A 45-year-old man with severe proximal muscle weakness had findings diagnostic of adult-onset nemaline myopathy. He also had a monoclonal gammopathy. This is the fifth report of adult-onset nemaline myopathy in a patient with monoclonal gammopathy, suggesting that the occurrence of these entities may be more than a chance association. Myocyte-bound immunoglobulin or light chains were not detected and immunotherapy was not effective in this patient. Other causes of adult-onset nemaline myopathy were ruled out, including the most common mutations of sarcomeric thin filament genes.

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Nemaline myopathy was described in 1963 as a nonprogressive myopathy of infancy.1,2 On muscle biopsy, characteristic intracytoplasmic granules and rods are found in muscle fibers that appear to arise from the Z-bands of sarcomeres.3 Although the molecular composition of the granules has been partially elucidated (actin filaments cross-linked by α-actinin),4 the pathogenesis of myocyte degeneration remains unclear.5

A unifying genetic feature of nemaline myopathy is the fact that heritable forms of the disease are associated with mutations of sarcomeric thin filament genes including α-tropomyosin (TPM3), α-actin (ACTA1), nebulin (NEB), β-tropomyosin (TPM2), and troponin T1 (TNNT1).5 Although additional genes associated with nemaline myopathy remain to be identified, some cases likely involve nemaline body formation as a nonspecific or secondary response to local pathophysiologic states.4

In 1966, A. G. Engel3 described an adult-onset form of the disease (adult-onset nemaline myopathy) with weakness of proximal limb and trunk muscles and sparing of the bulbar muscles. Most if not all adult-onset cases have been sporadic6 and in only 1 case has a mutation of ACTA1 been identified.7

In 1975, W. K. Engel and Oberc8 described a patient with adult-onset nemaline myopathy and monoclonal gammopathy. Since then, 3 similar cases have been reported.9-11 None have had an associated myeloma or identifiable lymphoproliferative disorder. We describe the fifth case of this unusual association.

In September 2003, a 45-year-old man with no family history of myopathy noted weakness of proximal limb muscles. The weakness spread and when last seen in January 2005, he could not stand or walk and was totally dependent in all activities of daily living. Weakness was still more severe proximally and he was using noninvasive ventilation. Dysphagia was severe and a percutaneous gastrostomy was performed after he had lost 60 pounds. Eye and tongue movements were normal and his speech was clear. He could not raise his head if supine. Fasciculations were not seen; tendon reflexes and sensation were preserved.

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An IgG λ spike was identified on serum electrophoresis. No lytic bone lesions or mass lesions were found on computed tomographic or positron emission tomographic scans of the chest, abdomen, and pelvis. The following were all within normal range: (1) erythrocyte sedimentation rate, (2) antinuclear antibodies, (3) acetylcholine receptor-binding, receptor-blocking, and receptor-modulating antibodies, (4) rapid plasma reagin, and (5) human immunodeficiency virus and hepatitis C virus antibodies. Serum creatine kinase activity was 496 U/L (normal = 51-294). An electromyogram showed spontaneous activity, fibrillations in proximal limb and trunk muscles, and full recruitment on moderate effort with short duration motor units of normal amplitude. Distal latency, amplitude, and conduction velocities were normal.

The results of a bone marrow biopsy showed trilineage maturation and a moderate, relative erythroid hyperplasia. Plasma cells were seen as single scattered cells and accounted for less than 5% of all nucleated cells on staining with CD138. A mild λ light chain excess was observed on staining for κ and λ light chains (κ:λ = 1:2).

In a muscle biopsy, most fibers were normal in size, but a few were atrophic and contained numerous fine granules in the sarcoplasm. In cryosections, the granules stained reddish on Gomori trichrome and eosinophilic on hematoxylin-eosin staining. These granules were also noted in the Epon-embedded semi-thin sections of the muscle biopsies in a variety of neuromuscular disorders and accounted for less than 5% of all nucleated cells on staining with CD138. A mild λ light chain excess was observed on staining for κ and λ light chains (κ:λ = 1:2).

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logic findings have suggested an autoimmune etiology. In 2 cases, immunoglobulins of the same type as the circulating protein were seen on the surface of the myofibers by immunohistochemical staining. No sarcomere-bound immunoglobulins were identified by immunofluorescence staining in 2 other cases. However, failure of immunohistochemical or immunofluorescence stains to show immunoglobulin or immunoglobulin light chains does not exclude the possibility of low titers of muscle binding antibodies. Neither immunoglobulin nor immunoglobulin light chains were identified by immunofluorescence staining in our patient, and the incubation of the patient’s serum with frozen sections of his muscle biopsy did not show evidence of sarcomeric or membranous staining.

Symptoms improved partially with plasmapheresis and immunosuppression (prednisone and cyclophosphamide) in 2 of the reported cases. While immunosuppression (prednisone) alone failed in another. In a third patient, plasmapheresis was unsuccessful, but immunosuppression (prednisone and azathioprine) improved symptoms. Unfortunately, all of these therapies as well as treatment with rituximab failed in our patient. Thus, although adult-onset nemaline myopathy with gammopathy may be more than a chance association, immunotherapy may not be effective in all cases.

**Author’s Note:** After this article had been submitted for publication, Chahin et al described 14 patients with adult-onset nemaline myopathy, including 7 with monoclonal gammopathy. Our patient died in June 2005, 21 months after onset of symptoms.

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**REFERENCES**


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