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Case Report

Rosai-Dorfman disease of thymus with elevated serum anti-acetylcholine receptor antibody: a case report

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Abstract: Rosai-Dorfman disease is a rare disorder of histiocytic proliferation in lymph nodes and at extranodal sites. We herein describe a patient with isolated Rosai-Dorfman disease in the thymus with elevated anti-acetylcholine receptor antibody. We examined the relationship between Rosai-Dorfman disease and elevated anti-acetylcholine receptor antibody. To our knowledge, elevated anti-acetylcholine receptor antibody has not been reported in isolated thymic Rosai-Dorfman disease.

Keywords: Rosai-Dorfman disease, thymus, anti-acetylcholine receptor antibody

Introduction

Rosai-Dorfman disease is a rare disorder of histiocytic proliferation affecting systemic lymph nodes and/or other organs [1]. We experienced a case with Rosai-Dorfman disease limited to the thymus, in which elevated serum anti-acetylcholine receptor (anti-AChR) antibody was detected. The thymus is a very rare site of Rosai-Dorfman disease. There are no reports describing elevated anti-AChR antibody in Rosai-Dorfman disease of the thymus. Thus, Rosai-Dorfman disease of the thymus may cause a high anti-AChR antibody level in serum.

Case report

A 70-year-old female presented for routine medical check-up. Her past medical history was unremarkable except for a renal stone diagnosed six years earlier. Chest computed tomography revealed an incidental nodular lesion in the anterior mediastinum. The lesion measured 2.7 × 1.5 × 1.2 cm, had a clear boundary, was internally uniform, and showed extensive contact with the pericardium (**Figure 1A**). On magnetic resonance imaging, the lesion had a higher signal intensity than the skeletal muscles on both T1-weighted (**Figure 1C**) and T2-weighed (**Figure 1D**) images. Fluorine-18 fluorodeoxyglucose positron emission tomography (FDG-PET) revealed FDG accumulation within the lesion, showing a maximum standardized uptake value of 3.5 (**Figure 1B**). The initial tentative clinical diagnosis was "suspicion of thymoma". The serum anti-AChR antibody level was 1.5 nmol/L (normal: <0.2 nmol/L). However, myasthenia gravis was ruled out by detailed examination. Thus, we performed surgery to obtain a definitive diagnosis of the lesion. The nodular lesion was located on the pericardium. We partially resected the pericardium because the lesion was firmly adherent to the affected portion of the pericardium.

The thymectomy specimen was examined pathologically. Histologically, proliferation of spindle epithelioid histiocytes with hyalinized fibrosis was demonstrated. Foamy macrophages were aggregated at sites of reactive lymphoid proliferation with germinal centers (**Figure 2A**,

