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Case Report

Isolated thymic Rosai-Dorfman disease with mediastinal bronchogenic cyst: a case report

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Abstract: Rosai-Dorfman disease (RDD) is a unique histiocytic proliferative disorder that occurs primarily in lymph nodes or extranodal sites. Isolated mediastinal thymic RDD is rare. Furthermore, the combination of this disease entity with mediastinal bronchogenic cyst is an even rarer phenomenon. A 45-year-old woman presented with two mediastinal masses that was detected using chest radiography. The patient underwent thoracoscopic surgery for the removal of the mediastinal masses. One lesion was diagnosed as thymic RDD. Histologically, a granulomatous lesion characterized with infiltration of lymphocytes, plasma cells, and histiocytes with lymphocytes engulfed in their cytoplasm was indentified. The other was diagnosed as primary mediastinal bronchogenic cyst. To the best of our knowledge, this is the first description of a thymic RDD and a bronchogenic cyst occurring simultaneously in the mediastinum. We discuss the clinical, pathologic findings as well as differential diagnoses.

Keywords: Rosai-Dorfman disease, mediastinum, thymus, bronchogenic cyst

Introduction

Rosai-Dorfman disease (RDD), also known as sinus histiocytosis with massive lymphadenopathy (SHML), is an uncommon macrophage-related histiocytic disorder [1, 2]. The disease is characterized with massive, painless bilateral cervical lymphadenopathy and histiocyte proliferation in young adults. Although RDD usually involves the lymph nodes, it may also involve extranodal organs or tissues [2]. Thymus involvement without detectable lymphadenopathy is rare in RDD cases. Bronchogenic cyst is an uncommon congenital anomaly of foregut origin and usually locates within the mediastinum. Bronchogenic cysts are usually unilocular, well-demarcated, lined with ciliated columnar epithelium, and filled with mucous content. The combination of two disorders occurring in the mediastinum of the same patient is extremely rare. Here, we report the first documented case of thymic RDD concomitant with congenital bronchogenic cyst.

Case report

A 45-year-old woman, who had no symptoms, was found to have two mediastinal mass on annual chest radiograph screening. She had no past medical history of disease and she denied fever, nausea, vomiting, hematochezia, appetite changes, or weight loss. Physical examination was unremarkable. No lymphadenopathy or abnormal mass was noted. The patient's complete blood count, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels were all within the normal range. Chest CT showed a triangle shape mass, measuring 5×4×1.5 cm, with clear boundary in the region of thymus (**Figure 1A**, **1B**). Uneven enhancement could be seen. Another lesion appeared as an oval shape mass with homogeneous low density and smooth margin, measuring 9×6.4×6 cm in size, on the right side of the posterior mediastinum in front of the spine. There was non enhancement on enhanced CT scan. Thoracoscopic surgery was performed.

