

## Early onset myotonic dystrophy in association with polyneuropathy

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**SYNOPSIS** A patient with early onset myotonic dystrophy, with associated neuropathy and epilepsy, is presented. It is postulated that his disorder was inherited through a recessive, pleomorphic gene. His differential diagnosis is discussed and the literature reviewed. The clinical variability of myotonic dystrophy is stressed and the diagnostic difficulties encountered in the younger age group.

The occurrence of myotonic dystrophy in children as compared with adults is relatively uncommon. There have been reports of its incidence between the ages 6 and 14 years by Maas and Patterson (1943). However, it was Vanier (1960), Dodge *et al.* (1965), and Pruzanski (1966) who put the subject into proper perspective, recognizing the atypical nature of the disease in children. They described, besides the classical type, the dysembryoplastic and dysphagic types (Dodge *et al.*, 1965; Pruzanski, 1966), and divided their patients into three groups according to the clinical manifestation. Watters and Williams (1967) added a fourth group.

The features considered to be characteristic in adults, such as ptosis, cataracts, baldness, endocrine abnormalities, and percussion myotonia, are seldom seen in the younger age group (Watters and Williams, 1967). Found instead are congenital anomalies such as high arched palate and skeletal abnormalities like talipes equinovarus and kyphoscoliosis (Aberfield *et al.*, 1965; Pearson *et al.*, 1967).

Recently there have been reports of evidence of neuropathy associated with myotonic dystrophy (McComas *et al.*, 1971; Caccia *et al.*, 1972; Kalyanaraman *et al.*, 1973).

The purpose of this paper is to stress the pleomorphism of myotonic dystrophy in the

younger age group and to report associated neuropathy.

### CASE REPORT

K. B. was an 18 year old male who complained of progressive weakness in all limbs. His parents were unrelated and his prenatal and postnatal histories were unremarkable. His motor milestones were delayed: he was late in sitting up and in being able to lift his head off the bed; he never crawled and did not walk till the age of 2 years. He began to talk 'at the usual time'. His mother had early noted occasional twitching movements of the left eyelids.

He had been seen by a neurologist at the age of 4 years: at that time episodes of left facial twitching were reported; there was universal motor weakness, particularly involving the neck flexors; and there was generalized hypotonia and areflexia. The face was 'hatchet shaped' and there was delayed relaxation of the handgrip.

At the age of 10 years he had a grand mal seizure preceded by dizziness and 'twinkling lights' in the left visual field, and was started on phenobarbitone and diphenylhydantoin.

There was no family history of similar difficulties; both his parents were in good health as was one younger sister.

He was a pleasant adolescent of normal intelligence. The face was long and thin; the head scaphocephalic; the neck thin and swan-like, with extreme wasting of the sternocleidomastoid muscles (Fig. 1) and marked weakness of the flexor muscles of the neck so that the head could not be lifted against gravity; the palate was high-arched and the teeth malaligned. The cardiac, respiratory, and gastro-

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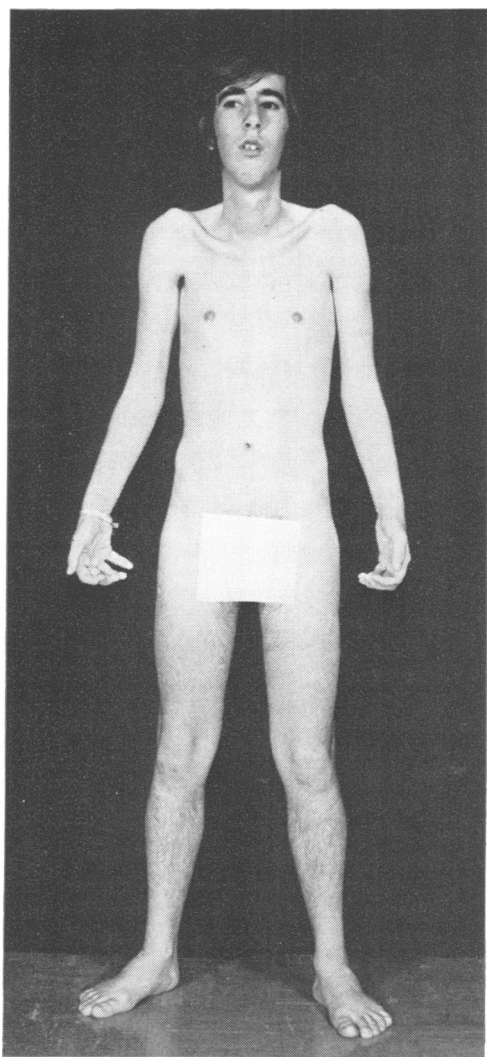


