Yonago Acta medica 1999;42:131–134

Chronic Fatigue Syndrome and IgA Nephropathy Occurring in the Same Patient

Kiyotaka Kohama

Second Department of Internal Medicine, Faculty of Medicine, Tottori University, Yonago 683-0826, Japan

We report a patient with a rare association of chronic fatigue syndrome (CFS) and IgA nephropathy (IgAN). The patient was a 45-year-old woman who presented initially with biopsy proven IgAN and 2 years later developed CFS. Because of proteinuria and hematuria, she was referred to our clinic. A renal biopsy done at that time revealed IgAN. Then she was struck by the sudden onset of profound fatigue. According to criteria published by the Centers for Disease Control and Prevention in the United States, we diagnosed her illness as CFS.

Key words: chronic fatigue syndrome; IgA nephropathy; chinese herbal medicine; immunology

Chronic fatigue syndrome (CFS) is characterized by a principal complaint of severe fatigue of at least 6 month's duration. No single pathogenic mechanism has been consistently identified using physical or laboratory tests, thus making the diagnosis of CFS one of exclusion (DeLuca et al., 1997; Komaroff et al., 1997). We report a patient with a rare association of CFS and IgA nephropathy (IgAN).

Patient Report

In August 1994, a 43-year-old woman was referred to our hospital because of episodes of proteinuria and occult hematuria. She was a housewife and a sales representative of the department store. A renal biopsy done at this time revealed IgAN to a moderate degree. Microscopic examination of her renal biopsy tissues showed a focal segmental proliferative glomerulonephritis (Fig. 1). Mesangial granular deposits of IgA and C3 were identified by immunofluorescence.

During the follow-up where she was given a 75 mg daily dose of dipyridamole she remained well, in a rather good condition, except for persistent microhematuria and proteinuria. In May 1995 she developed the sudden onset of profound fatigue, morning stiffness and low grade fever without any clear precipitating factor. Since that time, she has felt extraordinary weakness, finding herself unable to go to work. She could not even go about household chores. The exhaustion forces her to spend many hours in bed. Because of increasing severe myalgia and arthralgia, she was admitted to our hospital for the second time in November 1996.

On admission, her weight was 62.8 kg and her height was 150.2 cm. Her lower extremities were slightly edematous. Blood pressure was 150/72 mm Hg. Abnormal laboratory findings were: urinary protein 2+, occult hematuria 2+, urinary protein excertion 2.6 g/day, white blood cell count 21700/μL, blood urea nitrogen 43 mg/dL, serum creatinine 2.0 mg/dL, uric acid 9.7 mg/dL, total protein 5.0 g/dL, albumin 3.1 g/dL and β_2-microglobulin 2.85 mg/L. Serological tests for rheumatoid factor, antinuclear and antineutrophil cytoplasmic antibodies, hepatitis B and C, Epstein-Barr virus and herpes simplex virus were negative. Serum IgA 188 mg/dL, acylcarnitine 15.4 μmol/L, creatine phosphokinase 30 IU/L and C-reactive protein 0.01 mg/dL levels were within the normal range.

Abbreviations: CDC, United States Centers for Disease Control and Prevention; CFS, chronic fatigue syndrome; IgAN, IgA nephropathy; IU, International Unit

