CASE REPORT

Autoimmune Thrombocytopenic Purpura, Autoimmune Hemolytic Anemia and Gastric Cancer Appeared in a Patient with Myasthenia Gravis

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Abstract

We report a case of myasthenia gravis (MG) associated with autoimmune thrombocytopenic purpura (AITP) and autoimmune hemolytic anemia (AIHA), and after that gastric cancer appeared. A 51-year-old man began to suffer from fluctuated muscle weakness in 1985. Muscle weaknesses became exacerbated, and he was admitted to our hospital in 1989. He was diagnosed as MG associated with AITP. After a thymectomy (hyperplasia), prednisolone therapy was started, subsequently his condition was satisfactory. In March 1995, he developed severe anemia and icterus. He was diagnosed as Evans’ syndrome (AIHA and AITP) with MG. High-doses of immunoglobulin administration improved the anemia, but thrombocytopenia continued. In November 2002, he suffered marked petechia; the platelet count decreased to 1000/μl. Methylprednisolone pulse therapy and platelet transfusion were started. Gastrofiberscopy was performed and biopsy specimens revealed signet cell-type adenocarcinoma. On December 19, 2002, subtotal gastrectomy and splenectomy were performed. After that, his condition has remained satisfactory, without MG symptoms or thrombocytopenia. This is the first such case report in the literature.

Key words: myasthenia gravis, autoimmune thrombocytopenic purpura, autoimmune hemolytic anemia, gastric cancer

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Introduction

Myasthenia gravis (MG) is associated with many types of autoimmune diseases. The coincidence of MG and autoimmune thrombocytopenic purpura (AITP) (1-6) or autoimmune hemolytic anemia (AIHA) (7-11) has only occasionally been reported. While AITP and AIHA are frequently associated with cancer, gastric adenoma is an extremely rare association (12-14). We offer the first report, to the best of our knowledge, of a case of MG associated with AITP and AIHA, and after that gastric cancer appeared.

Case

A 51-year-old man begun to suffer from muscle weakness of the lower extremities in the middle of 1985. Subsequently, muscle weakness progressed to the upper extremities, leaving the subject unable to wash his face by the end of 1985. Muscle weakness fluctuated but he was able to continue with his duties at work. In 1989, these muscle weaknesses exacerbated, and he was admitted to our hospital. He had never experienced ptosis, diplopia or dysphagia. Manual muscle strength testing revealed 3-4/5 strength in both the upper and lower extremities. The edrophonium chloride test was positive. The serum anti-acetylcholine receptor antibody titer was 216.5 nmol/l. Repetitive median nerve stimulation testing of musculus abductor pollicis brevis showed decrements in muscle action potential amplitude of 66% at 3 Hz, 63% at 5 Hz and 59% at 10 Hz. He was diagnosed with MG associated with AITP (platelet 7.3-10.8x10^4/μl). After a thymectomy showing hyperplasia, daily 20

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mg prednisolone therapy was started. The dose of prednisolone was gradually increased to 100 mg/day, then gradually decreased and withdrawn in December 1992. After that, his condition was satisfactory without any muscle weakness. In May 1994, laboratory data suggested anemia. In March 1995, he developed severe anemia and icterus. He was readmitted with a diagnosis of Evans’ syndrome (AIHA and AITP) with MG. Both direct and indirect Coombs tests were positive; the red blood cell count was 170×10⁴/μl and the white blood cell count was 3000/μl. Severe splenomegaly was detected. Intravenous immunoglobulin 400 mg/kg was administered for 5 days. Subsequently, laboratory findings improved, but thrombocytopenia continued with platelet counts fluctuating between 6-8×10⁴/μl. Fifteen mg prednisolone was administered every other day starting in December 2001. In August 2002, platelet counts fluctuated between 1.6-2.1×10⁴/μl, and the dose of prednisolone was increased to 20 mg every other day. In November 2002, he suffered intra-oral hemorrhage and marked petechia of the lower extremities; the platelet count decreased to 1000/μl. He was readmitted for severe AITP. Methylprednisolone pulse therapy (1000 mg for 3 days) and 20 units of platelet transfusion were started; subsequently, prednisolone 60 mg/day was started. Platelets increased to 10.7×10⁴/μl. Gastrofiberscopy was performed because of gastric complaints. Biopsy specimens revealed signet cell-type adenocarcinoma. On December 19, 2002, subtotal gastrectomy and splenectomy were performed. He was discharged on January 11, 2003 with a platelet count of 24.4×10⁴/μl. After that, his condition has remained satisfactory, without MG symptoms or thrombocytopenia [Fig.]. He is working in usually good health in October 2005.

Discussion

Nineteen years ago, the patient suffered from MG with associated AITP. After extended thymectomy and high dose prednisolone administration, MG went into complete remission, but AITP persisted. After 3 years, Evans’ syndrome was diagnosed. After an additional 7 years, he developed severe AITP and gastric cancer. Fortunately, the gastric cancer was not advanced, and subtotal gastrectomy with splenectomy was successfully performed. Thrombocytopenia subsequently improved.

MG is often associated with hematological autoimmune disorders such as AITP, pure red cell anemia, pernicious anemia, AIHA and pancytopenia. AITP, AIHA, autoimmune leukopenia and Evans’ syndrome may occur in any combination and are associated with other diseases including collagen vascular diseases and malignancies.

MG, AITP and AIHA are disorders caused by failures in autoimmune mechanisms. Combined MG and AITP or AIHA has been infrequently described. The association of AITP (17-19) or AIHA (13-16, 20-22) with malignancy is well known; however, coincident AITP or AIHA and gastric cancer appears to be extremely rare (12, 13, 15). Inoue et al (13) reported that the most frequent cancer sites associated with AIHA were lung, ovary and colon, and the most highest frequent cancer histological type was adenocarcinoma. Some authors have claimed that cancer and metastasis exacerbate AIHA (13, 16, 20, 21). It has been suggested that mucin produced by the neoplasm plays an important role in the development of immune hemolysis (16, 20, 22); however, in the patient there was no evidence of malignancy when AIHA was diagnosed. In the present case, early stage gastric cancer exacerbated AITP. In an immunodeficient host
erythrocytes and platelets may produce tumorigenic substances, or, alternatively anti-erythrocyte and anti-platelet auto-antibodies may facilitate the development of a malignant tumor. We could not determine which therapy was effective for AITP, because the patient underwent simultaneous gastrectomy and splenectomy.

In summary, the coincidence of MG and extrathymic tumors has been reported, and the risk of these associations has been described in 1.7-9% (23-30) of MG patients. In the present case, however, malignancy appears to have been associated with autoimmune deficiencies such as AITP rather than MG.

References