FIG. 1 K.B.: showing extreme wasting of sternomastoids, proximal, and distal muscles in the upper extremities.

intestinal systems were unremarkable and the genitalia normal. The orbicularis oculi and lower facial muscles were weak bilaterally. Bilateral foot drop was obvious when he walked. In the upper limbs there was severe proximal and distal muscular atrophy, and the sternal heads of the pectoralis major muscles were absent. There was universal weakness in the lower limbs, with particular involvement of the extensors, flexors, and evertors of the ankles. The

calves showed pseudohypertrophy. There was generalized hypotonia and areflexia. No sensory changes were detected and sphincter function was intact.

Urinalysis, complete blood count, total plasma protein, plasma albumin-globulin ratio, immunoelectrophoresis, fasting blood sugar, serum aldolase, aspartate transaminase, alanine transaminase and lactate dehydrogenase levels were normal. Serum creatine phosphokinase was 343 I.U./l. Serum levels of phenobarbitone and diphenylhydantoin were normal. Radiographs of the skull, cervical spine, and chest were normal as were the EEG and brain scan. The electrocardiogram showed normal sinus rhythm. The spinal fluid protein was 0.89 g/l and the sugar 38.9 mmol/l (70 mg/dl).

Electromyography and nerve conduction studies were done under standardized conditions with a Teca Model TE-4 machine at a room temperature of 24°C with right forearm temperature being 34°C and the right leg temperature 32°C. Maximal motor nerve conduction velocities were as follows: right median 39.2 m/s; right ulnar 40.2 m/s, right peroneal 32.6 m/s, right tibial 35.7 m/s. Orthodromic sensory conduction velocities were: right median (finger to wrist) 40 m/s, right median (finger to elbow) 43.4 m/s, right ulnar (finger to wrist) 33.3 m/s, right ulnar (finger to elbow)—no evoked potential could be obtained.

The following muscles were tested on the right side with a concentric needle electrode: peronei, tibialis anterior, gastrocnemius, opponens pollicis, abductor digiti minimi, and biceps. The peronei and biceps showed classic myotonic discharges with 'dive bomber' sound and bizarre high frequency (pseudomyotonic) discharges. The other muscles showed increased insertional irritability and positive sharp waves. The motor unit potentials were reduced in number on maximal contraction and motor unit potentials were polyphasic and prolonged (10–15 ms in duration). These findings indicated a neurogenic atrophy of muscles in addition to the myotonia.

Biopsy of the left gastrocnemius muscle was carried out under local anaesthesia; paraffin embedded sections were stained with haematoxylin and eosin, trichrome, and PTAH. Rapidly frozen sections were also studied histochemically with phosphorylase, myosin-ATPase and DNPH-diaphorase.

Histological features such as rounding and variation of diameter of muscle fibres, central nucleation, and occasional necrosis were prominently myopathic (Fig. 2). Ring fibres, sarcoplasmic masses, and nuclear chains were absent. Histochemical studies showed normal fibre type differentiation with a tendency of type I fibre hypotrophy.