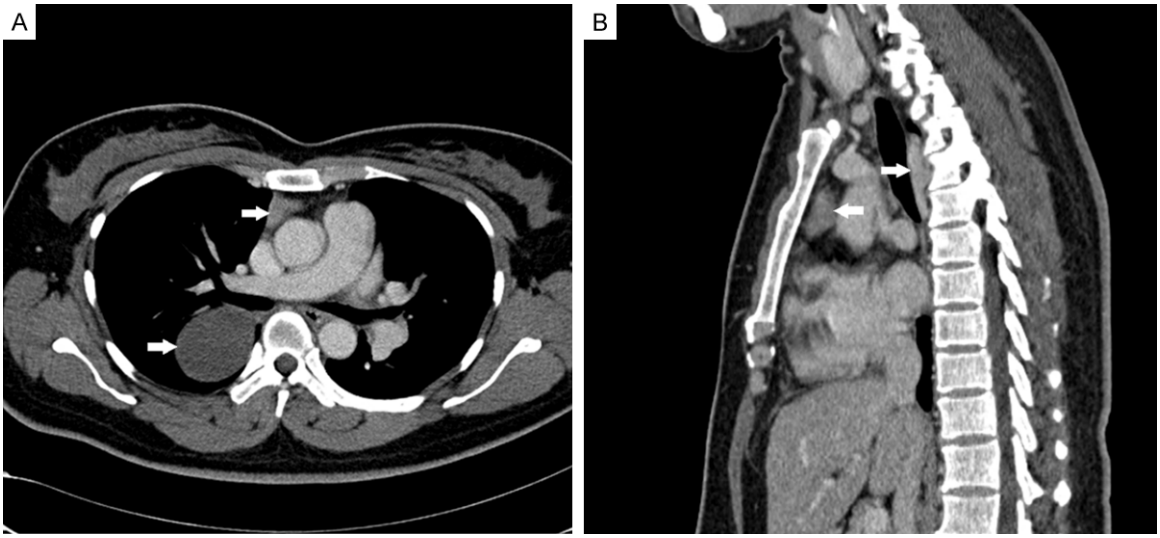

Figure 1. CT characteristics of lesions. A. Axial section. B. Sagittal section. Chest CT scan showed a triangle shape mass, measuring 5×4×1.5 cm, with clear boundary in the region of thymus (arrow). Another lesion appeared as an oval shape mass with homogeneous low density and smooth margin, measuring 9×6.4×6 cm in size, on the right side of the posterior mediastinum in front of the spine (arrow).

