A Case of Polymyositis Associated with Immunoglobulin A Nephropathy

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INTRODUCTION

Polymyositis (PM) is a chronic autoimmune inflammatory disease with a progressive course mostly involving muscles. It is characterized by symmetrical proximal muscle weakness, elevation of muscle-enzymes’ levels, characteristic electromyographic (EMG) features, and specific histopathological findings in a muscle biopsy specimen. Systemic organ involvement, including the respiratory and gastrointestinal tracts, is frequently observed in PM, but renal involvement is rare. Herein, we report the case of a 56-year-old woman presenting with weight gain, edema, and generalized myalgia. Laboratory tests revealed elevated creatinine kinase level, hypalbuminemia, and proteinuria. Histopathological examination of muscle biopsy revealed inflammatory myositis, and a renal biopsy confirmed immunoglobulin A (IgA) nephropathy. Based on the clinico-pathological results, the patient was diagnosed with PM with IgA nephropathy. This is a report of a rare occurrence of IgA nephropathy in a patient with PM presenting with chronic glomerulonephritis. (J Rheum Dis 2017;24:241-245)

Key Words. Polymyositis, IgA nephropathy, Proteinuria

A 56-year-old woman was admitted for a 1-month history of pruritus, weight gain (3 kg over a month), generalized myalgia, anorexia, and Raynaud’s phenomenon. Typical skin lesions were absent. Physical examination showed grade II bilateral pretibial pitting edema and grade IV muscle strength in the proximal muscles of all limbs.

Laboratory test results with their corresponding reference ranges were as follows: serum creatine kinase (CK), 8,493 (26 ~ 140 IU/L); lactate dehydrogenase, 653 (98 ~ 192 IU/L); aldolase, 90.1 (< 7.6 U/L); aspartate aminotransferase, 246 (0 ~ 37 IU/L); alanine aminotransferase, 190 (0 ~ 48 IU/L); C-reactive protein, 5.30 (< 1.00 mg/dL); erythrocyte sedimentation rate, 62 (< 20 mm/hr); serum albumin, 2.5 (3.5 ~ 4.8 g/dL); and serum creatinine, 0.8 (0.4 ~ 1.0 mg/dL). Urinalysis revealed 2+ protein, 2+ red blood cells, spot urine protein-to-crea-
tinine ratio (PCR) of 2,066.9 mg/g and urine albumin-to-creatinine ratio (ACR) of 81.1 mg/g. Anti Jo-1, anti-double stranded DNA, anti-ribonucleoprotein, anti SS-A(Ro), anti SS-B(La), anti-histone, anti-smith, anti-cardiolipin IgM/IgG, and anti-beta 2 glycoprotein IgM/IgG antibodies were all absent, except for antinuclear antibody (1:320 positive, speckled pattern). Serum complement and immunoglobulin G, A, and M levels were within normal limits.

EMG showed low amplitude polyphasic motor potentials of short duration in the upper and lower proximal muscles. Examination of the biopsy specimen from the left vastus lateralis revealed myopathic changes associated with inflammatory cell infiltrates (Figure 1), and immunofluorescence of the renal biopsy showed diffuse deposition of IgA in the mesangium, suggestive of IgA nephropathy (Figure 2).

The following biochemical parameters were elevated: CK, up to 11,312 IU/L; serum aldolase, up to 104.6 U/L; spot urine PCR, up to 4,345.5 mg/g and spot urine ACR, up to 350.7 mg/g. Administration of 60 mg oral prednisolone daily was initiated under the presumptive diagnosis of PM, according to the criteria of Bohan and Peter [1]. However, the severity of proximal muscle weakness was aggravated from grade IV to II. Muscle weakness deteriorated despite administering methylprednisolone (3 doses of 1 g daily each) and cyclophosphamide pulse therapies. Intravenous immunoglobulin was administered at a dose of 2 g/kg for 5 days. Thereafter, the patient’s proximal muscle strength gradually improved from grade
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II to IV and the CK level decreased to 780 IU/L. Malignancy workup to identify the cause of the rapid aggravation of PM revealed a 1.1 cm thyroid papillary carcinoma for which the patient underwent total thyroidectomy. CK level and PCR rapidly decreased to <300 IU/L and <60.1 mg/g, respectively, after surgery. The patient was maintained on oral prednisolone therapy. Up to 6 months after total thyroidectomy, disease activity of PM was well controlled and microscopic hematuria/proteinuria was not observed, even with low dose steroids alone.

