**ACTIVATED B CELLS IN THE THYMUS GLAND OF PATIENTS WITH MYASTHENIA GRAVIS**

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Myasthenia gravis (MG) is an autoimmune disease caused by the production of autoantibodies that damage acetylcholine receptors (AchR) at the myoneuronal junction. It is well documented that abnormalities of the thymus gland, including lymphofollicular thymitis and thymoma, may play a role in the pathogenesis of this disease. Association between acetylcholine receptor autoantibodies and thymic changes such as lymphofollicular hyperplasia (LFH) have been widely discussed. Although LFH is not pathognomonic for MG, it is the most common pathologic finding. Germinal centers (GCs) found in MG patients are larger and more frequent than those in normal individuals. Previous studies revealed hyperactivity of B and T cells in MG. Expression of AchR in the thymus gland, hypersecretion of thymopoietin, and anarchism in the immunoregulatory mechanism involving B and T cells are other proposed mechanisms.

To assess the role of B cells in the pathogenesis of MG, we performed an immunohistochemical study on frozen sections prepared from the thymus gland of seven MG patients who underwent thymectomy.

Over a 2-year period, from 1999 to 2001, seven patients were diagnosed by a neurologist as having MG on the basis of clinical features and electromyographic studies as well as response to anticholinesterase drug therapy. The treatment regimen included thymectomy to improve symptoms. Thymectomy sections were fixed in acetone and washed with phosphate buffer solution. Thereafter, they were treated first with methanol and then with diluted mouse monoclonal antibodies against CD21, CD23 and anti-IgM markers (Becton and Dickenson, USA). After drying, polyvalent goat antimouse Ig peroxidase conjugate (Dako, Denmark) was added to the sections. For staining the nuclei, the sections were processed with hematoxylin.

Immunohistochemical staining for studying the phenotype of B cells on sections revealed activated B cells expressing CD21, CD23 and IgM markers in the thymus glands with LFH present in all seven patients. B cells expressing IgM and CD21 markers were predominantly in the central parts of the GCs of the medulla, whereas activated B cells expressing CD23 were mostly in the outer zones of the GCs (Figures 1 and 2).

Several histopathologic changes can be seen in the thymus gland of MG patients. The most prominent pathologic feature is thymic hyperplasia, found in 50 to 60% of cases. This hyperplasia is accompanied by GCs containing B

![Figure 1. Sections of thymus gland from one myasthenia gravis patient showing B cells expressing IgM and CD21 markers in the germinal centers (indirect immunoperoxidase method with anti-CD23 monoclonal antibody [Bu38.MHM6]; original magnification X 400).](image-url)
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Lymphocytes, which may be a source of autoantibody production. This has been demonstrated by in vitro antibody (anti-AchR) production by cultured lymphocytes of the thymus gland of MG patients.9, 10 This study was undertaken to further clarify the phenotypic changes of lymphocytes by assessing activation markers.

CD21 and CD23 markers are among those expressed on the surface of activated B cells.11 These markers have been studied by Leprince et al on 12 thymus gland sections from MG patients with LFH using immunofluorescent antibodies against CD21, CD23, CD19, IgM and IgD. They showed that B cells with IgM and IgD markers were predominantly on the outer zones of GCs, while more mature B cells were mostly in the follicular part of GCs.9 We encountered the same findings in our study. CD21 and CD23 might also be found on follicular dendritic cells (FDC) and CD23 on activated T cells. Leprince et al separated FDC from thymus cells to examine pure B cells, which again expressed CD21 and CD23 markers.11 Higher amounts of anti-AchR antibodies were found in patients expressing more CD23. In conclusion, we investigated only CD21, CD23 and IgM markers of the thymus gland in MG subjects and showed that activated B cells might play a role in the pathogenesis of this disease, which is in accord with previous studies.9, 10, 12

References