Case Report

Myasthenia Gravis Associated with Lipodystrophy

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Patients with partial lipodystrophy frequently show hypocomplementemia but rarely have associated autoimmune diseases. We report here a patient of myasthenia gravis associated with limb lipodystrophy, a variant form of partial lipodystrophy, and hypocomplementemia.

Key Words: Myasthenia gravis, Lipodystrophy, Hypocomplementemia, Anti-acetylcholine receptor antibody, Autoimmune diseases

Partial lipodystrophy is a rare condition characterized by progressive and symmetrical loss of subcutaneous adipose tissue of the face, arms and trunk (cephalothoracic form) without antecedent clinical inflammatory or other pathologic changes¹⁾. The onset is usually in childhood and females are more frequently affected than males¹⁾. A variant form affecting fats in arms, legs and buttocks without facial and truncal involvement is called limb lipodystrophy²⁾. We report a patient of limb lipodystrophy which developed ten years after the onset of myasthenia gravis.

REPORT OF A CASE

A-29-year-old woman was in good health until November 1974 at the age of 19, when she developed left blepharoptosis. She was admitted to our hospital in April 1975 because of bilateral blepharoptosis, dysphagia and generalized muscular weakness. A diagnosis of myasthenia gravis was made on the basis of electromyographic evidence of neuromuscular fatigability and improvement of clinical signs with intravenous edrophonium. In May 1975, she underwent thymectomy. The thymus, which weighed 40 g, showed hyperplasia. After operation, alternate-day prednisolone was administered. The dosage was gradually increased. High doses (130 mg)

of prednisolone were continued for two months and then the dosage was gradually decreased. However, she sometimes experienced myasthenic crisis after the treatment of high doses of prednisolone.

In July 1980, she was reoperated because a remnant of the thymic tissue was thought to exist. However, no thymic tissue was found but only adipose tissue. After operation, 37.5 mg of alternate-day prednisolone was administered. Cyclophosphamide (300–500 mg) was administered intravenously twice a week for two months, and 100 mg of azathioprine subsequently. But immunosuppressive agents were withdrawn because of alopecia and leukopenia. In September 1980, the serum C3 level was 69.7 mg/dl (normal range: 55–120) and the C4 level was 21.1 mg/dl (20–50).

Because she sometimes had dyspnea or dysphagia, she had 12 sessions of plasma exchange in August 1982, followed by 100 mg of azathioprine and corticosteroid therapy. Her condition improved dramatically but she remained well only for several weeks. Anti-acetylcholine receptor (anti-AChR) antibody was measured by an immunoprecipitation method reported previously³⁾. The antigen was Triton extracted AChR obtained from human skeletal muscle at autopsy. The

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Table 1. Titers of anti-acetylcholine receptor antibody. Myasthenia developed in November 1974, and lipodystrophy in May 1983. After plasma exchange in August 1982 followed by treatment of immunosuppressive drugs, anti-acetylcholine receptor antibody decreased and her bulbar symptoms such as dyspnea or dysphagia disappeared.

Date	Anti-AChR antibody titer*
2 / 6 / 79	35
11 / 28 / 80	33
4 / 20 / 81	39
12 / 15 / 81	20
4 / 13 / 82	32
9 / 16 / 82	9.2
10 / 4 / 82	9.1
4 / 30 / 83	11
6 / 11 / 83	9.8

* $\times 10^{-9}$ M β -BuTX binding sites

range of the anti-AChR antibody titer of healthy individuals was $(0.32 \pm 0.12) \times 10^{-9}$ M α -bungarotoxin (α -BuTX) binding sites. Anti-AChR antibody titer was decreased by plasma exchange (Table 1). Prednisolone was administered as an alternate-day regimen with the dosage increased. She continued taking 100 mg alternate-day prednisolone for two months, then the dosage was gradually tapered down. At this time her bulbar symptoms disappeared.

In May 1983, she noticed a depressed area of her right thigh. There was no history of preceding induration, swelling or trauma to the affected sites. Physical examination revealed a demarcated atrophic area on the anteromedial surface of the right thigh (approximately 10 $\times$ 5 cm and 1 cm in depth), three linear atrophic lesions of the left anterior thigh (Fig. 1), and atrophic areas on the buttocks. No inflammatory or pigmentary changes were evident.

