



Surgical Removal of a Thymoma without Myasthenia Gravis Can Have a Therapeutic Effect on Concurrent Alopecia Areata: A Case Report

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Alopecia areata is a chronic organ-specific autoimmune disease and it could be associated with other autoimmune diseases. We, herein, report a case of alopecia areata in a patient with a thymoma without myasthenia gravis. Multiple hairless patches rapidly developed 6 weeks before the first visit on the patient who had been newly diagnosed with thymoma 2 weeks before the hairless patches occurred, and thymectomy was done 2 weeks before visiting dermatologic department. She had no symptoms associated with myasthenia gravis, and there were no abnormal findings on neurologic exams and acetylcholine receptor autoantibody was not detected in serum. Scalp biopsy showed numerous lymphocytic inflammations around hair follicles and in immunohistochemical staining, the aggregation of CD4+ and CD8+ T cells was observed around hair follicles and FoxP3+ T lymphocytes were rarely observed around hair follicles. The patient refused any treatment and her hairless patches were completely recovered 3 months after thymectomy, without being recurred 3 years after thymectomy. On the basis of both clinical manifestations and histologic findings, we concluded that alopecia areata in the patient had developed in association with thymoma and was recovered rapidly after thymectomy.

Keywords: Alopecia areata, Autoimmune diseases, Thymectomy, Thymoma

INTRODUCTION

Alopecia areata (AA) is a non-scarring hair disorder that develops once or more than once during the lifetime in 1.7% of the population¹. It is a chronic organ-specific autoimmune disease and is often associated with many other autoimmune diseases, such as vitiligo, lupus erythematosus, myasthenia gravis (MG), and scleroderma². The natural course of AA is highly variable, and more than 50% of the patients recover in a year without treatment; however, most of the patients will experience the recurrence³. Although AA is not a life-threatening disease, it can have an aesthetic and social or psychological impact on the patient temporarily or permanently.

Pathogenically, AA occurs due to an immune privilege collapse in the anagen hair follicles (HFs) and an inappropriate immune response of autoimmune CD8+ cytotoxic T cells to

follicular autoantigens^{4,5}. Furthermore, several studies reported that AA is also associated with the deficient function of FoxP3+ regulatory T cells (Treg cells) that contribute towards peripheral tolerance. The number of FoxP3+ lymphocytes around HF and in the peripheral blood decreased in AA patients, compared to that in the controls^{6,7}.

Thymoma, the most common tumor in the thymus, is histologically a heterogeneous tumor of thymic epithelial cells, and more than 95% of thymomas can generate thymocytes that mature into CD4+ or CD8+ cells^{8,9}. Thymomas are frequently associated with various paraneoplastic syndromes; among these syndromes, MG is the most common and develops in 30% to 44% of the patients⁹. AA occurs in 0.5% to 17% of the patients with thymoma, and various other autoimmune skin diseases, such as vitiligo and lichen planus can also develop^{9,10}.

Continuous efforts are being made to understand the



pathogenesis of AA. Herein, we report a case of AA in a patient with thymoma without MG, which improved rapidly after thymectomy and AA recurrence has not been observed to date. We hope this case report may aid in elucidating the pathogenesis of AA.

CASE REPORT

A 46-year-old Korean female presented with multiple hairless patches on her scalp (Fig. 1A, B). The patient was diagnosed with thymoma without MG since 5.6-cm-sized mediastinal mass had been found 8 weeks before the visit on chest CT (Fig. 1C) and any symptoms including muscle weakness or ptosis, any abnormal findings in neurologic examination, nerve conduction test, electromyography were not reported. Serum acetylcholine receptor autoantibodies was also not detected. Thymoma tissue removed by thymectomy showed predominant type B1 histology (2015 WHO classification), and diagnosis

of stage III was made. Multiple hairless patches were initially found on her occiput a month before the surgery and the number and the size of the patches rapidly increased. And at the first visit, multiple round or ovoid hairless scalp were observed on parietal and occiput areas (Fig. 1A, B). She had no previous history or family history of AA and had no other diseases except thymoma. Scalp biopsy showed numerous lymphocyte infiltration around HFs, and the miniaturization of the HF was not observed prominently (Fig. 2A). Immunohistochemical (IHC) staining revealed the presence of CD4+ T cells and CD8+ T cells around the HFs (Fig. 2B, C), and FoxP3+ lymphocytes were rarely observed (Fig. 2D) compared to the cell population observed in the normal scalp (Fig. 2E). And in the thymoma tissue removed by thymectomy, dense infiltration of lymphocytes with increased density of thymic epithelial cells were observed, and IHC staining showed increased number of CD8+ T cells and only a few FoxP3+ Treg cells (Fig. 3).