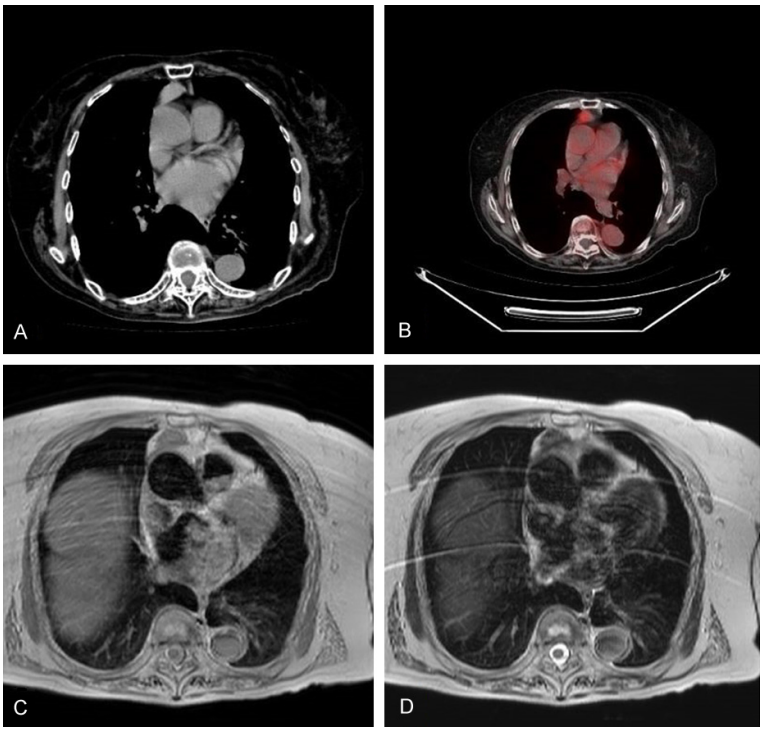

Figure 1. A. Chest computed tomography scan shows a well-defined nodular lesion located in the anterior mediastinum. B. Fluorine-18 fluorodeoxyglucose (FDG) positron emission tomography shows FDG accumulation in the lesion, with a maximum standardized uptake value of 3.5. C, D. Magnetic resonance imaging shows the lesion to have a higher signal intensity than the skeletal muscles on both T1(c)- and T2(d)-weighted images.

2E, **2F**). The cytoplasm of the foamy macrophages contained lymphocytes, plasma cells, and erythrocytes (**Figure 2A**, **2B**), a phenomenon termed "emperipolesis" which is among the characteristics of Rosai-Dorfman disease. Immunohistochemically, a Cytokeratin 19 and Cytokeratin AE1/AE3 positive meshwork of epithelial cells was observed in the background thymic tissue (**Figure 2C**). The macrophages expressed diffuse S-100 protein (**Figure 2D**), CD68, and limited amounts of CD163, but less than 1% of the macrophages stained for Ki-67. The diagnosis of Rosai-Dorfman disease of the thymus was thereby confirmed. No other focus of Rosai-Dorfman disease was identified anywhere else in the body.

At 24 months postoperatively, no recurrence of Rosai-Dorfman disease has been detected.

Discussion

Rosai-Dorfman disease is a rare disorder of histiocytic proliferation affecting systemic lymph nodes and/or other organs. Isolated Rosai-Dorfman disease rarely develops in the thymus and, to our knowledge, only two complete case studies have been reported to date in the English literature [2, 3]. In the first report, describing a case of isolated thymic Rosai-Dorfman disease, FDG-PET was performed and supported an accurate diagnosis. The other case had thymic Rosai-Dorfman disease with primary splenic lymphoma. In both cases, radiologic and clinical examinations indicated thymoma prior to pathological examination. Moreover, the patient with malignant lymphoma was pathologically misdiagnosed as having sclerosing thymoma but was then later diagnosed correctly at a facility based on pathological examination. As in the first case, even with FDG-PET a diagnosis of Rosai-Dorfman disease of the thymus can be difficult to confirm without pathological examination. The poor clinical outcome of the second case was suspected to be due to the splenic lymphoma rather than the thymic Rosai-Dorfman disease, because the latter usually has a favorable clinical outcome, and a watch-and-wait approach with or without a surgical excision is thus recommended [3].

This is the first report to document elevated anti-AChR antibody in Rosai-Dorfman disease of the thymus. Elevated anti-AChR antibody is thought to cause myasthenia gravis, and thymic disorders including hyperplasia of the thymus and thymoma are considered to trigger high anti-AChR antibody levels. In our present patient, lymphoid follicles with a germinal center were observed in the thymus. Rosai-Dorfman disease is related to abnormal immune responses, which could reflect an immune system deficit [4]. It is widely accepted that lymphoid follicles in the thymus are frequently identified in autoimmune diseases, being present at an especially high frequency in myas-

