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Massive thymic hyperplasia in an adult: A rare case report and literature review

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ABSTRACT

INTRODUCTION: Massive thymic hyperplasia is an extremely rare disorder, with fewer than 60 cases reported so far. Majority of the previous cases occurred in neonates, infants, and older children.
PRESENTATION OF CASE: A man was found to have an anterior mediastinal mass without any symptoms at 30 years of age. Operation was done successfully. The mass measured 112 mm × 191 mm × 184 mm and weighed 2141 g. Histological and immunohistochemical findings further confirmed the diagnosis of massive thymic hyperplasia. The complication of postoperative chylothorax occurred, which has not been previously reported in MTH. After undergoing conservative treatment, the patient finally recovered.
DISCUSSION: This is the first case of massive thymic hyperplasia reported in an adult (defined as ≥ 18 years old). Chylothorax is one of the potentially fatal complications. However, we carried out effective treatments, which are educational and clinically interesting to surgeons and clinicians.
CONCLUSION: Although not previously reported, massive thymic hyperplasia could also be found in adults. The main treatment for massive thymic hyperplasia is surgical removal. Good clinical effects on post-thymectomy chylothorax are available after undergoing conservative treatment.

1. Introduction

Most of the cases of massive thymic hyperplasia (MTH) have been characterized by enlargement in size, as well as increase in weight, of the thymus gland beyond the normal upper limit, without any known provocative systemic stress [1]. MTH is uncommon in adults and is usually found in newborns and younger children. Though the majority of cases were managed with surgical treatments, complications occurred rarely [2]. Although chylothorax after thymectomy in the treatment of myasthenia gravis has been previously reported, it was rare in cases of MTH. To the best of our knowledge, only 7 cases have been previously reported. However, neither perspective nor randomized studies were performed, so guidelines were not available for chylothorax so far. Here we present a special case in an adult, who was treated operatively, and developed the postoperative complication of chylothorax. This case has been reported in line with the SCARE criteria [3].

2. Case presentation

A 30-year-old male, a worker in China, was noted to have a large anterior mediastinal mass in his left thoracic cavity, with no symptoms. Physical examination was performed and we found absent breath sound and dull percussion in the left hemithorax in comparison with the right side. His past medical history was uneventful. Computed tomography (CT) revealed the mass to be 112 mm × 191 mm × 184 mm in size, located in the left anterior mediastinum, with a primary consideration of a lipoma (Fig. 1). Although it occupied most of the left hemithoracic cavity and caused segmental atelectasis and pneumonia as the CT revealed, he remained asymptomatic. The mass was adherent to the pericardium and the great vessels, but did not invade the adjacent structures. Left posterolateral thoracotomy was performed. During surgery, a tumor weighing 2141 g (Fig. 2), with the pedicle originating from the upper thymus gland on the left side, was excised. Microscopically, normal thymic tissue, normal thymic architecture, and adipose cells were demonstrated, and the ratio of adipose cells to thymocyte cells was approximately 7:3. Neither the presence of lymphoid cells with germinal centers nor evidence of malignancy was found (Fig. 3 A, B). On immunohistochemistry, the cells were diffusely positive for Ki67 and TdT and focally positive for CK19, CK5/6 and P63, while they were negative for TG and TTF1 (Fig. 3C–I).

Abbreviations: MTH, massive thymic hyperplasia; CT, computed tomography; NPO, non per os; TPN, total parenteral nutrition; IV, intravenous injection.