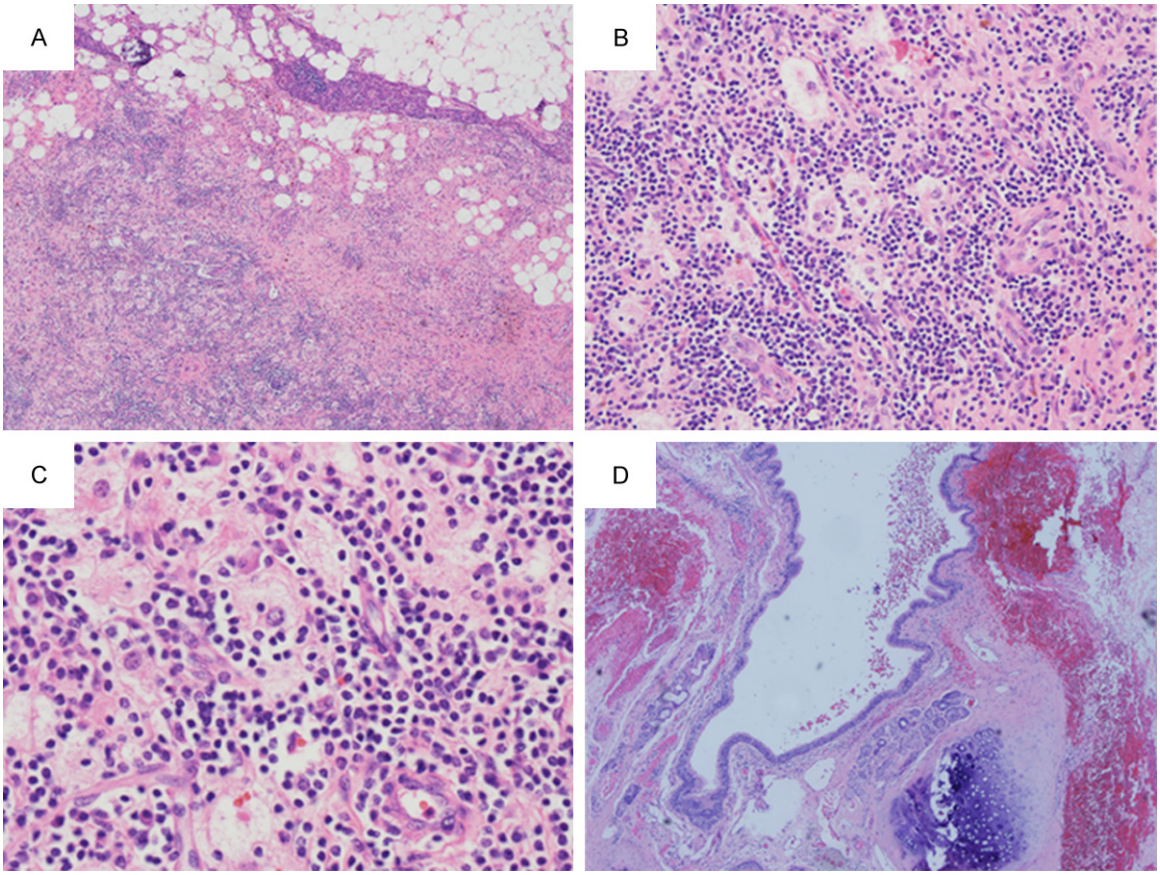

Figure 2. Microscopic features of the mediastinal mass. A. Atrophically thymic tissues in peripheral region were identified (hematoxylin-eosin, magnification ×40). B. These histiocytes demonstrated ample pale to slightly eosinophilic cytoplasm and vesicular nuclei (hematoxylin-eosin, magnification ×200). C. Emperipolesis or cellular penetration phenomena were observed in a few numbers of histiocytes (hematoxylin-eosin, magnification ×400). D. Histopathological examination revealed the mediastinal cyst lined by pseudostratified columnar ciliated epithelium

without cellular atypia. The cystic wall consisted of smooth muscle fibers, hyaline cartilage and focal mucous glands (hematoxylin-eosin, magnification ×40).

