Case Report

A Case of Myasthenia Gravis Associated with Thymoma, Multiple Schwannomas and Monoclonal IgA Gammopathy

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Myasthenia gravis, malignant thymoma, multiple schwannomas and monoclonal IgA gammopathy coexisted in a 54-year-old Japanese man. Serum acetylcholine receptor antibody activity was located in the IgG fraction, but not in the paraprotein peak. It was speculated that all these disorders might fall under the spectrum of the diseases associated with thymic abnormality or that some growth factors might induce neoplasms and activation of B cell clones of autoantibodies (including acetylcholine receptor antibody) in this case.

Key Words: Myasthenia gravis, Thymoma, Schwannomas, Monoclonal IgA gammopathy.

Myasthenia gravis (MG) may occur in conjunction with disorders of autoimmunity of thymus. But presence of monoclonal IgA gammopathy and multiple schwannomas is not typical of MG with thymoma. This is the first patient reported with this unusual combination of rare diseases.

CASE REPORT

A 54-year-old Japanese male was admitted because of generalized muscle weakness and bilateral hand tremor of five year's duration. At age 46, he was evaluated for a complaint of facial edema, dilated superficial veins in the neck and chest, and subcutaneous nodules in the left axillary and right popliteral fossa and on the flexor aspect of the right wrist. The routine tests of blood chemistry showed no abnormal findings. Serum protein immunoelectrophoresis was not done at that time. Chest roentgenogram revealed a large anterior mediastinal mass with small disseminated nodules in the lungs. The histologic study of the mediastinal mass disclosed the characteristic mixed epithelial and lymphocytic thymoma (Fig. 1a). The nodule in the axillary region was removed, and histologically it was a benign schwannoma (Fig. 1b). As other subcutaneous nodules had similar clinical manifestations to the biopsied one, they were also regarded as schwannomas. He had undergone radiation therapy under the diagnosis of superior vena caval syndrome secondary to compression by the mediastinal tumor. After radiation therapy, the mediastinal mass diminished in size and his facial edema significantly improved. But at age 49, he noted generalized muscle weakness and diplopia late in the afternoon and bilateral hand tremor, which was intensified by emotional stress. As these symptoms progressed, he was referred to our department. His family history was non-contributory. On admission, he had facial edema with dilatation of collateral veins in the upper thorax and neck. One cafe-au-lait spot was noted on his back. Two subcutaneous nodules were palpable; one in the right popliteral fossa and the other on the flexor aspect of the right wrist. Pressing the nodules caused tingling sensation which radiated distally. Neurological examination revealed muscle weakness, most pronounced in the proximal limb muscles, and postural and action tremor in the both hands. The muscle weakness improved dramatically with intravenous administration of edrophonium. The response to repetitive supra-maximal stimulation of peripheral nerves showed a decline of the evoked action potentials by 75% at 3 shocks per second with normal initial amplitude. Chest roentgenogram showed that the medi-

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astinal mass and small nodules in lungs did not enlarge in size since the radiation therapy.

Other laboratory investigations including complete blood counts, ESR and electrolytes were normal. Tests of liver, kidney, thyroid and adrenal functions were normal. Serum immunoglobulin concentrations were IgG 720 mg/dl (normal range 800–2000), IgA 988 (80–350), IgM 63 (50–230) and IgE 46 (below 750). Serum protein immunoelectrophoresis revealed a monoclonal peak in IgA area (Fig. 2). With specific antisera, the monoclonal fraction was identified as IgA (lambda). Electrophoresis of urinary proteins was normal and Bence-Jones protein was negative. Bone marrow aspirate showed no abnormality of plasma cells.

For the measurement of serum acetylcholine receptor (AChR) antibody activity, AChR was partially purified from human muscle. The receptor was labelled with $^{125}$I-α-bungarotoxin (New England Nuclear). The toxin-receptor complex was incubated with the patient’s serum sample for 16 hours. The toxin-receptor-IgG complex was precipitated with rabbit anti-human IgG, while the toxin-receptor-IgA complex was precipitated with anti-human IgA (Miles Yeda). The titre of AChR antibody in IgG was 42 nM/L (normal: below 0.6). With anti-human IgA, however, no AChR antibody was detected. Other serological tests revealed positive antinuclear antibody and LE test. The complement levels were normal. After administration of anticholinesterase (pyridostigmine 120 mg per day), marked improvement in the patient’s condition was noted without effect on the tremor. As he had no cerebellar signs and head CT scan showed no cerebellar atrophy, this tremor was regarded as essential tremor.

**DISCUSSION**

In the present case, the clinical symptoms, electrophysiological findings, response of cholinesterase inhibitor, association of thymoma and finally presence of AChR antibody in the serum make the diagnosis of MG unequivocal. Presence
of multiple schwannomas and monoclonal IgA gammopathy as observed in this patient, however, is not typical of MG. To our knowledge, this is the first patient reported with this unusual combination of rare diseases.

The incidence of extrathymic neoplasms is higher in MG with thymoma than the expected in a control group. Papatestas et al reported that the incidence of primary brain and CNS tumors in patients with MG having extrathymic neoplasms was 5.3% and there was a case report of MG with thymoma and ganglioneuroma.

On the other hand, it is known that neurofibromatosis is one of conditions associated with thymoma. One possible explanation for the relationship between thymoma and neoplasm of nervous system, might be that both tumors have a common origin in the neural crest, since embryogenetically the thymic mesenchyme is known to be predominantly derived from the neural crest.

According to the conventional criteria, the present case is compatible with the benign monoclonal IgA gammopathy. Several cases of thymoma with monoclonal gammopathies have been reported. Furthermore, four cases have been reported with apparent association of M-component and MG; one of the four had multiple myeloma and the others had benign monoclonal gammopathies (IgG and IgM).

On the assumption that the M-component (IgA) in this patient contained AChR antibody activity, we measured the antibody titre with rabbit anti-human IgA. But the antibody activity was not located in the IgA peak, but in the IgG group. Somer et al also reported a negative result in a case of MG with monoclonal IgG gammopathy.

The radiation therapy on the thymus is known as one of the treatments of MG. This treatment is useful for invasive thymoma. In this case, the symptoms of MG appeared after radiation therapy. As development of MG following thymectomy has been reported, similar effect might work in this case.

Although lack of enough definite insight regarding control mechanisms for oncogenesis and immunological regulations makes any attempt to explain multiple disorders (MG, multiple schwannomas and IgA gammopathy) in the present case purely speculative, there might be some growth factors which induce the development of neoplasms (thymoma and schwannomas) and also activate B cell clones (IgA gammopathy and autoantibodies, including acetylcholine receptor antibody and antinuclear antibody).

REFERENCES