Rehabilitation Practice and Science

Volume 18
Issue 1 *Taiwan Journal of Physical Medicine and Rehabilitation (TJPMR)*

Article 25

12-1-1990

Nemaline Myopathy: A casereport

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Nemaline Myopathy - A Case Report

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A 5 year-old boy had non-progressive myopathy since 2 years of age. Muscle enzymes were normal. Electromyography showed a myopathic feature. Prominantly disseminated nemaline bodies and predominant type I muscle fibers were found in muscle biopsy specimen. The clinical and morphological findings supported the existence of a rare form of congenital myopathy.

Key words: nemaline myopathy, congenital myopathy.

INTRODUCTION

Nemaline myopathy (NM) is a rare congenital non-progressive disease of skeletal muscles and was firstly described by Shy et al in 1963[1]. This special form of myopathy is characterized by the presence of subsarcolemmal aggregates of small rods or thread-like (Greek "nema"=thread) bodies in the muscle fibers.

The clinical manifestations vary. Patients with weakness and hypotonia may present from birth or infancy. The weakness is greater in proximal than in distal muscles of extremities. Further characteristics including myopathic face, high arched palate, and often chest deformities and scoliosis are not unusual [2,3]. In this report, we present a boy with NM and confirm histologically.

CASE REPORT

A 5 year-old boy was noticed to have weakness in upper and lower extremities, and gave rise to a waddling gait since 2 years of age. Birth history showed that he was born after a normal and uncomplicated gestation. No family member had neuromuscular disease.

His condition was rather stable without definite progression of muscular weakness till the age of 5 years. On physical and neuromuscular examinations, there was a mild dolichocephaly and high arched palate. Muscle power was grade 4/5 (Medical Research Council) in bilateral shoulder and pelvic girdle muscles. Mild muscular atrophy was noticed in bilateral gluteal muscles. Gower's sign was postive. There was no pseudohypertrophy of muscle. Muscle tone and deep tendon reflexes were normal. Electrocardiogram and echocardiogram showed normal features. Serum CPK and SGOT were within normal limits. Needle electromyography (EMG) done in left deltoid and quadriceps muscles showed a myopathic pattern.

HISTOPATHOLOGY

Muscle specimen was taken from left quadriceps femoris muscle via a needle biopsy. The pieces were frozen in isopentane which had been cooled in liquid nitrogen immediately and cut into

Figure 1 Title=Nemaline myopathy, Case report
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slices of 8 μm thick section for routine stainings of hematoxylin and eosine (H & E), modified Gomori-trichrome, nicotinamide adenine dinucleotide tetrazolium reductase (NADH-TR), periodic-acid-Schiff (PAS), oil red 0 and adenosine triphosphatase (ATPase, PH 9.5). For electron microscopy (EM), the muscle specimen was fixed in 3% glutaraldehyde and post-fixed in 1% osmium tetroxide. Ultrathin sections were cut with a diamond knife after dehydrated concentration and were stained with uranyl acetate and lead citrate.

In modified Gomori-trichrome stain, the nemaline bodies appear a purple red color in green bed of muscle fibers. They cluster in subsarcolemmal and paranuclear locations within the muscle fibers (Fig. 1). In EM study, the nemaline bodies measure 3 to 6 μm in length and 1 to 3 μm in width. They are usually parallel to the long axis of muscle fiber and oriented with perpendicular to the Z band of sacromere (Fig. 2). The proportion of containing nemaline bodies varies in muscle fibers. In ATPase stain, there were predominance of type I muscle fibers. NADH-TR stain showed a normal oxidative enzyme activity. Oil red 0 and PAS stains also showed normal lipid and glycolytic activities.

