



Growing thymic granuloma adjacent to a thymic cyst mimicking malignancy: a case report

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Abstract: An association between thymic cyst and thymic epithelial malignancy has been previously reported. However, several case studies have reported granulomas in the thymus with high metabolic activity, mimicking thymic malignancy. Additionally, an inflammatory response provoked by the rupture of cyst walls has been proposed as a pathogenesis of cholesterol granuloma in the thymus. However, the natural growth history of thymic granuloma remains unclear. We herein report the first case demonstrating the natural growth history of a thymic granuloma adjacent to a thymic cyst. Ten-year follow-up of the thymic cyst revealed a growing nodular lesion with high metabolic activity adjacent to the cyst. 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) showed a maximum standardized uptake value of 12.1 in a 2.5-cm solid mass. We performed total thymectomy given a high suspicion of a malignant thymic epithelial tumor. Histopathologic examination revealed a cholesterol granuloma in the thymus, which was directly connected to the thickened region of the cystic wall through a rupture of the wall. This case highlights the importance of considering thymic granuloma as a differential diagnosis for a growing anterior mediastinal nodule with high metabolic activity. Further, the clinical course and histopathologic findings of this case provide supporting evidence for the proposed pathogenesis of thymic granuloma.

Keywords: Thymic cyst; granuloma; thymic epithelial tumor; case report

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Introduction

An association between the thymic cyst and thymic epithelial tumors has been reported (1). 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) has been widely used to differentiate benign from malignant lesions in thymic pathology (2). However, several recent case studies have reported FDG-avid granulomas in the thymus mimicking thymic malignancy (3-5). Thymic cyst rupture has been suggested as a pathogenic mechanism for inflammatory granuloma (6). However, the natural growth history of thymic granuloma remains unclear. We herein report a case of a patient who was found to have a growing nodular lesion with high FDG avidity adjacent to

a long-term followed-up thymic cyst and underwent total thymectomy which revealed a granuloma in the thymus. To the best of our knowledge, this is the first reported case demonstrating the natural growth history of a thymic granuloma adjacent to a thymic cyst. We present the following case in accordance with CARE reporting checklist available at <http://dx.doi.org/10.21037/med-20-46>.

Case presentation

A 65-year-old man with no significant past medical history was found to have a thymic cystic nodule in a chest computed tomography (CT) scan (*Figure 1A*). Further workups including magnetic resonance imaging (MRI)

