Muscle involvement in association with filarial chyluria

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Twenty unselected consecutive patients of filarial chyluria were evaluated clinically, electromyographically, and histopathologically for neuromuscular dysfunction. None of the patients showed clinical evidence of muscle wasting or weakness suggesting myopathy, although generalized muscle weakness was complained by all of them particularly while climbing the stairs or on getting up or during lifting heavy weights. Electromyographic abnormalities were found in nine patients and slight histopathological abnormalities in two. The average duration of motor unit potentials and the mean amplitude were reduced, compatible with myopathy. There were no fibrillation potentials. Histological abnormalities consisted of a marked variation in muscle fibre size, sarcolemmal nuclear proliferation, and mild interstitial fatty infiltration.

None of the patients showed evidence of clinical neuropathy, abnormalities in conduction velocity along the nerves or signs of segmental demyelination in the biopsy of the nerve. Our data suggest that muscle weakness in these patients is myopathic in nature without peripheral nerve involvement, and is possibly due to hypoproteinaemia and hypolipidaemia, as these patients lose excessive amounts of protein and fat in their urine.

Key words: Filariasis – chyluria – myopathy – electromyography – muscle weakness

Among the various manifestations of filariasis, chyluria has attracted the attention of general physicians, surgeons, and nephrologists. The disease is common in North East India and investigations of the chyluric patients revealed that they were markedly hypoproteinaemic and hypolipidaemic due to urinary loss of protein and lipid (Kothari 1975, Singh 1975). Furthermore, patients with continuous chyluria of prolonged duration developed marked generalized muscle wasting. A prospective study was therefore planned to assess the neuromuscular status of these patients by clinical, electrophysiological, and histopathological methods.

MATERIAL AND METHODS

Patients
Twenty unselected consecutive patients with chyluria who attended this university hospital, and 20 age-and sex-matched controls, were evaluated for clinical, electrophysiological, and histopathological evidence of neuromuscular dysfunction. The male patients
and controls were 24 ± 8 years old, and the female patients and controls were 37 ± 15 years old.

**Diagnosis and the aetiology of Chyluria**
Patients who complained of passing “milky white urine” were investigated for the presence of chyle by the ether test, and by examining the urine for chylomicrons in dark ground illumination, or after staining with SUDAN – SGS III (Karanjivala 1970). The ether test was positive in all patients and the other tests in 16 patients (80%). Associated albuminuria was present in 17 (85%), haematuria in 12 (60%), and microscopic pyuria in four patients (20%). Frank pyuria, phosphaturia, bacteriuria and lipiduria which may simulate chyluria, were excluded.

The clinical diagnosis of filariasis was based upon the history of fever with chills (13 patients), urticarial rash and epididymo-orchitis (three patients each), and lymphadenitis and filarial hydrocele (two patients each). Microfilaria in the blood could be demonstrated in only two patients. Sixteen patients showed eosinophilia.

**Evaluation of neuromuscular dysfunction**

**Clinical.** A detailed history was taken and a neurological examination performed. Special attention was paid to the presence of weakness, wasting and fasciculations, the tendon jerks and sensory abnormalities. The muscle power was graded according to the Medical Research Council Memorandum (1943).

**Electromyography.** The E.M.G. was performed at a room temperature of 27° C using the “Medicor” 2-channel Myograph (Budapest) and the same concentric needle electrode (Buchthal et al. 1954). The “4-quadrant” method (Cohen & Brumlik 1968) was used for sampling from the deltoid, abductor pollicis brevis, gluteus maximus, and the extensor digitorum brevis muscles. Recordings were obtained on photographic films during minimal and maximal voluntary effort at an amplification of 100 μV/mm, using a sweep speed of 1ms/mm. The records were analysed for mean duration and amplitude of the motor unit potentials (M.U.P) and for the incidence of polyphasic potentials.

**Motor nerve conduction velocity.** The motor conduction studies were performed along the median, the ulnar, and peroneal nerves.