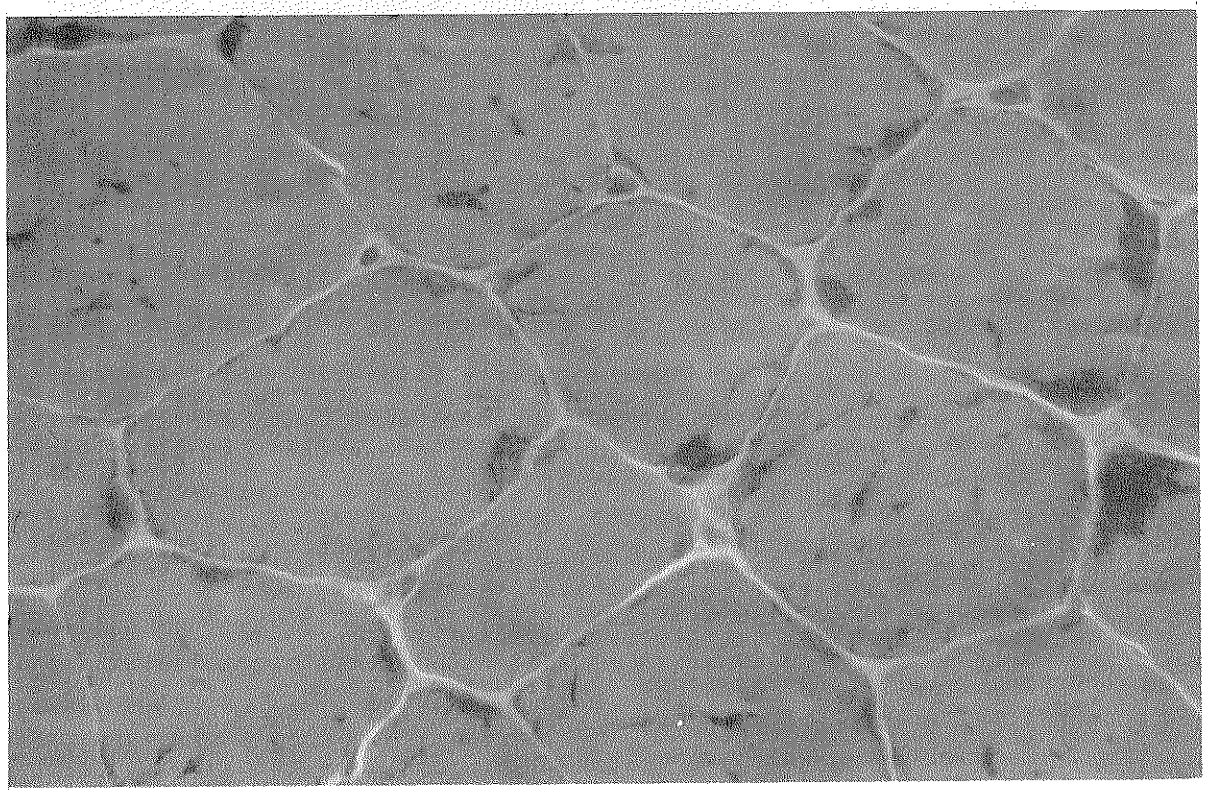

Fig.1 Frozen section muscle biopsy specimen with deposits of nemaline bodies (deep purple), modified Gomori-Trichrome, X 400.