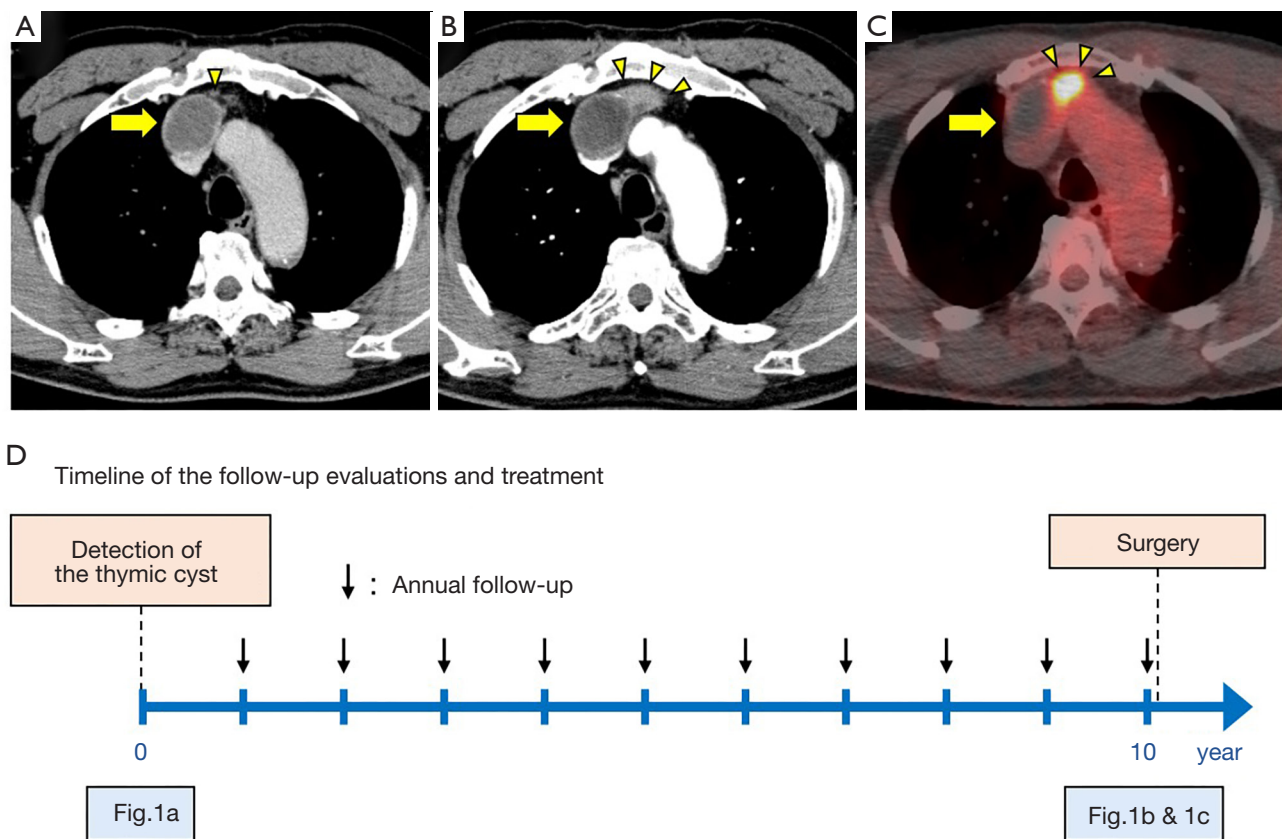


Figure 1 Radiological images. (A) Computed tomographic (CT) scan with contrast enhancement 8 years before surgery showed a 30-mm cystic lesion with a thickened wall (arrow) and a small solid nodular lesion adjacent to the cyst (arrowhead); (B) preoperative CT scan with contrast enhancement showed that the solid nodule adjacent to the cyst increased in size (arrowhead) whereas the size of the cyst did not change (arrow) compared with those 10 years ago; (C) preoperative 18F-fluorodeoxyglucose positron emission tomography scan showed that the solid nodule adjacent to the cyst had high metabolic activity (the maximum standard uptake value 12.1) (arrowhead) whereas there was no abnormal metabolic activity in the cyst (arrow); (D) timeline of follow-up evaluations and treatment for the thymic cyst and adjacent nodule.

with contrast revealed a nonenhanced thymic cystic lesion, which was suspected to be a thymic cyst. The patient was followed-up with annual CT scans, which showed a growing solid nodule adjacent to the known thymic cyst (*Figure 1B*). FDG-PET showed high metabolic activity with the maximum standardized uptake value (SUVmax) of 12.1 in a 2.5 cm solid mass adjacent to the cyst (*Figure 1C*). The timeline of follow-up evaluations and treatment for the thymic cyst and adjacent nodule is presented in *Figure 1D*. Chest CT scan and MRI with contrast demonstrated the innominate vein was compressed by the solid mass. We strongly suspected a thymic epithelial tumor arising on the wall of the thymic cyst with a direct invasion to the innominate vein.

We performed a total thymectomy via median sternotomy at ten years since the first detection of the thymic cyst when the patient was 75 years old. The cyst and solid mass attached to the innominate vein but there was no direct invasion to the vascular wall. Therefore, we were able to dissect the tumor from the vein. Histopathologic examination revealed a cystic lesion with a thickened wall, as well as accumulated foam cells and cholesterol cleft granulation. A solid mass adjacent to the cyst consisted of cholesterol cleft granulation which directly connected to the thickened part of the cystic wall through a rupture of the wall (*Figure 2*). The postoperative course was uneventful, and the patient was followed up without evidence of recurrence for 3 months after surgery. All procedures

