

Myasthenia Gravis and Chronic Lymphocytic Leukemia

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Myasthenia gravis, an autoimmune disease with a prevalence of 50 to 150 cases per 1 million persons, affects approximately 25,000 people in the United States.¹ Chronic lymphocytic leukemia (CLL) is the most frequent form of leukemia in adults in western countries.² Approximately 13,000 new cases of CLL are diagnosed in the United States each year, but because of prolonged survival associated with this disorder, the total prevalence is many times greater. The simultaneous occurrence of myasthenia gravis and CLL in the same person is quite rare. Only 10 such cases have been previously reported in the literature (Table 1).³⁻⁸ This article presents the case of a patient who developed CLL 15 years after receiving a diagnosis of myasthenia gravis.

CASE PRESENTATION

Initial Presentation and History

An 81-year-old white man with a 15-year history of myasthenia gravis came to the emergency department because of swelling in his neck, weight loss, and malaise over the past year. His myasthenic symptoms were well controlled with pyridostigmine. No thymectomy had been performed in the past.

Physical Examination and Laboratory Evaluation

On examination, the patient was obese but had significant loss of subcutaneous tissue; right partial ptosis; pallor; diffuse lymphadenopathy involving cervical, axillary and inguinal regions; marked hepatomegaly; massive splenomegaly; and bilateral lower-limb cellulitis.

Laboratory evaluation revealed a leukocyte count of $104 \times 10^3/\text{mm}^3$, with 90% lymphocytes, 6% neutrophils, 2% monocytes, and 1% eosinophils. Other laboratory measurements were as follows: hemoglobin, 8.8 g/dL; hematocrit, 26.3%; mean corpuscular volume, 122 fL; platelet count, $154 \times 10^3/\text{mm}^3$; reticulocyte count, 4 % of erythrocytes; serum lactate dehydrogenase, 523 U/L; and unconjugated bilirubin, 1.4 mg/dL. Results of uri-

nalysis and routine serum chemistry were within normal limits.

Diagnostic Studies

Chest radiography revealed no infiltrate, effusion, lymphadenopathy, or mediastinal widening. A computed tomography scan of the abdomen and pelvis confirmed marked splenomegaly, moderate hepatomegaly, diffuse lymphadenopathy, and cholelithiasis. Results of bone marrow aspiration with biopsy showed a hypercellular marrow with diffuse infiltration by small and medium-sized lymphoid cells.

DISCUSSION

Myasthenia gravis is an autoimmune disorder caused by antibodies^{9,10} directed against acetylcholine receptors¹¹ at the neuromuscular junction causing a decrease in the number of available receptors.¹² Myasthenia gravis has a bipolar incidence curve, with 1 peak in the second and third decades of life (affecting mostly women) and a second peak in the sixth and seventh decades of life (affecting mostly men).¹³

CLL is characterized by the clonal proliferation and accumulation of neoplastic B lymphocytes in the blood, bone marrow, lymph nodes, and spleen. The median age of patients diagnosed with CLL is 65 years, with only 10% to 15% of patients younger than 50 years.² The normal counterpart of CLL cells is a subpopulation of mature CD5+ B lymphocytes present in the mantle zone of lymph nodes and also in small numbers in the blood. The number of CD5+ B cells is greater in other autoimmune diseases (eg, rheumatoid arthritis, systemic lupus erythematosus, thyroiditis, Sjögren's syndrome).²

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Table 1. Reported Cases of Myasthenia Gravis and Chronic Lymphocytic Leukemia

Source	Year Reported	Sex	Age at Diagnosis of MG (years)	Age at Diagnosis of CLL (years)	Thymectomy Performed
Cohen and Waxman ³	1967	Male	28	58	No
Talvalkar and Meher-Homji ⁴	1968	Male	42	42	No
Vogel et al ⁵	1977	Male	63	63	No
Vogel et al ⁵	1977	Female	71	71	No
Vogel et al ⁵	1977	Unknown	28	58	No
Vogel et al ⁵	1977	Male	71	71	No
Vogel et al ⁵	1977	Female	29	58	No
Bennett et al ⁶	1980	Female	62	62	No
Kaplanski et al ⁷	1990	Female	47	65	Yes
Minard et al ⁸	1991	Unknown	51	50	No
Bawa and Rosner*	2002	Male	66	81	No

CLL = chronic lymphocytic leukemia; MG = myasthenia gravis.

*Present case.

The thymus has been implicated as the possible site of origin of the autoimmune response in myasthenia gravis,¹⁴ because 75% of affected patients have a thymic abnormality. Most of these patients have a hyperplastic thymus with active germinal centers, which contain dendritic cells and B lymphocytes; 15% of patients with myasthenia gravis have a thymoma. Thymectomy results in clinical improvement in most patients.¹⁵ A wide variety of other autoimmune diseases (eg, Graves' disease, thyroiditis, polymyositis, systemic lupus erythematosus, rheumatoid arthritis, skin disorders) have rarely been reported in patients with myasthenia gravis.¹³

In a retrospective study, 400 patients with myasthenia gravis underwent thymectomy and none developed CLL, whereas 5 of 1300 patients with myasthenia gravis and an intact thymus had CLL.⁵ In the past, thymic irradiation was used as treatment of CLL in nonmyasthenic patients.¹⁶ In all 11 cases (Table 1) thus far reported in the medical literature in which both diseases have occurred together, 5 patients had the simultaneous diagnosis of myasthenia gravis and CLL, 5 patients presented with myasthenia gravis first followed by CLL, and only 1 patient presented with CLL first followed by myasthenia gravis. In 10 of these 11 cases, no thymectomy was performed. In either disease, the inciting event or cause remains unknown. The occurrence of both diseases in the same patient may represent part of the wide spectrum of B-cell differentiation, with both conditions having a common pathogenesis. Alternatively, the occurrence of myasthe-

nia gravis and CLL in the same patient may be purely coincidental.

CONCLUSION

Myasthenia gravis and CLL are diseases that involve B lymphocytes. Both disorders are associated with other autoimmune disorders and malignancies; however, they rarely occur together in the same patient. The incidence of CLL is higher in patients with myasthenia gravis who have an intact thymus, compared with those who have had a thymectomy; the same finding occurs in rodents. The occurrence of both diseases in the case patient may be a chance association, may be caused by a defect in immunoregulation (as suggested in a previous study¹⁷), or may be linked to a certain genetic constitution.¹⁸ HP

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