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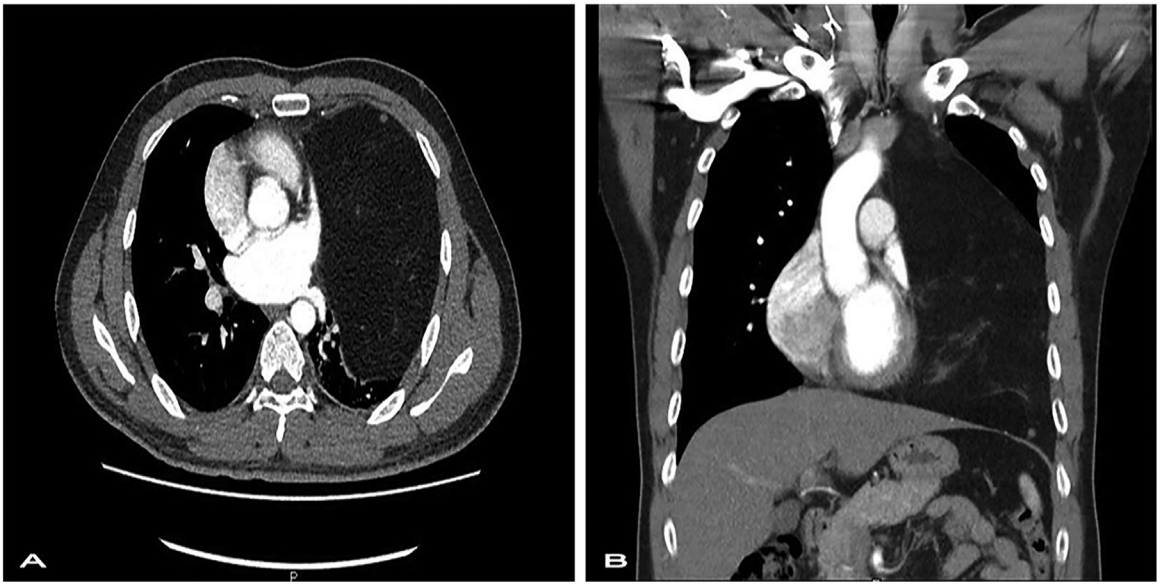

Fig. 1. (A, B) Computed tomography (CT) scan results, showing a large anterior mediastinal mass occupying most of the left hemithorax and compressing the adjacent structures.

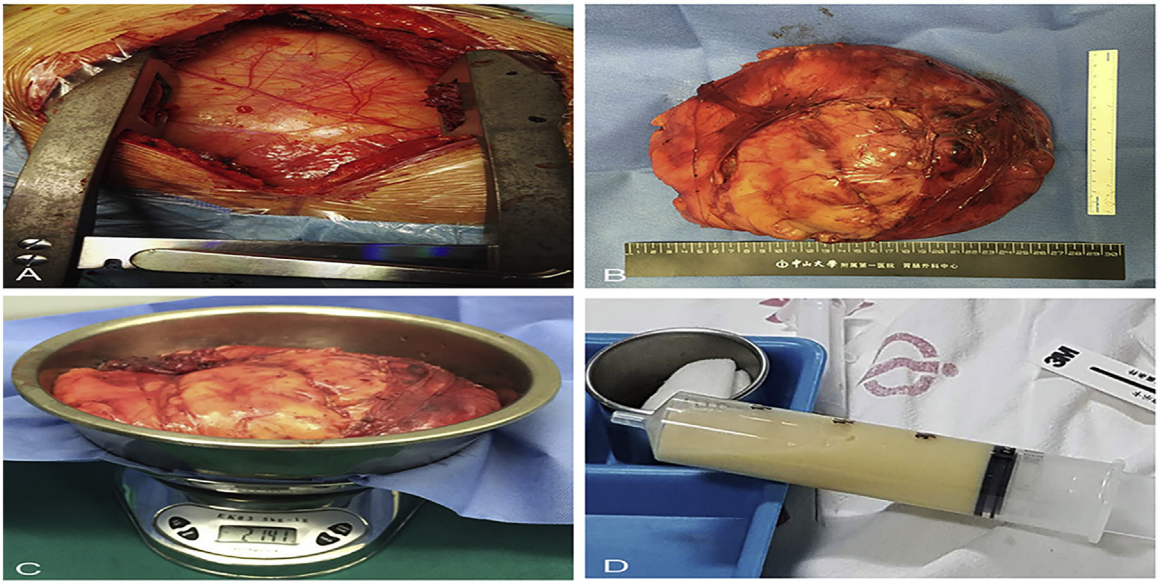

Fig. 2. (A) Left posterolateral thoracotomy was performed and the mass was glossy in appearance. (B, C) Completely resected, the mass measured approximately 112 mm × 191 mm × 184 mm in size and weighed 2141 g. (D) The pleural effusion was milky in appearance and sent for further examination.

Based on these histological and immunohistochemical findings, the final diagnosis of thymic hyperplasia was rendered.