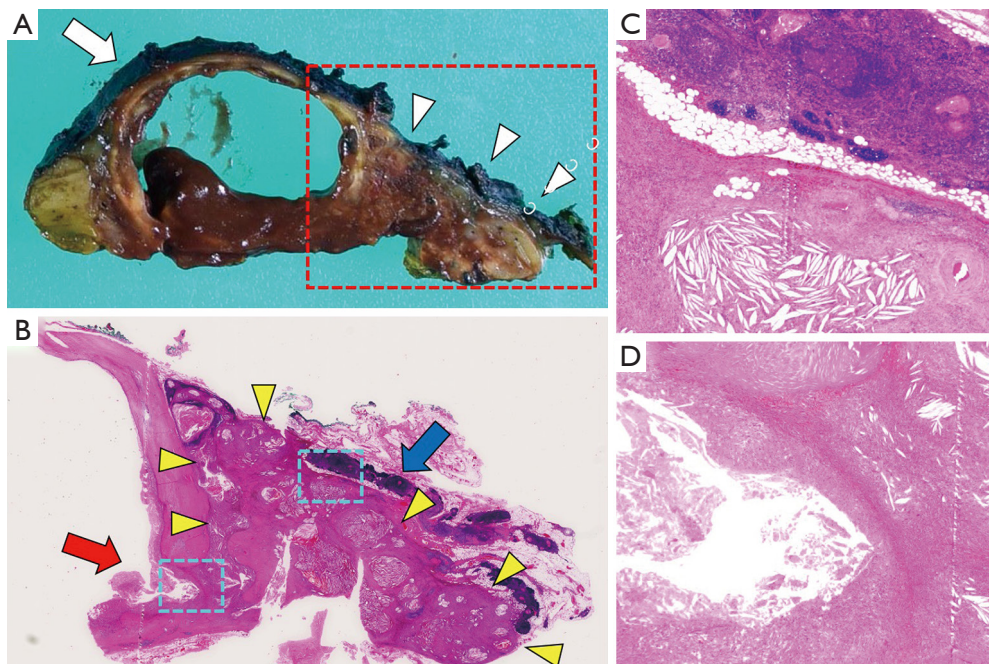


Figure 2 Gross and histological images. (A) The cross-sectional gross image showed a cyst (arrow) and an ill-defined solid nodule (arrowhead) adjacent to the cyst in the thymus. A red dotted-line square represented an area shown in B; (B) histological image of hematoxylin-eosin staining of the cyst and the adjoining nodule showed foam cell accumulation and cholesterol cleft granulation (yellow arrowheads). There was a rupture of the cyst wall (red arrow). There were thymic tissues around the granulation tissue (blue arrow). A blue dotted-line squares represented areas shown in C and D; (C) high magnification image ($\times 40$) showed a thymic tissue (upper) and a cholesterol cleft (lower). (D) high magnification image ($\times 40$) showed a rupture of the cyst wall through which the cyst and the nodule directly connected.

performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committees and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

Discussion

In the present case, we highly suspected a malignant thymic epithelial tumor based on its growing nature (7) and high metabolic activity (2). Furthermore, we assumed that the growing nodule could be associated with the adjacent thymic cyst (1).

Previous studies have demonstrated that the growth speed of thymic epithelial tumors was associated with their histologic grade, and reported the median tumor doubling time of thymic carcinomas ranges between 146 and 205 days (7-9). In this case, the tumor doubling time was calculated to be 193 days, which suggested malignancy.

On the other hand, studies have demonstrated that there is increased FDG avidity in high-risk thymic epithelial tumors compared with low-risk tumors, thus FDG-PET is useful to differentiate anterior mediastinal lesions (2,10,11). Inoue *et al.* demonstrated a SUVmax of 4.5 as a useful cutoff to differentiate high-risk (WHO type B2, B3, and thymic carcinoma) from low-risk (WHO type A, AB, and B1) thymic epithelial tumors (10). In our previous study on confined early-stage (Masaoka stage I or II) thymic epithelial tumors, a SUVmax of 3.5 was an optimal cutoff value to differentiate high- and low-risk tumors (11). The present case had a SUVmax of 12.1, which also suggested malignancy.

Thymic granuloma is a rare entity and has only been presented in a few case reports (3-6), some of which demonstrated cases with high metabolic activity mimicking thymic malignancy (3-5) as in our present case. Weissferdt *et al.* reported four cases of cholesterol granuloma in the thymus and proposed an inflammatory response provoked by the rupture of the cyst walls leading to the formation of

cholesterol cleft granuloma with foreign body-type giant cells as the pathogenesis of cholesterol granuloma in the thymus (6). Nagata *et al.* demonstrated granulomas in the lining of the ruptured cystic walls in the thymus (5). In the present case, the fact that a solid nodule adjacent to a thymic cyst increased in size during follow-up and the histopathologic findings as described above supported the proposed pathogenesis of thymic granuloma.

Conclusions

We report a case of growing granuloma adjacent to a thymic cyst. Although rare, a thymic granuloma should be considered as a differential diagnosis for growing, FDG-avid solid nodule in the thymus.

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Footnote

Reporting Checklist: The authors have completed the CARE reporting checklist. Available at <http://dx.doi.org/10.21037/med-20-46>

Conflict of interest: All authors have completed the ICMJE uniform disclosure form (available at <http://dx.doi.org/10.21037/med-20-46>). The authors have no conflict of interest to be declared.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committees and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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