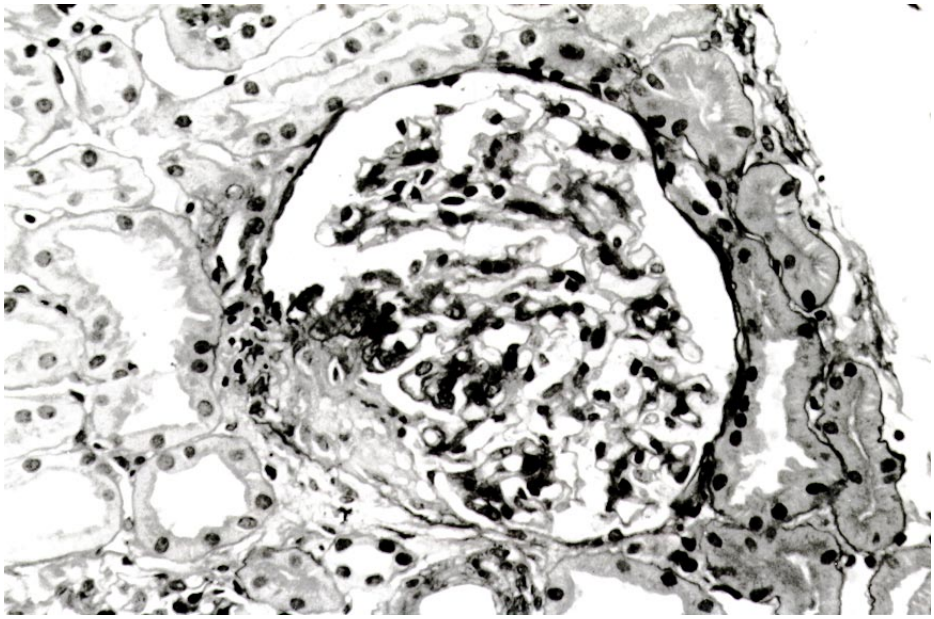

Fig. 1. Renal biopsy sample, periodic acid-Schiff-stained section (× 200).

All symptoms of the United States Centers for Disease Control and Prevention (CDC) criteria except lymph node swelling were satisfied in this patient. She complained of terrible muscle pain and multi-joint pain, even when she turned over in bed. As a result of remarkable muscle weakness, she could not go up stairs. At the same time, atopic symptoms flared up on her skin. A muscle biopsy on the biceps muscle of her arm was performed to exclude the possibility of polymyositis or dermatomyositis (Fig. 2). But her biopsy tissues did not show any abnormal findings.

Until now no controlled studies have provided convincing evidence of the efficacy of any treatment for CFS. However, a recent report revealed that circulating levels of cortisol in patients with CFS were relatively low (Mckenzie et al., 1998; Scott et al., 1998). To evaluate the efficacy of oral hydrocortisone as a treatment for CFS, a 30 mg daily dose of prednisolone was initiated. Severe fatigue, myalgia and fever were not improved. Then we tried Chinese herbal medicine (Hochuekkito) and a nonsteroidal anti-inflammatory drug (sulindac). After administration of these drugs her myalgia, arthralgia and even severe fatigue were remarkably reduced. She was discharged in May 1997.

Discussion

In 1988, the CDC proposed the term “chronic fatigue syndrome” and a definition for diagnosis. This definition was refined in 1994 by the International CFS Study Group (Nishikai, 1996). The revised CFS classification criteria requires

a) severe fatigue persisting for more than 6 months,
b) chronic fatigue of a new or definite onset, not the result of ongoing exertion, not substantially relieved by rest and resulting in a substantial reduction in previous levels of social or personal activities,
c) four or more of the following symptoms occurring concurrently: impairment of memory or concentration, sore throat, tender cervical or axillary lymph nodes, muscle pain, headache, unrefreshing sleep and postexertional malaise.

