception of MTH, there is usually no evidence of tracheal compression or deviation of mediastinal structures. Nonetheless, recognition of an anterior mediastinal mass as thymus is complicated by the variability of its appearance. In a report by Tausend and Stein[7], there was no prominence on either side in approximately 50% of thymus reviewed; and 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 a prominent right or left lobe. Indentation of the tissue by the anterior ribs is characteristic of normal thymic tissue and is a helpful sign. The distribution of fat density on the CT appears to be distinct from other fat-containing mediastinal lesions[8]. For instance, teratomas often have rounded or discrete areas of fat, and lipomas and thymolipomas are of predominately fat density. This difference may be useful in differentiating these lesions.

Clinically, thymic hyperplasia must be considered in a child with an anterior mediastinal mass, along with other anterosuperior mediastinal lesions including teratoma, lymphosarcoma, lymphangioma, haemangioma, substernal thyroid and thymic tumour. Presenting symptoms may influence the provisional diagnosis. Thymic enlargement is generally asymptomatic[9], though mediastinal compression, ie respiratory distress, dysphagia and airway obstruction and acute or recurrent pulmonary infection have been reported with MTH[3,10].

It is important to distinguish MTH from thymoma as it has immense prognostic impact, particularly in the paediatric age group. Unlike MTH, histopathologically, thymomas[2] usually are surrounded by a thick fibrous capsule and subdivided by fibrous trabeculae into irregular lobules which lack cortical-medullary zonation. Well-developed Hassall's corpuscles can be identified only rarely. Clinically, the outlook of thymomas occurring in the first two decades of life is sinister[11], especially those with anaplastic appearance and characterised by rapid local growth, low incidence of surgical resectability, and early metastasis[12]. On the other hand, MTH seems amenable to complete surgical extirpation and has not yet been associated with an unfavourable outcome.

Another anterior mediastinal mass to be considered in the differential diagnosis of MTH is so-called thymolipoma[13]. This lesion is poorly understood and it is uncertain as to whether it results from hyperplasia of one or both tissue components (ie, thymic parenchyma and fat) or whether it is indeed a true neoplasm of mixed type, as originally proposed. The pathological anatomy is not well-illustrated or defined, and it is conceivable that many thymolipomas are examples of true thymic

hyperplasia[14].

Thymolytic effects of steroids and their use as a technique to evaluate the enlarged cardiothymic shadow are well-documented[15,16]. Unfortunately, this test is inconsistent[17] and lacks specificity. Lymphoid tissue will also show the effects of steroids, and both normal thymic tissue and lymphomas may show rebound growth after the termination of steroid[18]. As there is no reliable method to differentiate thymic hyperplasia, especially the rare variant MTH, from other causes of massive anterior mediastinal mass, particularly thymoma and lymphoma, it is essential to establish a histological diagnosis in the management of thymic hyperplasia. This can be achieved with an incisional biopsy through an anterior mediastinoscopic window or limited thoracotomy, or excisional biopsy through a posterolateral thoracotomy. The latter is preferred especially in MTH which causes mediastinal compression. Moreover, MTH, if left unresected, are noted to undergo atrophy very slowly with reports of little or no change in size after months or after two years[3,19,20]. This is also noted in our first case and emphasises the need to monitor the patient closely if left untreated before it could possibly develop into airway obstruction and mediastinal compression.

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