**Histopathological studies.** The muscle biopsies were taken from the belly of the quadriceps muscle and the haemotoxylin and eosin-stained longitudinal and transverse sections were examined by light microscopy.

Sural nerve biopsies were obtained in 16 patients. The transverse and longitudinal sections were examined by light microscopy after staining with haematoxylin and eosin (16 patients). Bielschowsky's staining was done for the axons (nine patients). The osmic acid-fixed specimens were used for nerve fibre teasing. The fibre diameter and the internodal lengths were measured in 24 fibres of each nerve.

**Statistical analysis**
The mean M.U.P. duration and amplitude in the individual patients and in the group of patients were compared with those of the controls. If the mean M.U.P. duration and amplitude were below the mean minus 2 S.D. of controls, and if the pattern of activity showed no signs of loss of motor units, the E.M.G. was considered to be compatible with myopathic involvement. More significance was attached to the M.U.P. duration than the amplitude (Buchthal 1977).
The conduction velocities along the motor nerves of the patients were compared with those in controls. Similarly, the internodal lengths at different fibre diameters of all the nerve fibres of the patients were compared with those in controls. In two patients, the internodal lengths of each fibre were plotted against the corresponding fibre diameter (Fullerton et al. 1965) and compared with the regression lines obtained from the controls (Figure 1a, b).

![Graphical analysis of sural nerve from two chyluric patients showing the relationship between the internodal lengths and fibre diameter. Each vertical line represents one fibre which is plotted against its diameter, and the dots represent the internodal lengths. The continuous line is the mean regression line for control subjects and the interrupted lines indicate 95% confidence limits.](image)

**RESULTS**

**Clinical features**

The patients complained of muscle weakness. The weakness was generalized but 16 of the patients complained of difficulty in climbing stairs and in getting
up from a squatting position and 13 complained of difficulties in lifting heavy weights. None had muscle tenderness. None of the patients showed clinical signs of weakness or wasting, fasciculations or myotonia, or any abnormality of the gait. There were no motor or sensory symptoms and the tendon jerks were normal.

Electromyography
There was no spontaneous activity and all muscles showed a full recruitment pattern during maximal effort.

Motor unit potential duration: The M.U.P. duration was shortened in the deltoid (nine patients), abductor pollicis brevis (three patients), gluteus maximus (12 patients) and extensor digitorum brevis muscles (five patients) (Figure 2).

Motor unit potential amplitude: The M.U.P. amplitude was reduced in the gluteus maximus and the extensor digitorum brevis, in one patient each. In a given muscle, the mean M.U.P. amplitude from all patients was reduced as

![Figure 2. The duration of motor unit potentials in 20 chyluric patients and controls.](image-url)
compared to controls in the deltoid (P < 0.001) and the extensor digitorum brevis (P < 0.01) (Figure 3).

Polyphasic potentials: More than 10% polyphasic potentials were found in the deltoid and the abductor pollicis brevis (one patient each), the gluteus maximus (three patients), and the extensor digitorum brevis muscles (four patients) (Figure 4). The incidence of polyphasic potentials pooled from all muscles of the patients was the same as in controls.

Motor nerve conduction velocities
In the patients as a group, the mean motor nerve conduction velocity along the median, the ulnar and the peroneal nerves was the same as in controls. In two patients conduction was slightly slowed along the median nerve and in one patient along the ulnar nerve. The mean distal motor latency was

--- MEAN OF CONTROLS ---

--- ±2 S.D. ---

--- CONTROLS ---

--- PATIENTS ---

Figure 3. The amplitude of motor unit potentials in 20 chyluric patients and controls.
normal with the exception of a prolonged distal latency in the median nerve of one patient (Figure 5).

**Histopathological studies**

*Muscle.* Light microscopic studies showed remarkable changes, albeit mild, in only two patients. The changes consisted of a marked variation in the size of the muscle fibres (Figure 6) and sarcolemmal nuclear proliferation. The nuclei were often large and at places seen in continuous rows (Figure 7a, b). There was a slight increase in interstitial fat. Degenerative changes in the muscle fibre were absent.

