

# Myelin basic protein expression in thymoma after methylprednisolone administration for multiple sclerosis

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## Abstract

The relationship between thymic epithelial tumour and demyelinating disease (DD) is unknown and surgical resection has not been optimized. A 39-year-old woman was administrated methylprednisolone for newly diagnosed multiple sclerosis. A thymic tumour was found in the antero-superior mediastinum via computed tomography of the chest. Video-assisted thoracoscopic thymectomy was performed. Histologically, the tumour was diagnosed as Type AB thymoma. Immunohistochemical staining showed positive myelin basic protein (MBP) in the cytosol of spindle cells in the tumour specimen. Germinal centres or lymphocytes infiltration were not noted. Ectopic MBP presentation in thymoma might be correlated with DD.

## KEYWORDS

autoimmune disease, multiple sclerosis, thymoma, thymus, video-assisted thoracoscopic thymectomy

## INTRODUCTION

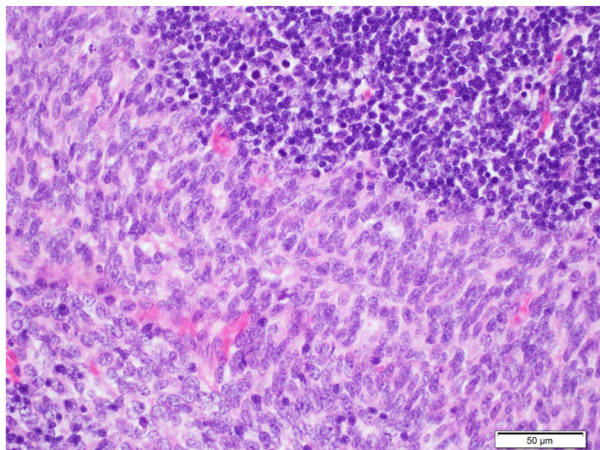
Multiple sclerosis (MS) is a demyelinating disease (DD) leading to demyelination and axon damage in the human central nervous system. MS is correlated with increased myelin basic protein (MBP) in cerebrospinal fluid.<sup>1</sup> MBP maintains the correct structure of myelin interacting with lipids.<sup>2</sup> Generally, MBP is strongly expressed in the central nervous system and not in the thymus, although mRNA expression of isoform MBP is found in foetal thymus and B cells, among others. In addition, the oligoclonal IgG band in the cerebrospinal fluid is positive in many MS patients, although the specific autoantibody for MS is still unknown.<sup>3</sup> MS is thought to be a T-cell-mediated autoimmune disease at the basis of an inflammation of nerve tissue and demyelination because invading peripheral immune cells are found in lesions and the production of immune molecules, including cytokines among others, has been noted.<sup>4</sup>

Thymoma is sometimes accompanied by an autoimmune disease, such as myasthenia gravis and red cell aplasia, among others. However, thymoma accompanied by MS has not been reported.

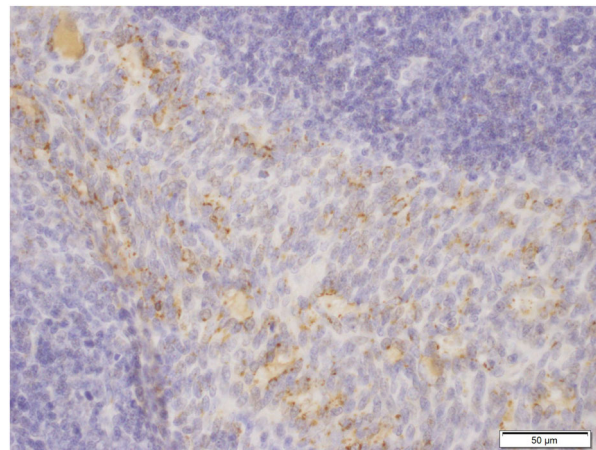
## CASE REPORT

A 39-year-old woman presented to the hospital with dysarthria and dysgraphia in the right hand. She had no significant medical history. Contrast-enhanced magnetic resonance imaging (MRI) of the head showed a high-intensity lesion with rim enhancement in the left corona radiata on diffusion-weighted imaging and T2 imaging. Another high-intensity lesion was also noted in the right cerebral cortex, which did not show enhancement. Cerebrospinal fluid testing was positive for MBP and negative for anti-aquaporin-4 antibodies. The oligoclonal band was positive. DD, especially MS, was suspected as one criteria for MS was fulfilled; dissemination in time and space.<sup>3</sup> Methylprednisolone (500 mg daily for 3 days and two courses of 1000 mg for 3 days, intravenously) was administered, and the symptoms improved. The lesions remained but the ring enhancement disappeared after MRI of the head.