**DISCUSSION**

PM not only affects muscles but also involves systemic organs. However, unlike respiratory and gastrointestinal tract involvement, renal involvement is infrequent in PM in comparison to other autoimmune diseases [2,3]. Acute kidney injury secondary to rhabdomyolysis and PM-associated glomerulonephritis are reported as the 2 chief renal signs of PM [4,5]. Otherwise, PM-associated IgA nephropathy is relatively uncommon.

The histopathological features of PM include myofiber injury caused by macrophages and activated CD8+ cytotoxic T cells that attack non-necrotic muscle fibers expressing class I major histocompatibility complex (MHC-I) [6-8]. Patients with IgA nephropathy are reported to be relatively deficient in suppressor T-cell activity and to have hyperactive IgA-specific helper T-cell [9]. Although

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**Figure 2.** Renal biopsy. (A) Light microgram showing mild mesangial expansion (black arrows) without cellular proliferation (Periodic acid Schiff, ×400). (B) Some glomeruli showed segmental sclerotic change and synechia with Bowman’s capsule (PAS-silver stain, ×400). (C) Immunofluorescence staining revealed moderate positivity for IgA on the mesangium and para-mesangium (Immunofluorescence staining, ×400). (D) Electron microgram demonstrating deposits in the mesangium and para-mesangium (Uranyl acetate, ×6,000).
cellular immunity is the main player in PM, humoral immunity may also be involved via the production of IgG that reacts with IgA, causing IgA nephropathy. The pathophysiological mechanisms linking IgA nephropathy to PM remain unknown [10].

IgA nephropathy is a primary glomerulonephritis characterized by IgA deposition in the glomerular mesangia. Most patients with IgA nephropathy have primary disease, but a secondary form is frequently reported with liver disease, inflammatory bowel disease and connective tissue disorders [11]. Very little is known about the incidence of secondary IgA nephropathy compared to that of primary IgA nephropathy. Moreover, the specific interrelations between autoimmune status, regulation of IgA synthesis, and development of IgA nephropathy remain uncertain.

The lack of renal biopsy result after improvement of the underlying autoimmune disease, due to the patient’s refusal to repeat it, was a limitation in this report. Determining whether the cause was primary or secondary to other diseases such as autoimmune disease was very challenging. Moreover, a repeat renal biopsy would not discriminate between primary and secondary IgA nephropathy. Although our patient showed hypoalbuminemia with nephrotic range proteinuria and was diagnosed with IgA nephropathy, the proteinuria might have been of non-glomerular origin because urinary albumin to total protein concentration ratio was <0.4. Since most patients with IgA nephropathy have isolated hematuria or hematuria with glomerular proteinuria, the non-glomerular proteinuria in this case suggests secondary IgA nephropathy, or incidental IgA nephropathy combined with PM. Furthermore, the decrease in CK level and resolution of hematuria after treatment of PM indicate the secondary nature of IgA nephropathy.

Our patient was found to have thyroid cancer shortly after being diagnosed with PM. The relationship between inflammatory myopathy and malignancy has been well known since PM associated with stomach cancer was first reported by Stertz in 1916 [12]. Further studies suggest that cancer and myositis have common autoantigens such as Mi-2, HRS, DNA-PKc [13]. However, the presence of these antibodies was not checked in this patient because most of them are not used clinically. Based on the timing of muscle weakness onset, worsening pattern of PM despite methylprednisolone pulse therapy, and dramatic decrease in disease activity after total thyroidectomy [13], PM in this case was more likely to be a paraneoplastic syndrome secondary to thyroid cancer.

To the best of our knowledge, this is the first case of idiopathic inflammatory myopathy, particularly PM, diagnosed with IgA nephropathy to be reported in Korea, and the second worldwide [14].

**SUMMARY**

Renal involvement makes the poor prognosis in many autoimmune diseases. Renal biopsy is important for diagnosis in patients with worsening renal function or increasing proteinuria. Our findings suggest that IgA nephropathy secondary to PM may cause proteinuria; therefore, renal biopsy should be considered in patients with myositis presenting with proteinuria.

**CONFLICT OF INTEREST**

No potential conflict of interest relevant to this article was reported.

**REFERENCES**