The compressed lung was completely re-expanded and he was discharged on the 7th day after operation. On the 12th day, the patient complained of fatigue and dizziness. The chest radiograph showed a huge pleural effusion on the left side. Thoracentesis was performed and the fluid was milky in appearance, with suspended fat droplets (Fig. 2). The chylous qualitative tests of the liquid specimen were positive, and consequently, postoperative chylothorax was diagnosed. Since the daily volume of the drainage was below 500 ml, conservative treatments, including non per os (NPO), total parenteral nutrition (TPN), thoracic drainage, and administration of octreotide (250 μg intravenous per hour), were performed. The volume of drainage decreased sharply after treatment was instituted and the qualitative tests of the effusion were negative for 3 times, taken sequentially. We removed the chest tube on the 19th day and he was again discharged. The patient well tolerated to our treatment and no adverse events occurred. The patient is satisfactory about treatments because he did not complain any symptoms related to treatments and no radiological evidence of recurrence revealed by CT scan, was found in the follow-up period.

3. Discussion

Levine et al. [1] reported that thymic hyperplasia could be divided into two types. One is true thymic hyperplasia. The other type is lymphoid hyperplasia, which was often closely associated with myasthenia gravis and other autoimmune diseases [4]. Interestingly, previous study also reported that thymic hyperplasia may correlate with Graves disease and degenerate after treatments of thyroid diseases [5].