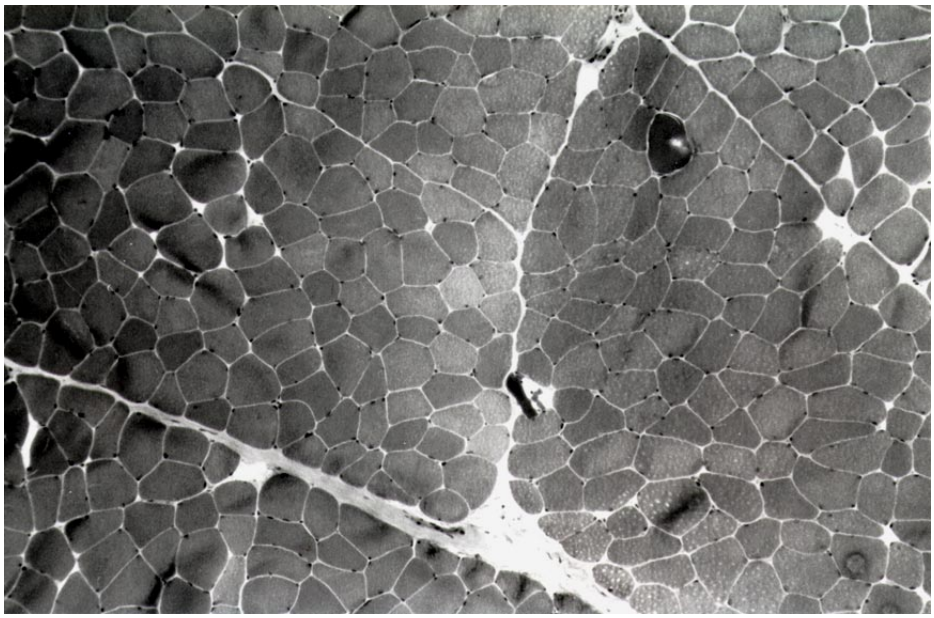

Fig. 2. Muscle biopsy sample (× 200).

This report is the first description of CFS associated with IgAN. Because immune-mediated mechanisms may be a cause of IgAN and CFS, we hypothesized that this association might be linked with a common pathogenesis.

IgAN is the most common form of glomerulonephritis, with a prevalence ranging from 10% of renal biopsies in the United States to 30–40% in Japan (Hemmen et al., 1997). The mean age range is generally in the second or third decade. Haematuria as the presenting symptom is found in 80% and proteinuria in 71% of the patients. In 40% of the patients with IgAN, the progressive disease leads to end-stage renal failure. Recently, the role of the monocyte system and IL6 secretion in the pathogenesis and progression of IgAN has been emphasized (Tsimaratos et al., 1996). It has been suggested that age-dependent variations in the development of the IgAN mucosal system or individual differences in antigen exposure or handling of immune complexes may play an important role. The prevalence of DQ4/8/9 and DR4 is high among Japanese patients with IgAN (Taniguchi et al., 1997).

Immunologic abnormalities are also reported in CFS (Plioplys et al., 1997): decreased function in natural killer cells and macrophages; reduced mitogenic response of lymphocytes; B-cell subset changes, and activation of CD8 cells. There have also been reports of the presence of circulating immune complexes, decreased complement, and the presence of anti-cardiolipin and antiphospholipid antibodies. However, the evidence for an immunological basis for CFS is as tantalizingly non-specific as is the evidence for a viral etiology (Dickinson, 1997).

The present patient may provide further immune-mediated mechanisms for IgAN and CFS.

References

1 DeLuca J, Johnson S, Ellis S, Natelson B. Cognitive functioning is impaired in patients with chronic fatigue syndrome devoid of psychiatric disease. J Neurol Neurosurg Psychiatry 1997;62: 151–155.

2 Dickinson CJ. Chronic fatigue syndrome: aetiological aspects. Eur J Clin Invest 1997;27:257–267.

3 Hemmen T, Perez-Canto A, Distler A, Offermann G, Braun J. IgA nephropathy in a patient with Behcet's syndrome: case report and review of literature. Br J Rheumatol 1997;36: 696–699.
4 Komaroff A. A 56-year-old woman with chronic fatigue syndrome. JAMA 1997;278:1179–1185.
5 McKenzie R, O'Fallon A, Dale J, Demitrack M, Sharma G, Deloria M, et al. Low-dose hydrocortisone for treatment of chronic fatigue syndrome. JAMA 1998;280:1061–1066.
6 Nishikai M. Chronic Fatigue Syndrome: current perspectives. Iryo 1996;50:747–752 (in Japanese with English abstract).
7 Plioplys AV. Antimuscle and anti-CNS circulating antibodies in chronic fatigue syndrome. Neurology 1997;48:1717–1719.
8 Scott LV, Medbak S, Dinan TG. Blunted adrenocorticotropin and cortisol responses to corticotropin-releasing hormone stimulation in chronic fatigue syndrome. Acta Psychiatr Scand 1998; 97:450–457.
9 Taniguchi Y, Yorioka N, Kanbe M, Okushin S, Oda H, Nishida Y, et al. Parent and child cases of IgA nephropathy associated with von Recklinghausen's disease. Nephron 1997;75: 113–114.
10 Tsimaratos M, Brunet P, Dussol B, Michel G, Mege JL, Casanova P, et al. Kostmann's syndrome and IgA nephropathy: an unknown association. Nephron 1996;74:478.

(Received December 22, 1998, Accepted February 2, 1999)