Continuous remission of myasthenia gravis
with the recurrence of thymoma

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[Summary]

The etiologic role of the thymus and thymoma in myasthenia gravis (MG) is still obscure. In this report, we presented a MG patient affected with thymoma whose myasthenic symptoms had disappeared after the surgical removal of thymoma together with non-thymomatous thymus. The patient had been continuously in remission when the thymoma recurred 6 years after.

We have speculated that there is a possibility that either the thymomatous or non-thymomatous thymus can have an effect positively or negatively on the development of myasthenic symptoms.

Key words: Myasthenia Gravis,
Thymoma

【症例報告】

胸腺腫再発時に筋無力症状の再燃をきたさなかった重症筋無力症の1例

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【Summary】

The etiologic role of the thymus and thymoma in myasthenia gravis (MG) is still obscure. In this report, we presented a MG patient affected with thymoma whose myasthenic symptoms had disappeared after the surgical removal of thymoma together with non-thymomatous thymus. The patient had been continuously in remission when the thymoma recurred 6 years after.

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【症例報告】

重症無力症（以下 MG と略す）は，高率に胸腺過形成あるいは胸腺腫などの胸腺異常を伴い，胸腺・胸腺腫摘出術により MG 症状の改善が得られることが知られている。通常，胸腺腫を合併した患者では MG 症状の自然緩解はま
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I. Introduction

MG は脳胞内の視覚基盤と呼ばれる自己免疫疾患である。MG 症状が増悪し、脳胞腫瘍出あるいは反射性療法などの脳胞腫瘍に対する治療が奏効した場合に MG 症状も改善することもあると考えられている。しかし、われわれが検索した限りでは脳胞腫瘍合併 MG において、脳胞腫瘍の再発と MG 症状の関係を明確にした報告を見出すことはできなかった。

今回、われわれは脳胞・脳胞腫瘍摘出後、MG 症状はほぼ完全覚解した後に、脳胞腫瘍は再発したが MG 症状の再然を認めなかった脳胞腫瘍合併 MG の 1 例を経験した。このような症例は MG と脳胞、脳胞異常との関連を考えるうえで示唆に富む症例と考えられたので報告する。

症例は 40 歳男性。1977年4月脳性下垂体で発症。同年6月 Osserman 分類で II A の MG と診断、気管内視鏡にて脳胞腫瘍の存在を認めたため同年7月外科的摘出を施行した。脳胞腫瘍は脳胞の一部と激していたが、これを含め非絵画性脳胞とともに全摘した。術後 MG 症状は徐々に改善し3年後には抗コリンエステラーゼ剤もまったく必要となっていた。術後6年後に脳胞腫瘍の再発を認めたが MG 症状は覚解状態を維持し続けた。この間に、抗アセチルコリン受容体抗体価にも変動を認めなかった。

本症例の MG 症状と脳胞腫瘍および非絵画性脳胞との関連について考えると、脳胞腫瘍そのものは MG 症状の発現には関与しておらず、脳胞異常脳胞が MG 症状の発現に関与していたと考えられる。

文献的には、脳胞腫瘍摘出後に MG が発症した例や、脳胞腫瘍摘出後に覚解状態にあった MG 症状が再現出した例、脳胞腫瘍摘出後に MG 症状が急性増悪した例、覚解状態にあった MG 患者で脳胞腫瘍がはじめて認められるようになったときに MG 症状が再現しなかった例などが報告されており、本症例も含め脳胞腫瘍には MG 症状発現に促進的因子が働く場合、抑制的に働く場合および本症例のように一時的には関与していないと思われる場合があることが示唆された。また脳幹外、脳胞腫瘍以外に甲状腺腫瘍および肺巣腔形腫瘍を合併しており、脳胞異常と腫瘍性疾患との関連をうかがわせる症例であった。

II. Case report

40 years-old female, she had developed blepharoptosis in April, 1977, and had been treated with anticholinesterase (anti-ChE) drugs under the diagnosis of MG. In June, 1977, she was referred to our hospital because of gradual worsening of her myasthenic symptoms involving generalized muscles (Osserman's type II A). Her symptoms were definitely reactive to...
the injection of edrophonium chloride. A waning phenomenon was demonstrated by repetitive supra-maximal nerve stimulation. The presence of thymoma was suggested by pneumomediastinography, and she underwent thymothymectomy with a trans-sternal approach plus a right thoracotomy. The thymoma was found in the right thymic lobe and had partially invaded into the pleura. The thymoma was totally removed with the pleura and non-thymomatous thymus was also resected completely. The weight of the resected thymus was 50 g. Histopathological diagnosis was lymphocyte-predominant mixed type thymoma (Fig. 1). Capsular and pleural invasion of the thymoma were also confirmed histologically. Follicular hyperplasia was demonstrated in non-thymomatous thymus (Fig. 2). Prednisolone (5 mg/day) had been added to anti-ChE drug (Mestinon) for the control of myasthenic symptoms 4 weeks after the thymothymectomy.

The patient had noticed an increasing thyroid mass in the right lobe since May, 1978, and hemithyroidec-tomy was performed in February, 1979. The patho-

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**Fig. 1.** Microphotograph of thymoma: The histopathological diagnosis was lymphocyte-predominant mixed-type thymoma (H & E staining, ×400).