*Nerve.* Light microscopic studies on sections from the sural nerve biopsies using H and E as well as Bielschowsky's axonal staining did not show pathologic changes. The distribution of nerve fibre diameters and the relation of fibre diameter to the internodal length were normal. An occasional fibre in a few patients showed a shortened internodal length suggesting remyelination.

**DISCUSSION**

Weakness, fatigue and weight loss are frequent complaints of chyluric patients and some of them show severe muscle wasting in the late stages. In the

![Graph showing the percentage of polyphasic potentials in 20 chyluric patients and controls. The graph includes different muscle groups and statistical significance levels marked with asterisks and p-values.](image-url)
present study, although none of the patients showed weakness on clinical testing, the duration of motor unit potentials was shortened in nine patients and slight unspecific histopathological abnormalities were present in two. The peripheral nerves were normal on clinical, electrophysiological, and histopathological investigations with the exception of two patients in whom the nerve conduction velocities were reduced.

The electromyographic diagnosis of myopathy was based on a reduction in the M.U.P. duration and 45% of our patients showed evidence of predominant proximal myopathy, the gluteus maximus muscle being most severely involved. The M.U.P. amplitude was reduced in the deltoid and extensor digitorum brevis muscles. The incidence of polyphasic potentials was not increased.

The electrophysiological and histopathological abnormalities that have

![Graph](image)

*Figure 5. Motor nerve conduction velocities and terminal latency time in 20 chyluric patients and controls.*
been observed in these patients are not specific for chyluria because similar changes have been observed in muscular dystrophies and in various endocrine and osteomalacic myopathies (Kugelberg 1949, Pinelli & Buchthal 1953, Adams 1964, Harward 1962, Ramsay 1965, 1966, Skaria et al. 1975). However, in the absence of electrophysiological or histopathological abnormalities in the peripheral nerves, these changes point toward a primary muscle involvement.

The pathogenesis of myopathy in chyluria remains unclear. Since these patients developed hypoproteinaemia and hypolipidaemia in 50 and 87% of the patients, respectively (Singh 1975), it is likely that either protein deficiency or excessive loss of fat soluble vitamins in the urine may in some way be related to the pathogenesis of myopathy in these patients. It is well known that patients of kwashiorkor and tropical sprue who have protein deficiency develop muscle weakness and wasting (Sachdeva et al. 1971, Iyer et al. 1973). Similarly, among the fat soluble vitamins, deficiency of vitamin E or of vitamin D is known to produce myopathy (Skaria et al. 1975, Gordon & Nitowsky 1956). None of our patients had osteomalacia. Unfortunately, vitamin E determinations were not done on our patients. In the literature, there is experimental and clinical data in favour of vitamin E myopathy. Muscular dystrophy has been produced in various laboratory animals by vitamin E deficiency (Burr et al. 1937, Pappenheimer 1939, Shimotori 1940, Mackenzie & McCollum 1940, Safford et al. 1954, Dinning & Day 1957).

![Figure 6. Histogram showing the variation in muscle fibre diameters in two patients indicating the scatter, as compared to a normal muscle (P < 0.001).](image)
Also, in patients with cystic fibrosis of pancreas and biliary atresia, mild histopathological alterations in the muscles have been observed due to malabsorption of vitamin E (Gordon & Nitrowsky 1956).

Figure 7a. Light microscopy of the quadriceps muscle of a chyluric patient showing increased sarcolemmal nuclear proliferation. The nuclei are seen to be large with finely stippled chromatin. × 160 (H & E).

Figure 7b. Light microscopy of the quadriceps muscle of a chyluric patient showing increased sarcolemmal nuclear proliferation. The nuclei are seen to be large with finely stippled chromatin. × 630 (H & E).
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