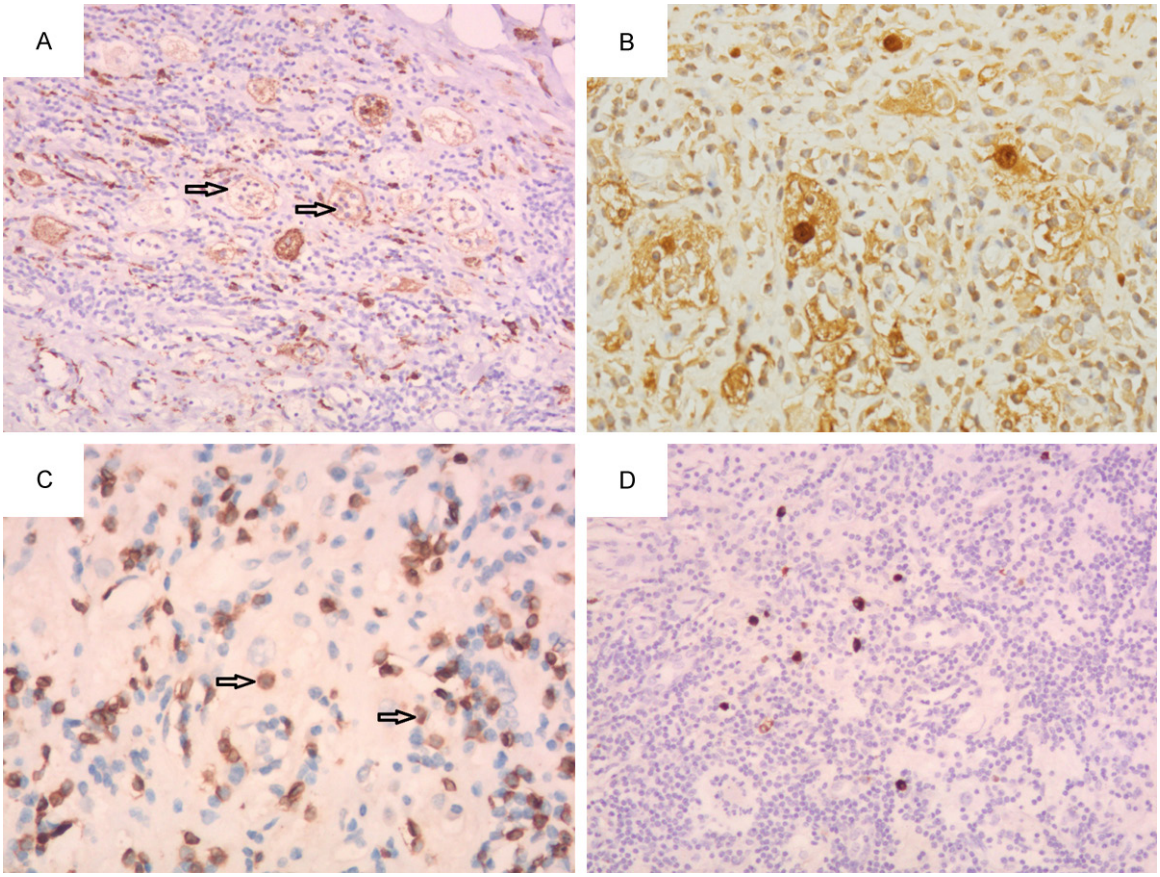

Figure 3. Immunohistochemical staining features of the thymic RDD. A. Large macrophages were weakly positive for CD163 (arrow) but the small histiocytes were strongly positive (magnification ×100). B. The histiocytes were positive for S-100 protein (magnification ×200). C. CD3 staining showing the phagocytized cells are CD3 positive (arrow) (magnification ×200). D. There were only a few IgG4-positive plasma cells present within the lesion (magnification ×100).

On gross examination, the thymus mass was 4.5×3.5×1.2 cm. The cross section was grayish white to yellow in coloration. Microscopic examination revealed a granulomatous lesion composted of abundant histiocytes, mature lymphocytes and plasma cells. Part of the surrounding tissue had dense fibrosis and sclerosis. Atrophically thymic tissues in peripheral region were identified (**Figure 2A**). These histiocytes demonstrated ample pale to slightly eosinophilic cytoplasm and vesicular nuclei (**Figure 2B**). Emperipolesis or cellular penetration phenomena were observed in a few numbers of histiocytes (**Figure 2C**). The second lesion in the posterior mediastinum is a cyst with intact capsule. The cyst contained thick mucinous fluid. Histopathological examination revealed a cyst lined by pseudostratified columnar ciliated epithelium without cellular atypia. The cystic wall consisted of smooth muscle fibers, hyaline cartilage and focal mucous glands (**Figure 2D**). Immunohistochemical study of the thymic mass indicated that the large macrophages were weakly positive for CD163, but the small histiocytes were strongly positive (**Figure 3A**). The histiocytes were also positive for S-100 (**Figure 3B**) and CD68 protein, but were negative for CD1a. CD3 staining showing the phagocytized cells were CD3 positive (**Figure 3C**). There were only a few IgG4-positive plasma cells present within the lesion (**Figure 3D**). No elements of the lymph node

were seen. According to the histological and features, final diagnosis of thymic RDD with bronchogenic cyst was made.

To date, two years after operation, the patient was symptom free with no evidence of recurrence.

Discussion

RDD was first recognized as a distinct clinicopathologic entity by Rosai and Dorfman in 1969 [3]. Although the disease primarily involves the lymph nodes, extranodal involvement occurs in approximate 40% of patients [1]. The most commonly involved extranodal sites are the skin and soft tissue, nasal cavity and paranasal sinuses, followed by eye, orbit, and ocular adnexa, bone, salivary gland, central nervous system, oral cavity, kidney and genitourinary tract, respiratory tract and liver [2]. In rare circumstances, the thymus can be affected. To our knowledge, only two cases of isolated thymus RDD have been previously reported [4, 5]. The first case was a 43-year-old man with a 2 cm anterior mediastinal mass. The patient initially presented with a chief complaint of a neck mass [4]. However, this finding that had been suspected as cervical lymphadenopathy remitted spontaneously in a few days and subsequent physical examination and CT results were negative. The second one was a 42-year-old male with isolated thymus RDD. Although bilateral painless cervical lymphadenopathy was not observed, the patient presented symptoms of persistent fever, leukocytosis and elevated ESR. Moreover, the patient's condition quickly deteriorated due to primary splenic diffuse large B-cell lymphoma. As for our patient, she presented with a solitary mediastinal mass, and the excised tissues contained thymus but had no relationship to the lymph node. Obviously, the present case appears to be the first report of solitary RDD localized in the thymus without any symptoms and signs.

