Pharmacogenomics and Personalized Medicine

Dovepress

open access to scientific and medical research

Open Access Full Text Article

CASE REPORT

Giant Multilocular-Cystic Metaplastic Thymoma: A Case Report

Lihua Han[1], Bo Gao[2], En-Hua Wang[3], Liang Wang[3]

[1]The Central Laboratory of Morphology, Shenyang Medical College, Shenyang, People's Republic of China; [2]Department of Pathology, Cancer Hospital of China Medical University, Shenyang, People's Republic of China; [3]Department of Pathology, First Affiliated Hospital and College of Basic Medical Sciences, China Medical University, Shenyang, People's Republic of China

Correspondence: Lihua Han, The Central Laboratory of Morphology, Shenyang Medical College, Shenyang, People's Republic of China, Email hanlihualn@163.com

Abstract: The metaplastic thymoma with giant multilocular-cyst formation had not been documented. The metaplastic thymoma is an extremely rare primary thymic epithelial tumor with an indolent clinical course. It is characterized by a histologic biphasic appearance, which is consisted of solid epithelial areas and spindle cells as the background. This specific pattern can be easily mistaken as the type A thymoma or the type A components of type AB thymoma. When cystic change occurs in metaplastic thymoma, it will bring more challenges for both imaging and pathological diagnosis. Herein, we reported an extremely rare case of a 14.9-cm giant tumor located in the anterior mediastinum of an elderly female. The tumor is consisted of both multilocular cysts and solid components, with the largest cyst measuring 6 cm in diameter. The multilocular cyst contained hemorrhage, calcification, and cholesterol crystal cracks without cell lining. In the solid area, the epithelial cell nests were surrounded by spindle cells with scattered lymphocytes. With immunostains, neither type of cells was CD20 positive. The epithelial cells were positive for CK and P63, while the spindle cells expressed vimentin and EMA. Fluorescence in situ hybridization analysis revealed that the tumor harbored *YAP1-MAML2* gene fusions. Accordingly, although the multilocular cystic pattern set a diagnostic challenge, the diagnosis of metaplastic thymoma was rendered due to the immunohistochemistry staining and *YAP1-MAML2* gene rearrangement detection.

Keywords: metaplastic thymoma, thymoma, thymic cyst, FISH, *YAP1-MAML2*

Introduction

The metaplastic thymoma is a rare type of thymoma and only limited cases have been reported in the literature.[1] Histologically, it shows biphasic differentiation, consisting of epithelial cell nests disposed among delicate spindle cells.[2] In general, it lacks the general histological characteristics of common types of thymoma, such as a lobular growth pattern, perivascular spaces, and an unequal proportion of TdT-positive immature lymphocytes. Clinically, most cases have been reported to follow indolent courses except for extremely unusual cases with malignant transformation and local recurrence, and are not associated with myasthenia gravis (MG).[3] Immunohistochemistry plays a very important role in diagnosis and differential diagnosis. Recent studies have shown that the rearrangement of *YAP1-MAML2* is a very key genetic change in metaplastic thymoma,[4] which is of great significance for the diagnosis and differential diagnosis of those challenging cases.

Case Presentation

The patient was a 74-year-old woman who found a giant mass in the mediastinum during a routine examination before surgery on her right breast lesion (ductal carcinoma in situ). The mediastinal lesion resection was performed one month after breast surgery (February 2022). The patient had no cough, expectoration, dyspnea, chest tightness, or chest pain before the operation. No MG or other related symptoms were evident. Chest computed tomography (CT) revealed a giant mass located in the anterior mediastinum, with a size of 149 mm × 107 mm. Upon enhancement, the mass was in a cystic-solid pattern with a clear boundary, and the septa and calcification can be seen. The tumor protruded to the right chest cavity, and the adjacent lung was severely compressed (Figure 1A and B).