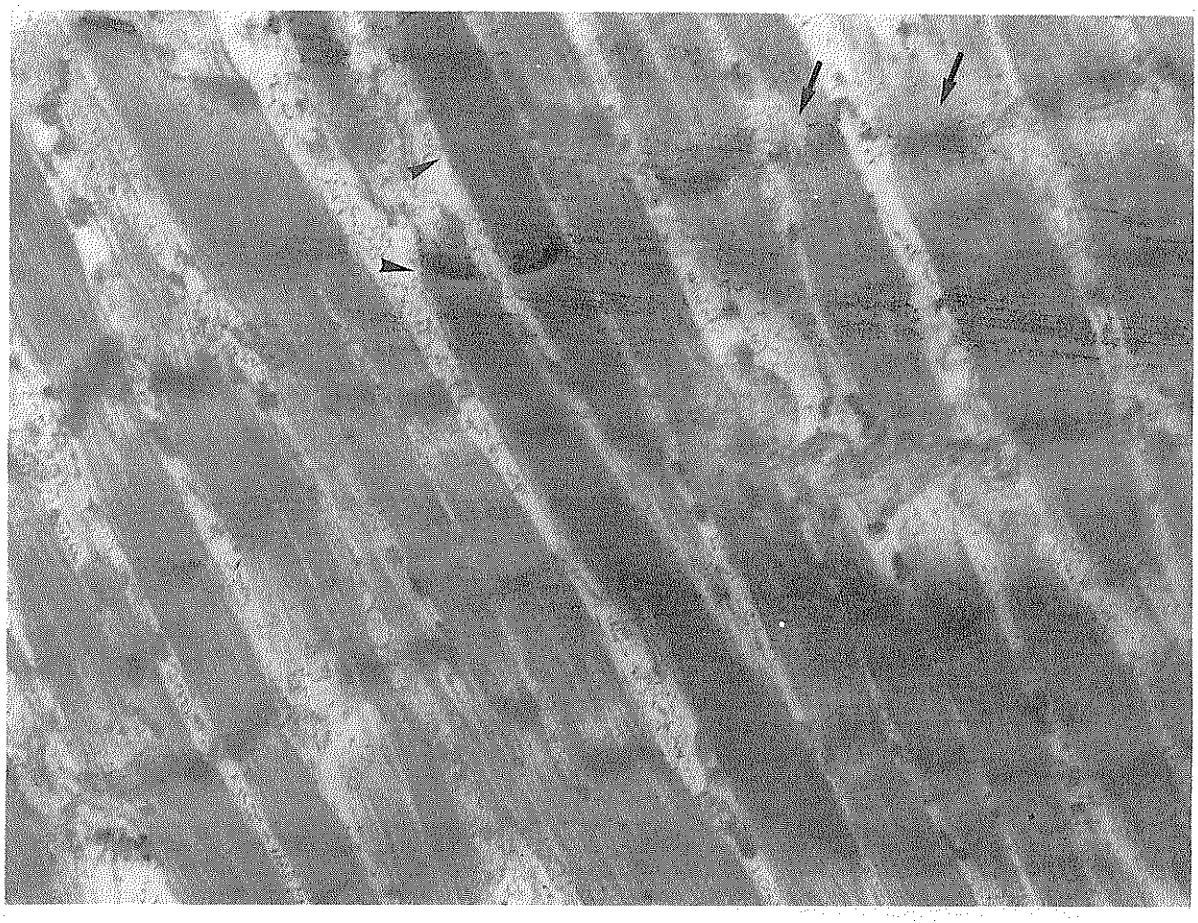

Fig.2 By electron microscopy, nemaline bodies (short arrows) appear as elongated structures parallel to the muscle fibrils and perpendicular to Z disks (long arrows), X 12000.

DISCUSSION

The clinical manifestations of NM varied widely. Four forms of this myopathy have been recognized [3] :1) a congenital and rapidly fatal myopathy; 2) a congenital and relatively non-progressive or slowly progressive type; 3) an asymptomatic form; and 4) an adult-onset form. The non-progressive or slowly progressive form is the most common. In the majority, the myopathy is relatively mild and the disease course was non-progressive as in our case. The age at which progression becomes apparent varies significantly. It may start in childhood but does not occur until middle or late life [4]. Although our case has no family member to be identified. NM has a genetic basis [2]. In some families, it is inherited as an autosomal dominant, whereas in others it occurs as an autosomal recessive [5]. The lack of transmission from father to son has been emphasized and the possibility of an X-linked dominant inheritance has been raised [4,6]. The sex distribution has been recognized to even between male and female [5].

As in many of the congenital myopathies, serum enzyme studies are always normal in NM.