The patient was diagnosed with AA and was suggested for

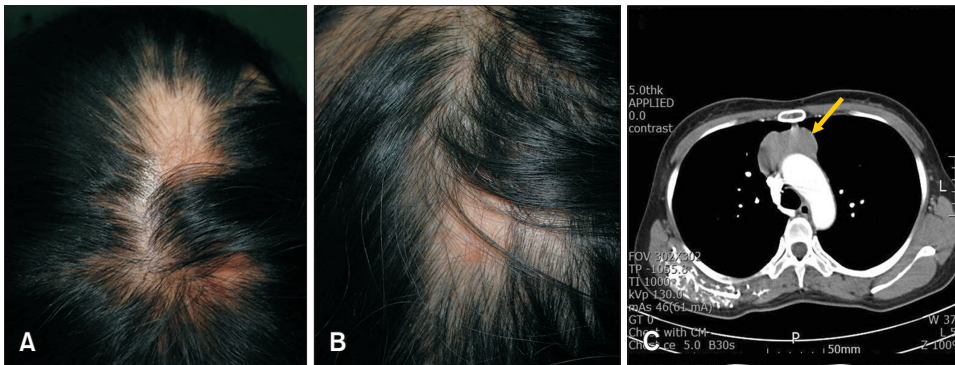


Fig. 1. Clinical presentation. (A, B) Multiple hairless patches observed on the scalp at the first visit. (C) Chest computed tomography showing round soft tissue attenuation located between the sternum and great vessels, indicative of a thymoma (arrow).

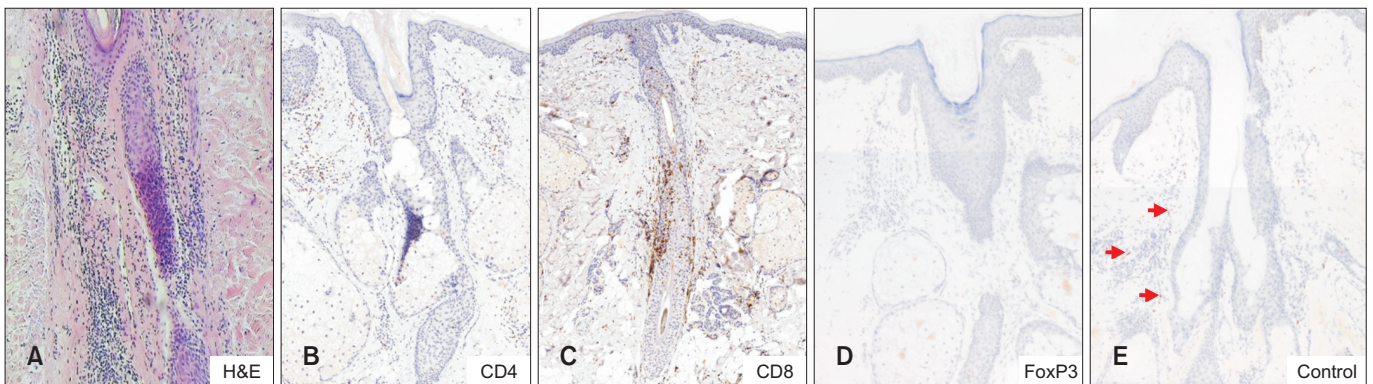


Fig. 2. Histopathological findings of alopecia areata lesion. (A) Scalp biopsy specimen obtained from the alopecic patches showing inflammatory cell infiltration around the hair follicles (HFs) (H&E, 200 \times). (B, C) Immunohistochemical staining showing that CD4+ and CD8+ lymphocyte infiltration around the bulge and bulb of the HFs (B: CD4 staining, 100 \times ; C: CD8 staining, 100 \times). (D) Immunohistochemical staining confirmed the scarcity of FoxP3+ lymphocyte in alopecia areata lesion. (E) A small number of FoxP3+ lymphocytes gathered around the HFs (arrows) in normal scalp (D, E: FoxP3 staining, 200 \times).