Received: 23 March 2023
Accepted: 18 May 2023
Published: 19 May 2023

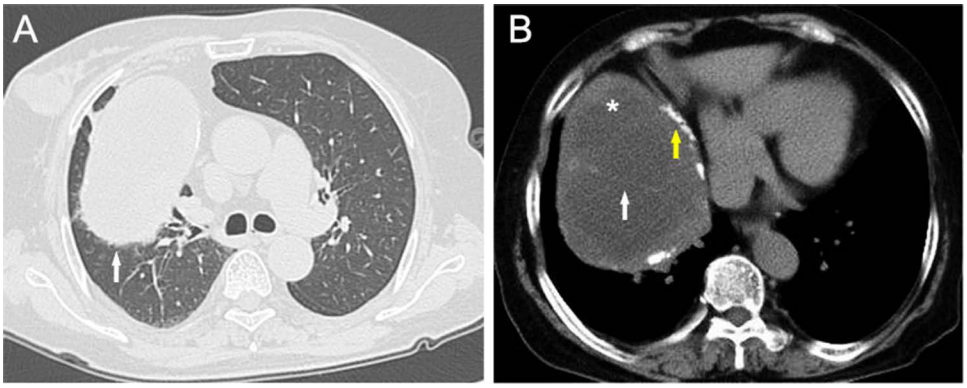

Figure 1 Enhanced CT showed that the tumor was located in the anterior mediastinum, presenting a mixed mass of cystic and solid, compressing the right lung (white arrow (**A**), lung window). The tumor boundary was clear ((**B**), mediastinal window), with arc-shaped calcification shadows (yellow arrow), solid components (asterisk), and internal septa (white arrow).

A partial thymectomy with video-assisted thoracic surgery was performed. A giant mass with a maximum diameter of 15 cm was resected. In gross, the tumor was encapsulated and the cross-section revealed multilocular cysts, which were measured 0.5–6 cm in the greatest diameters. The cysts were filled with pink-brown fluid. Solid gray-white lesions were in irregular shape and the maximum diameter was 7 cm.

Microscopically, the inner side of the cysts lacked epithelial cell lining and there were hemorrhage, calcification, cholesterol crystal cracks, and edema within cavities (Figure 2A and B). The fibrous septa varied in thickness and contained epithelioid cells with a small number of scattered lymphocytes (Figure 2C). In the solid area, the epithelial cell