**Fig. 2.** Microphotograph of the non-thymomatous thymus: This figure shows a germinal center and a Hassal's body in the thymus (H & E staining, ×100).
Fig. 3. Clinical course of the patient: This figure indicates the changes of muscle strength and anti-AchR antibody titers.

Fig. 4. Multiple metastases of the thymoma: This picture shows multiple metastases at the time of recurrence of the thymoma on the diaphragmatic, parietal and pulmonary pleura.

Fig. 5. Microphotograph of the metastatic thymoma: The histopathological diagnosis was mixed-type thymoma. The proportions of lymphocytes within the thymoma were variable among the tumors obtained from different metastatic portion (H&E staining, ×100).
logical diagnosis was follicular adenoma of the thyroid.

Both medication were tapered-off and finally discontinued during the time when her myasthenic symptoms had gradually improved and then disappeared by 1981 (Fig. 3).

In 1983, right ovarian tumor was found at the time of her regular gynecological examination, and removed surgically. The pathologic diagnosis was cystic teratoma of ovary. On the chest X-ray study at the time of her admission, multiple nodular lesions were found in the right pleural cavity. Recurrence of the thymoma with multiple pleural metastases was diagnosed by mediastinoscopy. All lesions were removed surgically with the invated pleura and diaphragm (Fig. 4). The pathological diagnosis was mixed type thymoma (Fig. 5). She received radiation therapy (Lineac 3000 R) post-surgically.

Since 1979, the serum anti-AchR antibody in this patient has been determined by radioimmunossay (Binding assay; anti-human IgG method, normal: less than 0.8 p moles/ml). The titer was always weakly positive and not increased when the thymoma was recurred. We could not determine the antibody, however, at the time of the first thymectomy.

Her muscle strength has been followed regularly and presented in Fig. 3. Both the myasthenic symptoms and thymoma had been in remission by the time of March, 1986.

III. Discussion

Spontaneous remission of myasthenic symptoms has been reported to be rare in MG patients affected with thymoma. In general, myasthenic symptoms worsen with the extension of thymoma and improve after the surgical removal of thymoma. It has been also considered that the symptoms relapse at the time when thymoma recurred, although we could not find any definitive report addressing the relationship between the recurrence of thymoma and myasthenic symptoms in this regard. We believe that this is the first case report of MG whose myasthenic symptoms had been in remission when the thymoma recurred after the previous thymectomy.

The myasthenic symptoms of the present patient disappeared after the surgical removal of both the thymomatous and non-thymomatous thymuses, whereas the symptoms did not relapse when the thymoma recurred. We can suggest, therefore, that the thymomatous thymus in the patient was not be primarily related to the development of MG symptoms, but the non-thymomatous thymus was. No increase in the anti-AchR antibody titer was observed with the recurrence of thymoma in this patient. This also supports our speculation on the role of thymoma in the patient.

In MG with thymoma, however, spontaneous remission has only rarely been reported. On the other hand, either occurrence, exacerbation or recurrence of the MG symptoms after the surgical removal of thymoma has been reported in the medical literatures. Two patients have been reported whose myasthenic symptoms did not relapse upon the recurrence of thymoma after the radiation therapy for thymoma. Another two patients also have been reported in which the thymoma became visible after remission of MG symptoms. Consequently, we considered, that, the effect of thymoma on development of MG could be variable.

The thymic epithelial cells are well known to have an important role in the maturation and differentiation of T-lymphocytes. The function of epithelial cells in the non-thymomatous thymus could be defective in MG patient, and the thymomas could preserve some of the function. We presented our concept of the relationship between MG and thymic abnormalities in Fig. 6. The T-lymphocytes from either the thymoma or non-thymomatous thymus would migrate to the peripheral lymphoid organs and regulate the anti-AchR antibody production of B-lymphocytes. The follicular hyperplasia has been known as one of the extra-thymic lymphoid tissue. The result here shown, the T-lymphocytes would stimulate or suppress the antibody production. In the patients whose MG occurred, exacerbated or recurred after the removal thymoma, the T-lymphocytes produced by the thymoma might be considered to have a negative effect on the antibody production. In this regard another possibility should be considered in both our
Fig. 6. Relationship between myasthenia gravis and thymic abnormalities: The function of thymic epithelial cells in the non-thymomatous thymus could be defective in MG patients, and the thymomas could preserve some of the function. The T-lymphocytes from either the thymoma or non-thymomatous thymus would regulate the anti-AchR antibody production positively or negatively. The follicular hyperplasia of the thymus has been known as one of the extra-thymic lymphoid tissue.

patient and the two patients whose MG did not relapse when the thymoma recurred after the radiation therapy for thymomas. The function of thymic epithelial cells has been changed, either over the time or by treatment, at the time of the recurrence of thymoma. Furthermore the T-lymphocytes being responsible for the development of thymoma.

Finally, another interesting point in this patient was that she developed three neoplasmas in different organs; the thymus, thyroid and ovary. All neoplasmas developed in the right side of organs. At present, we do not know whether any etiological relation should be considered among these neoplasmas.

References


