SHORT REPORT

A case of inclusion body myositis with benign monoclonal gammopathy successfully responding to repeated immunoabsorption

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Abstract

A 69 year old woman with inclusion body myositis is described. She presented with benign monoclonal gammopathy. She was resistant to steroid therapy, but responded to repeated immunoabsorption. Up to now, there has been no established therapy for inclusion body myositis, including IVIg. It is suggested that immunoabsorption could be an alternative therapy for inclusion body myositis, when it was accompanied by immunological abnormality.

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Inclusion body myositis is a common acquired myopathy in patients older than 50. The characteristic pathological features are inflammation, vacuolated muscle fibres, amyloid deposits and 15-18 nm tubulo filaments.¹ Mendell *et*

al postulated the diagnostic criteria of inclusion body myositis.¹ They diagnosed patients who exhibited all the above pathological features as definite inclusion body myositis and if the muscle only showed inflammation without the other pathological features, as possible inclusion body myositis. Dalakas *et al* reported that inclusion body myositis was often associated with monoclonal gammopathies.² We examined a 69 year old woman with inclusion body myositis associated with IgG- γ , BJP- γ type benign monoclonal gammopathy, which was successfully treated with repeated immunoabsorption.

Case report

A 69 year old woman developed muscle weakness from 66 years of age. There was no family history of neuromuscular disorders and no consanguinity. She was employed at a clothing shop as a deskworker. History disclosed dysaesthesia on the palmar side of her right second to fourth fingers at 67. She was

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Figure 1 Clinical course of the patient. MMT=Manual muscle strength test; arrows indicate immunoabsorption treatments; clinical improvements are underlined.

Figure 2 (A) Haematoxylin-eosin stain. ($\times 33$); Increase of connective tissue, variation in muscle fibre size, round muscle fibres in some groups, and increase of intermyonuclei are found. Some basophilic round nuclei in some regeneration fibres and rimmed vacuoles in a few muscle fibres are present. One basophilic fibre mononuclear infiltration is seen. (B) Muscle MRI of the right thigh muscle; T2 weighted images. The left image shows muscle atrophy in the thigh before prednisolone therapy. After repeated immunoabsorption, progression of muscle atrophy is not shown in the right image.

diagnosed with carpal tunnel syndrome from the delayed distal latency of the right median nerve shown in a nerve conduction study. Endoscopic ligament resection was performed and her dysaesthesia disappeared.

At 66 years of age, she noticed weakness in her thigh muscles. At 67, she needed support standing up from a chair. At 68, she went up stairs one step at a time and she walked more slowly than before. Later she could not go up stairs and needed help with housework. She could not stand up from a squat position, so she was admitted to our hospital in September 1996.

On admission, her weight had decreased by 6 kg over 3 years. Neurological examination showed atrophy of her hip and hamstring muscles, proximal dominant muscle weakness (manual muscle strength test gave the follow-

ing results: neck flexion 3, extension 4, arm 4, forearm 4, hip extension 3-, hip flexion 2+, knee extension 2+, knee flexion 2-, ankle dorsiflexion 4, ankle planter flexion 5-), and dysaesthesia at the bilateral palmar site of the second to fourth fingers. Laboratory studies showed the following; creatine kinase and lactate dehydrogenase were moderately increased to 550IU/l and 400IU/l, homogeneous type of antinuclear antibody was detected at 40 times dilution, IgG and BJP monoclonal gammaglobulins were detected. IgG was 650 mg/dl, IgA was 78.2 mg/dl, and IgM was 114 mg/dl. Urinalysis gave a %creatinine : creatinine ratio of 50%. Bone marrow aspiration showed hypocellular bone marrow and its plasma cell concentration was 8.2%. Bone radiography showed osteolytic lesions on the left temporal bone, the right fifth and sixth ribs and the left

second and third ribs. Therefore, we concluded that her gammopathy was benign monoclonal gammopathy of uncertain significance (MGUS) from the Southwestern Oncology Group criteria for multiple myeloma.

Needle electromyography showed early recruitment of all examined muscles and at voluntary contraction polyphasic, low amplitude, and short duration unit potentials were revealed. At rest, a fibrillation and positive sharp wave was shown. We concluded that these were myogenic changes. Muscle CT showed severe atrophy of the bilateral gluteus maximum muscle and the hamstrings. Moderate atrophy of the paraspinal and bilateral posterior tibial muscles was also found.