The etiology of the RDD remains unknown, although associations between the disease and immune dysfunction or viral infections such as Epstein Barr virus and human herpes virus infections have been suggested. Bronchogenic cysts are congenital cysts occurring due to a developmental malformation in the foregut during embryogenesis [6]. We considered co-existence of these two diseases in the present case seems to be coincidental. However, careful long-term follow-up was required.

Histologically, RDD is characterized by a proliferation of abudant histiocytes within lymph node sinuses and lymphatics in extranodal sites. Emperipolesis, defined as the active penetration by one cell into and through a larger cell, is the hallmark of the disease [7]. RDD presenting in extranodal sites can be difficult to diagnose because these diseases often exhibit a nonspecific fibro-inflammatory lesion with stromal sclerosis and varying amounts of lymphocytes and plasma cells. In some cases, more fibrosis and fewer histiocytes with emperipolesis can often make the diagnosis difficult. Outline of the individual histiocytes can be clearly assessed by S-100 protein staining, which facilitates the search for emperipolesis. Diagnosis of mediastinal bronchogenic cysts is established based on histopathological findings which show the pseudostratified columnar epithelium, seromucous glands, hyaline cartilage, and smooth muscle fibers. The presence of cartilage tissue is important for establishing the final diagnosis.

When RDD is suspected, it is important to exclude other anterior mediastinal lesions with histiocytic or lymphoid differentiation, including langerhans cell histiocytosis (LCH), thymoma and lymphoma. LCH can occur at any age and has been described in thymus [8]. The histiocytes in LCH are characterized by eosinophilic cytoplasm and grooved nuclei admixed with eosinophils, and are lack of the emperipolesis. In contrast, the large histiocytes in RDD have round nuclei and vesicular chromatin. Moreover, langerhans cells were strongly reactive for S100 protein and CD1a, but only rare CD1a-positive cells are found in RDD. Another differential diagnosis considered is thymoma, which is the most common tumor of the anterior mediastinum. The tumor is typically composed of neoplastic thymic epithelial cells and a variable number of lymphocytes that can be confused with RDD. The epithelial cells may be round, polygonal, oval or spindle-shaped. Immunohistochemistry can also help bacause the tumor cells can express cytokeratin (CK), carcinoembryonic antigen (CEA) and epithelial

membrane antigen (EMA), and lymphocytes express CD4 and CD8. Whereas the expression of S-100 is typically negative. Lymphoma can be separated from RDD by their dispersed cell population, distinctive cytologic features, positive staining for specific protein in corresponding type and negative staining for S-100, CK and CEA.

IgG4-related disease can also be confused with RDD. This disease is characterized by the presence of abundant IgG4+ plasma cells infiltration, with tissue sclerosis and elevated serum IgG4 concentration [9]. This disease can occur in a variety of anatomic locations all over the body including thymus [10]. Because IgG4-related disease shares some common characteristics such as abundant plasma cells infiltration and stromal sclerosis with RDD, several studies have presumed that RDD and IgG4-related disease might overlap to some extent [11, 12]. As to the current case, immunohistochemical staining for IgG4 failed to exhibit increased number of IgG4 plasma cells and higher ratio of IgG4 to IgG, so it did not meet the criteria of IgG4-related disease.

Most RDD patients have a benign clinical course, but some patients with RDD involving extranodal sites or autoimmune disease can have an unfavorable course [2, 13]. Recurrence is common in extranodal RDD [14]. Thus, complete excision is the treatment of choice. As to the mediastinal bronchogenic cyst, considering cyst enlargement leading to compression of adjacent organs, surgical resection is recommended. Our patient has the thymic RDD, along with bronchogenic cyst completely removed simultaneously. No additional treatment was initiated, and the patient remained disease-free for the following two years.

We present a rare case of isolated thymic RDD with mediastinal bronchogenic cyst. This diagnosis was made based on the typical morphological and immunohistochemical features. When considering RDD, it is important to exclude other common mimickers, including LCH, thymoma, lymphoma, and IgG4-related disease.

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Disclosure of conflict of interest

None.

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