On the other hand, chest computed tomography before steroid administration showed a homogeneous and hypodense mass of 30 mm in size with smooth contours and heterogeneous enhancement in the antero-superior mediastinum. Serum levels of soluble interleukin-2 receptor,



**FIGURE 1** Haematoxylin and eosin stain of Type AB thymoma with demyelination disease ( $\times 400$ ). The neoplasms were composed of short spindle-like epithelial cells and polygonal epithelial cells with lymphocytes



**FIGURE 2** Immunohistochemical staining of myelin basic protein ( $\times 400$ ). Positive staining was observed in cytoplasm of spindle-like cells in Type AB thymoma

carcinoembryonic antigen and anti-acetylcholine antibody were within normal range. Thymoma was suspected. Video-assisted thoracoscopic thymectomy using a subxiphoid approach was performed. There was a lobulated and elastic mass in the thymus, measuring  $40 \times 25 \times 20$  mm. Histologically, the neoplasms were composed of short spindle-like epithelial cells and polygonal epithelial cells with lymphocytes (Figure 1). No lymphoid follicles or germinal centres were observed in the thymus. This tumour was diagnosed as a Type AB thymoma (Masaoka Stage I, T1aN0M0 Stage I) based on the World Health Organization classification. Immunohistochemical staining of wide spectrum cytokeratin was positive in spindle cells and almost negative in polygonal cell areas. Immunohistochemical staining of MBP was positive in the cytoplasm of spindle-like cells in the thymoma (Figure 2). The thymus was completely negative for MBP.

The post-operative course was uneventful. At the 12-month follow-up, no evidence of tumour recurrence was detected. Currently, the patient has no difficulty speaking or writing with the right hand without any medication. The two lesions found via MRI of the head remain unchanged and no new lesions have appeared without treatment. The final diagnosis is mild MS, after differential diagnosis including with anti-gamma aminobutyric acid A receptor antibody-positive encephalitis and autoimmune encephalitis, among others based on good clinical courses.

## DISCUSSION

We showed positive ectopic MBP in Type AB thymoma in immunohistochemical staining. We could not find any report of thymic tumour with MS. To the best of our knowledge, this is the first report to show MBP expression in

thymic tumour. However, the role of MBP in thymoma or MS is still unknown.

Previous studies support the fact that external factors such as viral or bacterial infection, environmental agents or smoking cause dysregulation of immunological tolerance towards myelin structures, including MBP. If central tolerance in the thymus is broken, autoreactive T cells can escape central tolerance and be released into the periphery from the thymus. Central nervous system-directed autoreactive B cells and T cells can also be activated in the periphery by cross-reactive immune response occurring with mimicry between a foreign microbial antigen and auto-antigen, leading to inflammation and tissue damage.<sup>4</sup> MBP in the thymoma might have played a similar role to microbial antigens in causing MS or contributed to impairment of central tolerance in the thymus in our patient. If this hypothesis is correct, removing ectopic MBP by thymectomy might not avert relapses and drive chronic progression. The reason is that adaptive immunity must be completed, and this is a plausible reason why relapse and chronic progression are found in many MS patients after recovery from infection. Adapted immunity towards MBP may continue to exist and cause relapse and disability progression after thymectomy.

The thymus might not be involved in MS. Thymectomy showed no evidence of benefit in a previous study in which 34 MS patients underwent thymectomy followed by 3-year follow-up.<sup>5</sup> No abnormal finding was found in the thymus in our case. We have no reason to consider additional thymectomy for our patient in case of future exacerbation. On the other hand, we should consider the possibility that methylprednisolone administration before surgery might have changed the image of the thymoma and thymus. If abnormal autoantibodies are produced in the thymus before methylprednisolone administration, thymectomy is one choice for MS treatment.

Further accumulation and study of cases are necessary to unveil the relationship between DD and thymic tumour.

#### CONFLICT OF INTEREST

None declared.

#### AUTHOR CONTRIBUTION

Tomomi Isono: Data collection, analysis and discussion. Naoko Ose: Data collection, analysis and discussion. Keisuke Kawasaki: Analysis and discussion. Ayumi Shibata: Data collection, analysis and discussion. Soichiro Funaki: Discussion. Yasushi Shintani: Data collection, analysis, discussion and supervision.

#### ETHICS STATEMENT

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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