Laboratory findings in June 1983 were as follows: the hematocrit was 38.7%; the white cell

Fig. 1. Moderately demarcated atrophic area arrow on the anteromedial surface of the right thigh and three linear atrophic lesions of the left anterior thigh.

count was 1800/mm³, with 57% neutrophile and 35% lymphocytes. The glucose was 84 mg/dl, the total protein was 6.8 g/dl (albumin 64.4%, α 1-globulin 2.6%, α 2-globulin 6.3%, β -globulin 9.2%, γ -globulin 17.4%). CRP and rheumatoid factor were negative. Serum C3 level was 44.1 mg/dl (86 to 140), C4 14.6 mg/dl (20 to 55), C3 activator 14.0 mg/dl (11.5 to 225.6), and CH50 30 U/ml (30 to 45). Urea nitrogen, creatinine, glutamate oxaloacetate transminase, glutamate pyruvate transaminase, alkaline phosphatase, serum lipids, serum immunoglobulin (Ig) G, IgM, IgA, triiodothyronine and thyroxine were normal. Serum anti-microsomal antibody was positive, but anti-thyroglobulin antibody, anti-white blood cell antibody, anti-nuclear antibody, anti-smooth muscle antibody, and anti-mitochondrial antibody were negative.

Atrophic and apparently normal adipose tissue of the right thigh were biopsied in June. The adipose tissue in the depressed area was thinner than that of the normal area, but the size of the adipose cells of the depressed area were similar to those of the normal area. No inflammatory reaction was seen in the skin or adipose tissue.

The patient's myasthenic symptoms did not deteriorate after the appearance of lipodystrophy. Lipodystrophy progressed for only two months and later spontaneously ceased.

COMMENT

In post-steroid panniculitis, the subcutaneous nodules often associated with pruritus and tenderness appear one to thirteen days after discontinua-

tion of high doses of corticosteroid administration and heal with pigmentation without skin atrophy^{4, 5}). Post-steroid panniculitis develops not only after complete withdrawal but also during reduction of dosage after high dose administration of corticosteroid⁶). In our patient, although she had lipodystrophy after 100 mg alternate-day prednisolone, no subcutaneous nodule existed in the affected areas and the biopsy specimen did not reveal fat necrosis or cellular infiltrations. Thus the lipodystrophy of our patient was not a sequela of post-steroid panniculitis.

On rare occasions, partial lipodystrophy is accompanied by autoimmune diseases such as systemic lupus erythematosus⁷), Sjögren's syndrome⁸) or Goodpasture's syndrome⁹). Some patients with partial lipodystrophy have associated mesangiocapillary glomerulonephritis, hypocomplementemia due to depression of C3 and the presence of C3 nephritic factor, an autoantibody (IgG) against C3bBb^{10, 11}). Complement abnormalities have not been known to cause lipodystrophy or vice versa, however, it may be possible that partial lipodystrophy is associated with autoimmune mechanisms. Our patient showed low concentrations of C3, C4 and CH50 which are compatible with classical-pathway activation. The complement abnormalities of our case may be associated with lipodystrophy since serum complement levels were normal before the onset of lipodystrophy. We could not examine the C3 nephritic factor in her serum. Sissons et al.¹²) described a similar case (Case 25) of limb lipodystrophy with very low serum concentrations of C1q, C4 and C2. Although limb lipodystrophy is considered to be a variant form of partial lipodystrophy²), the relationship between limb lipodystrophy and complement activation is still unclear. Myasthenia gravis associated with lipodystrophy is extremely rare. Wilson et al.¹³) reported a case of lipodystrophy within bilateral third lumbar dermatome with thyrotoxicosis, myasthenia gravis, idiopathic thrombocytopenic purpura, bilateral optic atrophy and sensorineural deafness.

Because biopsy specimens from the atrophic and the apparently normal area revealed that the sizes of the adipose cells were normal, lipodys-

trophy in our patient is attributable to decrease of the number of adipocytes rather than to reduction of the volume of adipocytes as reported previously¹⁴). The mechanism of the reduced number of adipocytes had not been known, however, in our case it may be associated with autoimmune phenomenon.

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