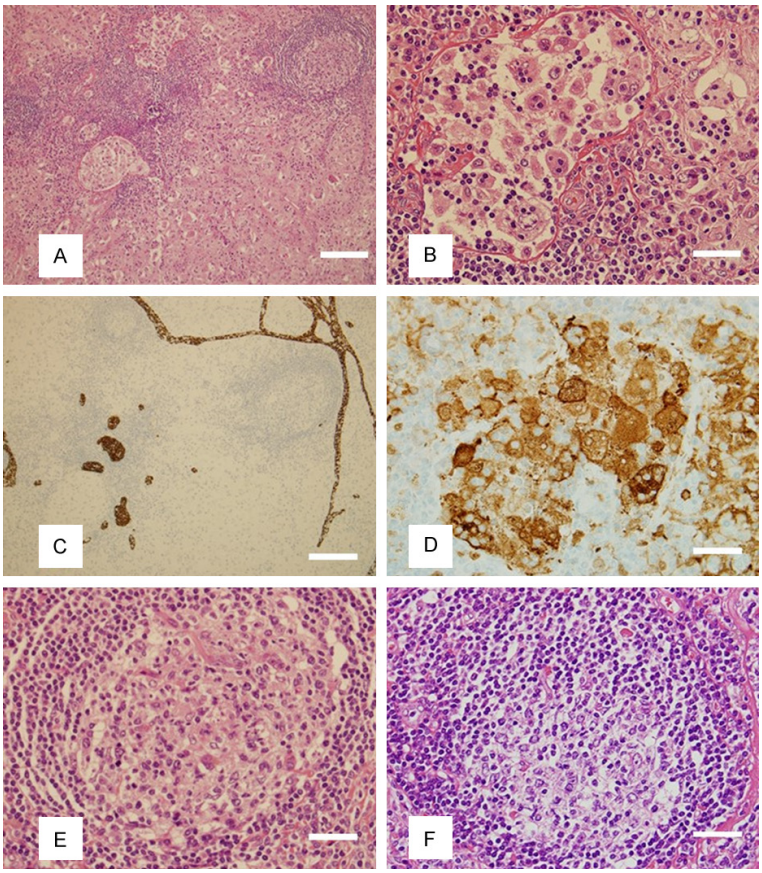

Figure 2. (A) Epithelioid histiocyte proliferation with hyalinized fibrosis. Foamy macrophages show aggregation at reactive lymphoid proliferative sites with a germinal center. (Hematoxylin and eosin (H&E) 100×) (bar is 200 μm). (B) The foamy macrophages contain lymphocytes, plasma cells, and erythrocytes in their cytoplasm, i.e. "emperipolesis" (H&E 400×) (bar is 50 μm). (C) Cytokeratin 19-positive meshwork of epithelial cells in the background. (100×) (bar is 200 μm). (D) The macrophages diffusely express S-100 protein. (400×) (bar is 50 μm). (E) Germinal center seen in (A). (H&E 400×) (bar is 50 μm). (F) Germinal center seen at another site in the thymus (H&E 400×) (bar is 50 μm).

thenia gravis, while lymphoid follicles with germinal centers are rare in the normal thymus [5]. Although in this patient myasthenia gravis was absent, the state of elevated anti-AChR antibody seen in this patient is common in patients with myasthenia gravis. Thus stimuli from activated macrophages, such as chemokines, inducing proliferation of lymphoid follicles and germinal centers are thought to have existed in the thymus of this patient [6, 7]. As was hypothesized in a previous report, we speculate that a signal disturbance was transduced to germinal center B-cells, thereby leading to B-cell activation and the prevention of B-cell apoptosis [8]. Activation of the germinal centers was thought to underlie the high level of anti-AChR antibody production by nonspecific surviving auto-reactive B-cell clones producing autoantibodies [8]. Rosai-Dorfman disease of the thymus can cause anti-AChR antibody elevation.

In conclusion, we experienced a rare case with Rosai-Dorfman disease of the thymus and have discussed herein its relationship with elevated serum anti-AChR antibodies. This is the first report to document elevated anti-AChR antibody in Rosai-Dorfman disease of the thymus.

Disclosure of conflict of interest

None.

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