Left semitendinosus muscle biopsy was performed. Haematoxylin-eosin staining showed increased connective tissue, variation in muscle fibre size, round muscle fibres in some groups, and increased intermyonuclei. We found basophilic round nuclei in some regenerating fibres; therefore, internuclear inclusions were suspected (fig 1 A). Immunocytochemistry showed mononuclear infiltration around one basophilic fibre, prominent CD3 positive T cells, and dominant CD 8 positive cells. Gomori-trichrome stain showed rimmed vacuoles in a few muscle fibres. Tiny deposits of tau-positive profiles were detected. Characteristic filamentous inclusions were not disclosed by electron microscopy in the cytoplasm or myonuclei. We concluded that the patient had inclusion body myositis by the clinical criteria Mendel *et al.*²

Prednisolone (50 mg/day) was given from December 1996. Muscle power increased, but on tapering prednisolone the power decreased again. The %creatinine : creatinine ratio of about 50% did not alter with the tapering of prednisolone. Steroid myopathy was excluded.

In April 1997, prednisolone was tapered to 30 mg/day and methotrexate at 5 mg/week was administered. Her hip flexor power was decreased to 2- and we concluded that immunosuppressive therapy with prednisolone and methotrexate had little effect.

Next we examined monoclonal gammopathy; we started immunoabsorption at the end of May 1997, 2–3 times a month. After the fourth absorption, monoclonal gammaglobulin in the urine disappeared and that in serum reduced. After the seventh absorption her knee flexion power was increased to 3-. After the ninth absorption, she could flex the knee at a right angle, and keep her leg up in a prone position; with assistance she could stand up from a chair, and her creatine kinase concentration reduced to 50IU/l. We tapered prednisolone gradually to 20 mg/day from the the seventh absorption onwards and she showed no progression of muscle weakness. She was discharged from our hospital at the end of August 1997 and we continued absorption once a month, because monoclonal gammaglobulin in her urine reappeared 3 to 4 weeks after absorption. Her clinical course is shown below (fig 2) In April 1998, she had maintained the strength of her hamstring muscles. Muscle MRI of her thigh muscle showed muscle atrophy of the thigh

similar to that before therapy; progression of muscle atrophy was not shown (fig 1 B).

Discussion

Many studies have reported myopathy associated with MGUS or multiple myeloma. Telemann-Toppet *et al* reported myositis with perifascicular atrophy associated with MGUS.³ Kiproff *et al* performed combination therapy of plasma exchange and treatment with prednisolone and cyclophosphamide for three cases of inflammatory myositis with perifascicular atrophy associated with IgG- γ type MGUS.⁴ The treatment produced clinical improvement in all three patients. Examination of muscle biopsy specimens by direct immunofluorescence showed linear deposits of IgG- γ along the sarcolemmal basement membrane. Muscle biopsy specimens after treatment showed no immune deposits. Sheehan-Dare and Simmons treated amyloid myopathy in association with IgG- γ chain myeloma by melphalan and prednisolone⁵ which resulted in the remission of both the myeloma and myopathy. Eymard *et al* reported that plasmapheresis and immunosuppressive agents produced partial clinical improvement of late onset rod myopathy with MGUS,⁶ however, therapy interruption led to remission. As shown above, reduction of serum monoclonal gammaglobulin by chemotherapy, plasma exchange, or immunoabsorption improved the myositis.

Dalakas *et al* reported that inclusion body myositis was often associated with monoclonal gammaglobulin,² but there was no report of plasma exchange or immunoabsorption to inclusion body myositis with gammopathy. Chad *et al* reported that plasma exchange produced no improvement of inclusion body myositis in Sjögren's syndrome⁷ but no control study was performed. Dalakas *et al* concluded that plasmapheresis was not helpful⁸ for inclusion body myositis because plasmapheresis was ineffective in a double blind controlled study conducted in polymyositis and dermatomyositis. Dalakas reported that IVIg treatment produced only modest improvement for inclusion body myositis⁹ and the efficacy of IVIg remains debatable.^{9–10}

We examined inclusion body myositis with MGUS. Repeated immunoabsorption reduced urinary and serum monoclonal gammaglobulin and her muscle weakness was improved. The good response to immunoabsorption was similar to that of myositis with monoclonal gammaglobulin. It would be useful to look hard for immunological abnormalities such as MGUS or multiple myeloma in patients with inclusion body myositis and, if there, to consider immunoabsorption or plasmapheresis.

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