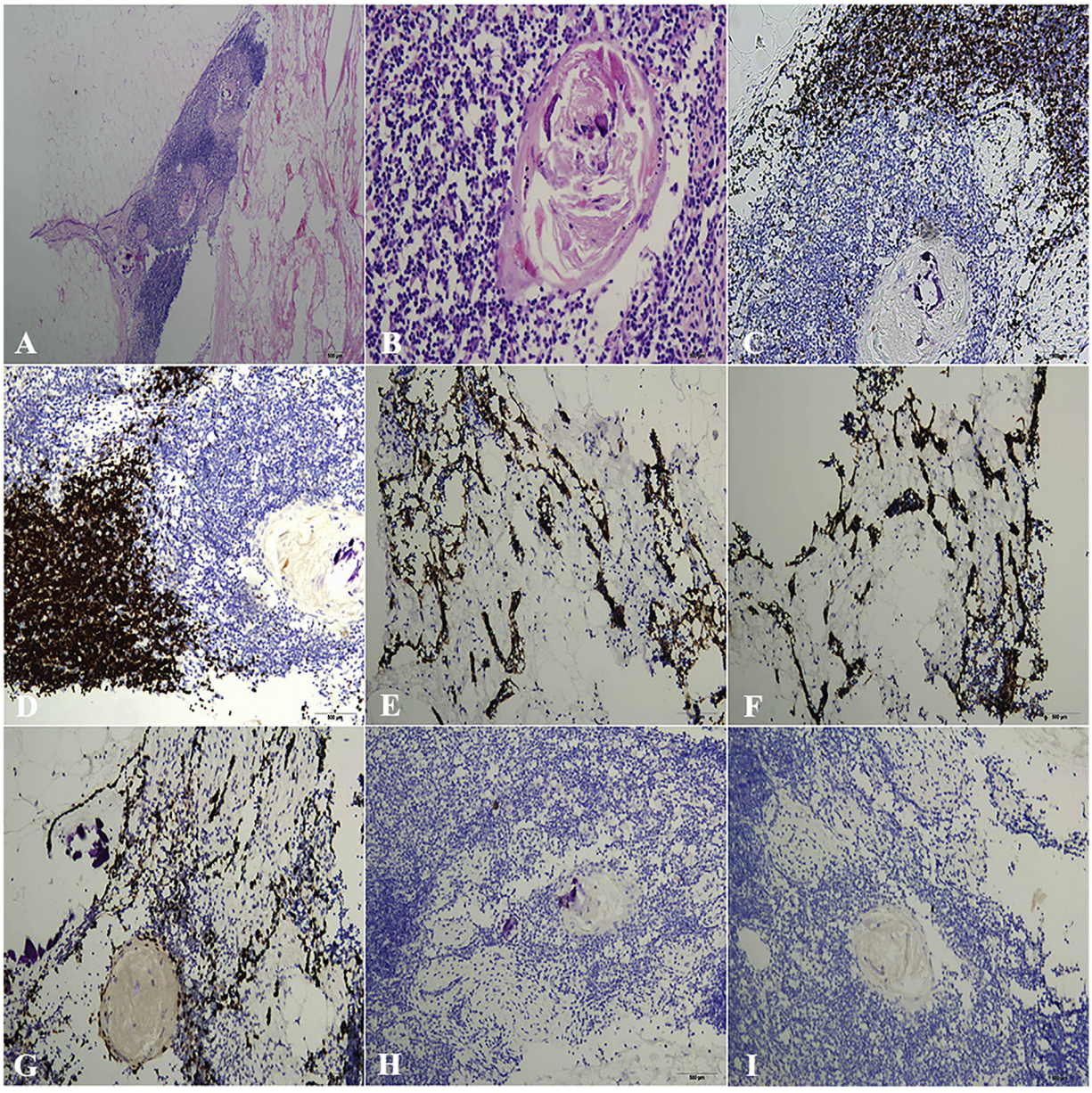

Fig. 3. (A, B) Thymic hyperplasia: the thymic architecture is conserved, consisting of a corticomedullary differentiation and the presence of Hassall's corpuscles in the medulla (H&E stain, A × 20; B: ×200). (C, D) The cells were diffusely positive for Ki67 and TdT, indicating that they are medullary thymic epithelial cells. (E–G) The cells were focally positive for CK19, CK5/6 and P63, suggesting that they were from thymic cortex. (H, I) The cells were negative for TG and TTF1, revealing that they weren't derived from thyroid gland. (Immunohistochemical tests, C-I: ×100).

When it came to the criteria to characterize "massive" in true thymic hyperplasia, Linegar et al. [2] recommended the guidelines below: (1) The size on chest radiograph is larger than the heart shadow; (2) The weight of the thymus should be several times the normal weight for the specific age and sex group; and (3) The weight of the thymus should be above 2% of the mass. Our case met all the criteria above. Consequently, he was definitely diagnosed as massive thmic hyperplasia.

It has been reported that the normal weight of the thymus ranges from 23 to 55 ± 13 g in younger children, to peaking at puberty, to an average of 34 ± 10 g by 16-31 years of age [6]. In our case, the mass, removed from the cavity, weighed 2141 g. To the best of our best knowledge, this is the second largest case for true thymic hyperplasia among all literature. The largest one for MTH was reported in 1996 by Obaro, with a weight of 3550 g [7].

Perhaps due to the active function of the thymus in pre-adults, the majority of the previously reported cases occurred in neonates, infants, and older children, typically under the age of 15. This case appears to be the first case of MTH reported in an adult, which is significantly different (Table 1).

Although thymic hyperplasia is the most common anterior mediastinal mass in infants, it is extremely rare among adults [8]. The differential diagnosis in adults must take into consideration the following: thymoma, lymphoma, teratoma, and benign thyroid tumors [9]. One of the special features of our case was that the CT imaging revealed an anterior mediastinal mass with fat attenuation. Quint et al. [10] reported that only 3 major possible etiologies are considered in these kinds of masses, specifically teratoma, thymolipoma, and Morgagni hernia. Surprisingly, our case, with a density similar to that of adipose tissue, turned out to be MTH,

Table 1
Timeline for diagnosis and treatments.

Time	Informations
The year of 2004	Firstly found a mass in pleural cavity.
2016-11-04	CT revealed a mass, with a primary consideration of a lipoma.
2016-11-15	He was admitted to hospital.
2016-11-18	Left posterolateral thoracotomy was performed.
2016-11-24	Pathological examinations suggested massive thymic hyperplasia.
2016-11-28	He recovered and was discharged.
2016-12-03	The patient complained of fatigue and dizziness.
2016-12-05	He was readmitted to hospital.
2016-12-06	The chest radiograph showed a huge pleural effusion on the left side. The chylous qualitative tests were positive. Thoracentesis was performed.
2016-12-07 to 2016-12-22	Conservative treatments, including non per os (NPO), total parenteral nutrition (TPN), thoracic drainage, and administration of octreotide (250 μg intravenous per hour), were performed.
2016-12-23	The chylous qualitative tests were negative for for 3 times, taken sequentially.
2016-12-25	He recovered and was again discharge.
2018-1-17	No clinical or radiological evidence of recurrence.

similar to the case presented in a 15-year-old adolescent whose CT imaging also revealed fat contents [11]. Whether this phenomenon is associated with the patient's age still remains unknown. The rarity of MTH in adults and the distinctive CT imaging may lead to a preoperative misdiagnosis of a lipoma.