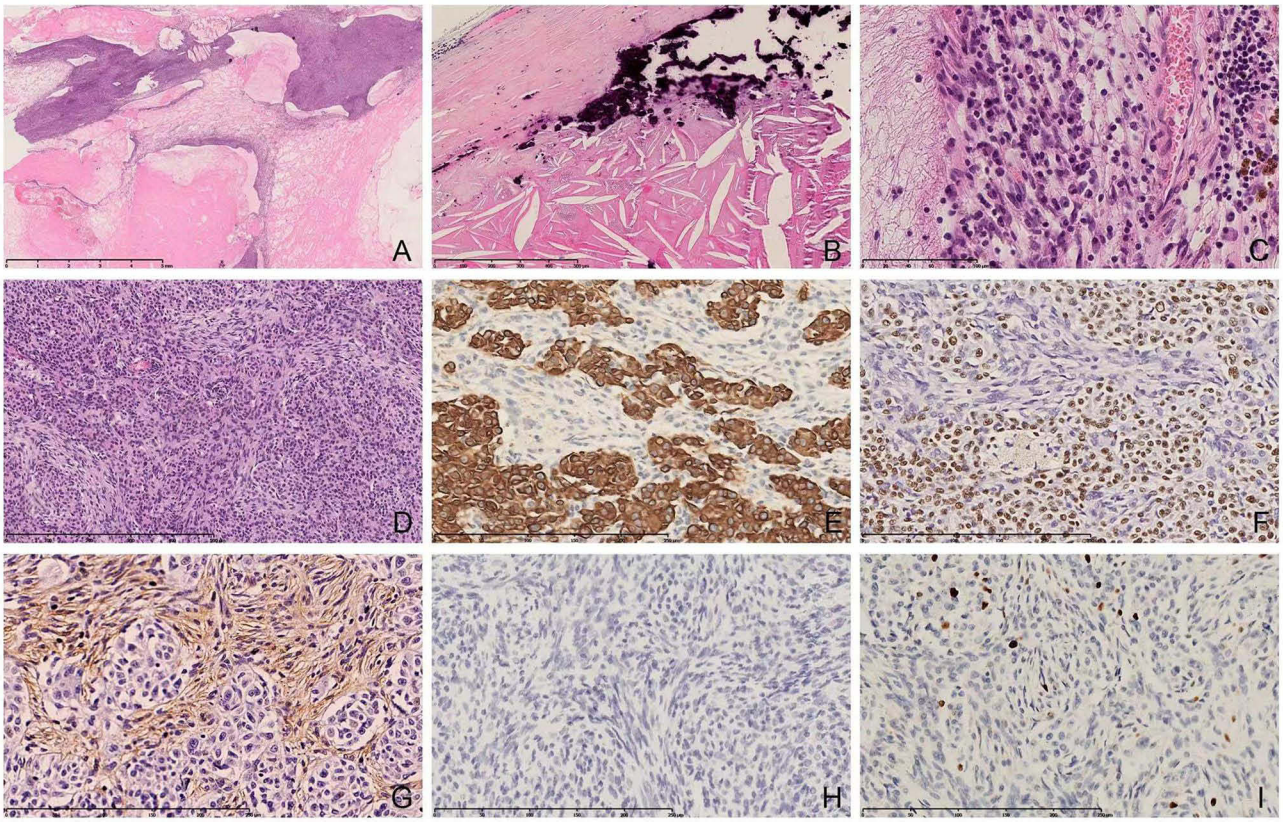

Figure 2 Under the microscope, the mass was multilocular-cystic. The cyst walls varied in different thicknesses, and the solid epithelioid components were like islands (**A**). The hemorrhage, cholesterol crystal crack, calcification, and edema were in the cyst (**B**). The epithelioid components were lined in the inner side of some cyst walls, and a small number of lymphocytes were scattered in the epithelioid cell (**C**). The solid epithelioid areas were surrounded by spindle cell bundles (**D**). The epithelial cells expressed CK (**E**) and P63 (**F**), and the spindle cells expressed Vimentin (**G**), but the CD20 was negative in both types of cells (**H**), and the Ki-67 index was less than 5% (**I**).

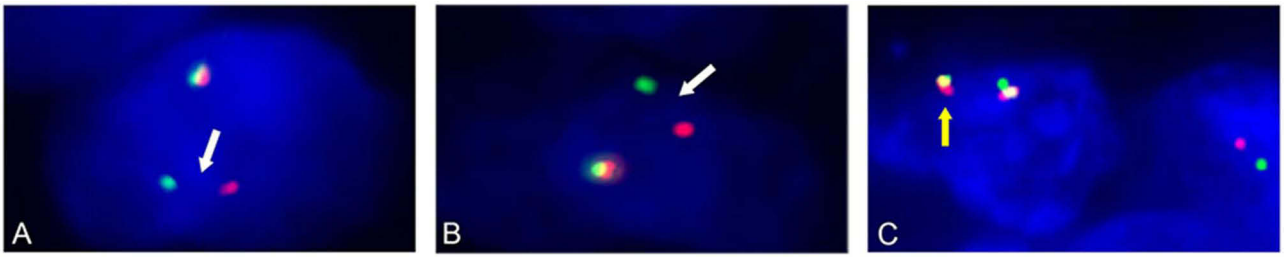

Figure 3 The dual-color separation signal of *YAP1* (**A**) and *MAML2* (**B**) was detected by FISH (the green fluorescent probe was directly hybridized with the distal end of the *YAP1* gene, the Orange fluorescent probe was directly hybridized with the proximal end of *YAP1* gene; the green fluorescent probe was directly hybridized with the proximal end of *MAML2* gene, and the Orange fluorescent probe was directly hybridized with the distal end of *MAML2* gene), white arrows indicating separating signals. The *YAP1-MAML2* fusion probe detected that there was a yellow fusion signal (**C**), the Orange probe was 5' of *YAP1* and the green probe was 3' of *MAML2*, the yellow arrow indicating the merged signals).

nests were deposited in the background of spindle cells, presenting a biphasic differentiation with scattered lymphocytes (Figure 2D). Both types of cells were bland-looking and small nucleoli can be seen in epithelial cells. No perivascular spaces or Hassall's corpuscles were found.

Immunohistochemistry was performed. CK-pan (Figure 2E), P63 (Figure 2F), and E-cadherin were expressed in epithelial cells. The spindle cells were positive for Vimentin (Figure 2G) and EMA. Neither type of cell expressed CD20 (Figure 2H), and the Ki-67 index was less than 5% (Figure 2I). A small number of CD3 and CD5 positive T lymphocytes can be evident. However, these lymphocytes were all negative for CD1a, TdT, and CD99.

Fluorescence in situ hybridization (FISH) analysis of the *YAP1* and *MAML2* break-apart probes and *YAP1-MAML2* fusion probes were performed with a FISH detection kit (HealthCare Biotechnology, Wuhan, China). It was found that the separation signal of *YAP1* (Figure 3A) and *MAML2* (Figure 3B) were both over 20%; *YAP1-MAML2* fusion-positive signal is more than 10% (Figure 3C). Accordingly, the final diagnosis was rendered as metaplastic thymoma with multilocular-cystic formation. With no further treatment, the patient survived without evidence of recurrence for 12 months.