Our case showed normal CPK value of 56 IU/L. This is a critical clue in differentiating NM from muscular dystrophy. EMG in NM has usually show "myopathic" features, but a number of researchers describe diverging results of normal findings [7,8] or a neuropathic pattern [6]. Recently, Wallgren-Pettersson et al [9] used single fiber EMG to examine 13 patients with NM. They stated that active degeneration and regeneration of muscle fibers takes place in NM suggest that the neuropathic motor unit potentials seen in their patients may be secondary to myopathic disease activity.

The most significant in diagnosis of NM is the histopathological findings with presence of abundant nemaline bodies in the muscle fibers and often predominance of type I (slow) muscle fibers. Nemaline bodies have been considered to originate from the Z disks of sacromere [10,11]. They oriented with their long axis perpendicular to the Z disk. The filaments that remain in nemaline body are thin and are oriented longitudinally and parallel to the long axis of the extracted nemaling body [3]. Experiments in which EM studies were combined with biochemical techniques suggested that a major component of the nemaline bodies was α -actinin [12,13].

The cause of weakness in patients with NM is still unclear. By several observations [3], the nemaline body is not the main cause of muscular weakness. In patients with NM, the proportion of fibers containing nemaline bodies varies considerably from muscle to muscle, and the number of fibers containing nemaline bodies within a muscle does not correlate with the degree of weakness of that muscle [4]. Usually, the weakness may affect proximal muscles predominantly as in our case, while the nemaline bodies are more conspicuous distally[4]. The nemaline bodies can not well reflect the functional abnormality in the muscle fibers. Muscle atrophy is not identical to the decreased nemaline bodies but to the loss of muscle fibers.

The predominance of type I muscle fibers is suggested to have strong correlation to the muscular weakness in NM. Volpe et al [14] found that the type I muscle fiber predominance was associated with a practically pure slow myosin light-chain pattern. Weeds et al [15] suggested that the myosin phenotype is controlled through the nervous system, because switching nerves switches the myosin pattern. Engel and Warmolts [16] also proposed that the type I muscle fiber predominance was an abnormality of innervation. On the basis of their assumption, it has been suggested the predominant type I muscle fiber in NM indicates a primary alternation in the lower motor neuron [3] and that nemaline bodies result from anterior horn cells [3]. The weakness of muscle may be related to the neuronopathy or the existing nemaline bodies associated with a major Z disk alternations. In conclusion. We found the case of non-progressive congenital NM has the more significantly histopathological diagnosis rather than the clinical features, muscle enzymes study or EMG examination.

ACHNOWLEDGEMENTS

The authors are greatly obliged to Miss. Yuh-Ling Lee and Mr. In-Chan Chen for their assistances in muscle histology and electron microscopy techniques.

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先天性桿狀肌病——病例報告

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桿狀肌肉病變是一種少見的非進行性先天性肌肉病變，台大醫院復健科最近發現一位5歲男孩，無家族病史，嬰兒時期發育正常，自2歲起被發現有上下肢肌肉無力現象，成長中無明顯進行性退步。理學檢查發現病童有Gower氏現象，上下肢近端肌肉無力(MRC 4/5)，且臀部肌肉稍有萎縮現象，但肌肉張力正常，沒有假性肌肉肥大(pseudohypertrophy)，也沒有其他骨關節系統的畸型變化。病童血中肌肉酵素檢查CPK 56 U/L，神經傳導速度檢查正常，針肌電圖檢查在左三角肌及四頭肌有明顯肌病變變化，但病童的心臟超音波檢查正常。在左四頭肌的肌肉切檢查中，發現大多數肌細胞外側有明顯桿狀體(nemaline body)沈積，肌細胞沒有明顯退化萎縮現象，第一類型肌細胞明顯增加，電子顯微鏡下發現此種桿狀體不規則排列在細胞外圍，長度約3至6微米，寬度約1至3微米，濃度與Z線相似，有的桿狀體則散佈在細胞纖維之間。

此少見的先天性肌肉病變，在復健科常見的肌病變病童中需作鑑別診斷，以作爲治療上及預後評估上的參考。

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