The diagnosis relied on histological analysis. However, whether or not biopsy should be advocated still remains controversial. Two cases that underwent mediastinoscopic biopsy were proven to be thymoma after complete resection of the mass. On the other hand, Bangerter et al. suggested that fine needle aspiration cytology might be reliable in the diagnosis of thymic hyperplasia [12]. In our opinion, therapies should be designed on different classification criteria, as follows: (1) If the mass can be excised completely, we would advocate operation without biopsy, to avoid destroying the integrity of the tumor and spread; and (2) If the mass cannot be resected completely, biopsy is suggested first.

Although oral administration of adrenocorticosteroids is not always completely reliable in conservative treatment, it was still one of the non-specific options for diagnosis [6,13]. However, conservative management might result in some uncertain complications progression, recurrence, and delayed treatment of potential malignancies. Consequently, surgical interventions, including median sternotomy, posterolateral thoracotomy, and video-assisted surgery, were advocated to obtain specimen for histological analysis and/or exclude differential entities and/or relieve compression for mediastinal structures. From a review of literature, 82% of MTH patients underwent thoracotomy, without any complications reported [2].

To the best of our knowledge, only 7 cases have been previously reported. The main limitation of our case was that the uncommon but potentially life-threatening complication occurred, probably due to injury of the left bronchomediastinal trunk when we dissected the pedicle of the mass. Great attention should be given to the development of chylothorax, because it might lead to fatal complications, including nutritional troubles, immunodepression, respiratory distress, and dehydration [14,15]. However, we managed successfully. Conservative, surgical, and interventional treatments are available when dealing with this annoying problem. Conservative treatment is recommended as the first-line therapy, with a success rate varying from 67% to 87% in recent years [14]. Conservative treatment was recommended for low-volume drainage, especially when less than 500 ml per 24 h; This often failed, necessitating more invasive treatment, in cases of high-volume situations, when the output was more than 1000 ml per 24 h [16]. For conservative treatment, the application of somatostatin or octreotide may be a good choice. In our case, administration of octreotide (250 μg IV per hour) was performed. However, more invasive treatment, especially surgical treatment, is the first-line option for adults to reduce mortality, based on the following [14,15]: (1) Daily volume of drainage more than 1000 ml; (2) Daily volume of drainage more than 500 ml during the first day after conservative treatment based on NPO and TPN; (3) Malnutrition and metabolic problems; (4) Leak persistent over 14 days; (5) Daily volume of drainage more than 1000 ml after conservative treatment lasting for 5 days. Interventional treatment, although not available in every hospital, was also reported as another safe option with high success rates in treating chylous leakage. Interventional methods reportedly led to higher cure rates along with lower complication rates, and might replace the traditional treatments for chylothorax [16].

4. Conclusion

Although rare, massive thymic hyperplasia could also be found in adults. Fortunately, the prognosis remains favorable after undergoing complete surgical removal. During operative procedure, great attention should be paid to the protection of the branches of the thoracic duct in order to prevent the complication of post-thymectomy chylothorax. As for post-thymectomy chylothorax, conservative treatment is effective and associated with good outcomes when drainage is less than 500 ml per 24 hours. However, more invasive treatment should be necessitated once it fails.

Conflicts of interest

The authors declare that they have no competing interests.

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Ethical approval

Ethical approval was obtained from the Ethic Committee of the First Affiliated Hospital of Sun Yat-Sen University. Informed consent to participated in the study was obtained.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

DWZ – Conception of study, acquisition of data, analysis and interpretation of data, drafting the manuscript.

HHL – Management of case, revision of article, final approval of the version.

YFF – Management the histopathological analysis, revision of article.

BZ – Analysis of data, revision of article.

YYL – Conception of study, acquisition of data, analysis and interpretation of data, drafting the manuscript, final approval of the manuscript.

Registration of research studies

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Guarantor

Yiyan Lei.

Availability of data and materials

The datasets used and/or analysed during the current study available from the corresponding author on reasonable request.

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