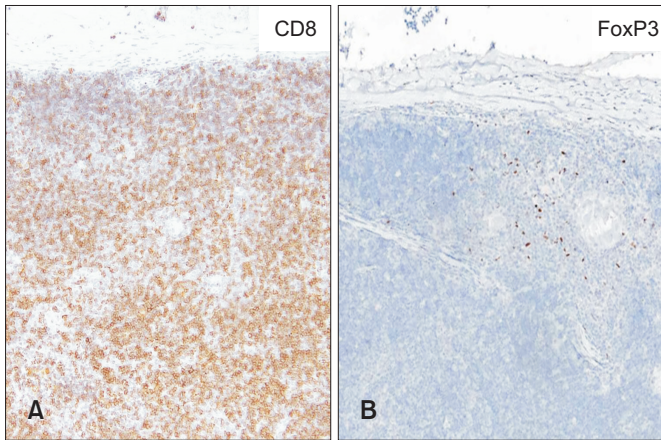


Fig. 3. Immunohistochemical staining of thymoma tissue removed by thymectomy (A: CD8 staining, 100 \times ; B: FoxP3 staining, \times 100). Immunohistochemical staining of the thymoma tissue removed during thymectomy showing predominantly increased CD8+ T cell counts (A) and only a few FoxP3+ T cells (B).

the treatment, but she refused any treatment and just wanted regular checkups. During regular follow-ups, newly growing hair appeared on the alopecic patches and the result of hair pull test also improved, reaching negative results 3 months after the surgery. The patient's hairless patches were also fully and steadily recovered 3 months after the surgery without any intermittent worsening during the period, and it has never recurred for 3 years after the surgery. The thymoma has also not recurred. Written informed consent about publication of this case report and accompanying images was obtained from the patient.

DISCUSSION

We report a case of AA that developed concurrently with a thymoma without MG in a 46-year-old Korean female and were resolved after thymectomy. In MG, the most studied autoimmune disorder associated with thymoma, pathogenetic mechanism mainly involves CD4+ T cells¹¹. But in AA, role of CD8+ T cells was known to be important, and several studies have been attempted to explain the mechanism underlying thymoma-associated autoimmune diseases such as AA¹²⁻¹⁴. Shelly et al.¹⁴ suggested the following mechanisms based on the aspect that the 'sick thymus' generates mature but impaired T cells: first, thymoma-derived thymocytes that are immature and have insufficient self-tolerance bypass the medullary areas in which self-tolerance was achieved, escape into the circulation, and become autoreactive; second, the cortical thymo-

cytes in the thymoma show increased turnover rate, which can induce genetic mutation, and neoplastic epithelial cells can also affect autoimmunity due to the impaired expression of HLA-DR; last, the CD8+ T cells with impaired tolerance from the thymoma can additionally induce the activation of CD4+ T cells that produce autoantibodies at the periphery. Moreover, improperly educated or lower counts of Treg cells may be produced due to thymomas compared to that produced by the normal thymus, thus, resulting in the decrease in the Treg cell count in both the thymus and peripheral blood, and decreased regulation of the thymoma-derived CD8+ T cells^{7,15}.

Thymoma without MG is generally diagnosed later than thymoma with MG because it is asymptomatic in many cases¹¹. Thymomas may be associated with autoimmune diseases, including AA; however, the association is not as common as that observed in case of MG. And literature review confirmed five cases of AA associated with thymoma, in which all patients were accompanied by MG, and three cases reported the improvement of AA after thymectomy^{10,16-20}.

In our patient, the development of AA could be an indicative of the association between AA and thymic dysfunction, as AA improved after thymectomy. Before thymectomy, her AA lesion was getting worse but it was resolved steadily and completely cured 3 months after the surgery. And the hair regrowth observed in this case was faster than those observed in other AA patients. Although there is no absolute evidence for whether CD8+ T cells from the thymoma were autoreactive toward the HFs, we found the increased CD8+ T cells and decreased FoxP3+ T cells in both alopecic patches and thymoma tissues, and the patient's clinical course also suggested that her AA was caused by thymoma.

Herein, we report a rare case of AA that developed concurrently with thymoma without MG; the alopecic patches were fully resolved after thymectomy. We hope that our case findings may aid in elucidating both the pathogenesis of AA and the association of AA with other autoimmune diseases.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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