Discussion

The cystic formation of the thymus can be caused by congenital, inflammatory, and tumor.[5] Although thymoma can occur based on thymic cyst,[6] it is different from the cystic formation in thymoma. The latter lacks epithelial cell lining or its wall is continuous with the main component of thymoma.[7] The cystic formation of thymoma is relatively common, but the giant cystic formation is extremely rare.[8] Metaplastic thymoma with giant cystic formation has never been reported. The current case showed multilocular-cystic change with up to 6cm in the greatest diameter, which may be related to intracapsular hemorrhage.

The metaplastic thymoma is extremely rare and indolent, accounting for less than 1% of all types of thymoma.[1] Its most distinctive histological feature is bidirectional differentiation, that is, solid epithelial cell nests deposited within the spindle-shaped cell background.[2] Immunohistochemistry played an important role in its differential diagnosis, such as the expression of CK, P63, and E-cadherin in epithelial cells, while the spindle cells expressed vimentin and EMA. CD20 is generally positive in type A thymoma but negative in metaplastic thymoma. In addition, a small number of CD3 and CD5 positive cells in type A thymoma showed positive expression of CD1a and TdT, while T cells in metaplastic thymoma showed negative expression of CD1a and TdT.

It is noteworthy that a very important molecular marker in metaplastic thymoma was recently identified, namely the gene rearrangement of *YAP1-MAML2*.[4] We adopted FISH to confirm this specific genetic change in the current case. For those challenging cases, NGS and other methods can also be used to detect whether there is a mutation of *GTF2I* c.74146970T>A,[9] which exists in type A and AB thymomas.

In conclusion, we reported a case of giant metaplastic thymoma with multilocular-cystic change, which was challenging in imaging and histopathological diagnosis. Although metaplastic thymoma had specific histological patterns, it was necessary to be distinguished it from other types of thymoma. The immunohistochemistry and *YAP1-MAML2* gene rearrangement detection were of great help.

Data Sharing Statement

The datasets supporting the conclusions of this article are included within the article.

Ethical Approval and Consent to Participate

Ethical approval for this study was obtained from the institutional ethic review boards of the First Affiliated Hospital of China Medical University.

Patient Consent for Publication

Informed consents were obtained from the patients for publication.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or all these areas; took part in drafting, revising, or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Funding

This study was supported by grants from the Natural Science Foundation of Liaoning to Liang Wang (2021-MS-160).

Disclosure

The authors declare that there is no conflict of interest regarding the publication of this article.

References

1. Liu B, Rao Q, Zhu Y, Yu B, Zhu HY, Zhou XJ. Metaplastic thymoma of the mediastinum. A clinicopathologic, immunohistochemical, and genetic analysis. *Am J Clin Pathol*. 2012;137(2):261–269. doi:10.1309/AJCP0T1JFYLMPHMI
2. WHO Classification of Tumours Editorial Board. *Thoracic Tumours*. 5th ed. Lyon (France): International Agency for Research on Cancer; 2021:347.
3. Zhao J, Zhao R, Xiang C, Shao J, Guo L, Han Y. YAP1-MAML2 fusion as a diagnostic biomarker for metaplastic thymoma. *Front Oncol*. 2021;11:692283. doi:10.3389/fonc.2021.692283
4. Vivero M, Davineni P, Nardi V, Chan JKC, Sholl LM. Metaplastic thymoma: a distinctive thymic neoplasm characterized by YAP1-MAML2 gene fusions. *Mod Pathol*. 2020;33(4):560–565. doi:10.1038/s41379-019-0382-x
5. Rieker RJ, Aulmann S, Schnabel PA, et al. Cystic thymoma. *Pathol Oncol Res*. 2005;11(1):57–60. doi:10.1007/BF03032408
6. Ascani S, Carloni A, Agostinelli C, Martini E, Bravi I, Pileri SA. Thymoma arising in the wall of a thymic cyst. *Pathologica*. 2008;100(6):476–477.
7. Shen X, Jin Y, Shen L, Sun Y, Chen H, Li Y. Thymoma and thymic carcinoma associated with multilocular thymic cyst: a clinicopathologic analysis of 18 cases. *Diagn Pathol*. 2018;13(1):41. doi:10.1186/s13000-018-0719-7
8. Sakaguchi Y, Komatsu T, Takubo Y, Terada Y. Resected case of giant cystic thymoma with spontaneous intracystic hemorrhage. *Surg Case Rep*. 2019;5(1):30. doi:10.1186/s40792-019-0586-9
9. Wells K, Lamrca A, Papaxoinis G, et al. Unique correlation between GTF2I mutation and spindle cell morphology in thymomas (type A and AB thymomas). *J Clin Pathol*;2022. jclinpath-2021-207837. doi:10.1136/jclinpath-2021-207837