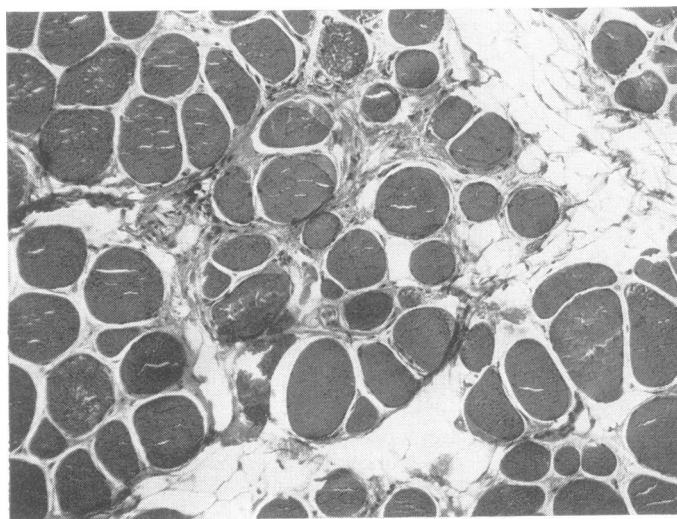


FIG. 2 Biopsy of left gastrocnemius: showing rounding and variation of muscle fibre size and areas of necrosis. H and E,  $\times 250$ .

#### DISCUSSION

The clinical and laboratory data pointed to early onset myotonic dystrophy. The clinical features were classical: the delayed milestones, hypotonia, facial spasms, poor relaxation of handgrip, weakness and wasting of neck muscles, hatchet-shaped face, and high-arched palate. The EMG and muscle biopsy confirmed the diagnosis. However, the EMG study raised some questions discussed below.

**INHERITANCE** The mode of inheritance of myotonic dystrophy is thought to be autosomal dominant (Tyler, 1954; Vanier, 1960; Caughey and Myrianthopoulos, 1963; Dodge *et al.*, 1965; Pearson *et al.*, 1967). In our case, the parents and sister were studied clinically and by EMG and were normal. The inheritance is therefore presumed to be recessive; or the case may have been sporadic.

The genes transmitting the early-onset and adult types of muscular dystrophy may be different (Carter and Bundy, 1972). The adult cases with neuropathy seen by us were sporadic (Kalyanaraman *et al.*, 1973). It is therefore possible that myotonic dystrophy with neuropathy differs genetically from the classical type.

**NEUROPATHIC FEATURES** Engel (1971) postu-

lated that the peripheral nerve has an 'inhibitory' influence on myoneural function and that the loss of this inhibitory influence is manifested as myotonia. McComas *et al.* (1971) were of the opinion that the changes in the muscle were the result of a primary neuropathy.

In the cases of myotonia associated with neuropathy studied by Caccia *et al.* (1972), there was conclusive EMG and histopathological evidence for neuropathy. The two cases of adult onset myotonic dystrophy reported by Kalyanaraman *et al.* (1973) showed evidence of neuropathy by EMG and muscle biopsy.

Our present patient had electromyographic evidence of neuropathy in the form of slowed motor conduction. In addition, the spinal fluid protein was elevated; an abnormality noted by Refsum *et al.* (1967) in nine of their 16 cases.

The question also arose whether the diphenylhydantoin he was taking for epilepsy could have been responsible for the neuropathy and the elevated spinal fluid protein. Rawson (1968) studied the spinal fluid in four patients with diphenylhydantoin intoxication: the protein was elevated in all, as was the serum level of the drug; and they all had clinical signs of cerebellar dysfunction. When, in these patients, the serum levels of the drug were lowered to the therapeutic range, the clinical signs cleared and the

spinal fluid protein returned to normal. Our patient showed no clinical signs of diphenylhydantoin intoxication, and had normal serum levels of the drug. We do not think it likely, therefore, that diphenylhydantoin contributed to his neuropathy. Diphenylhydantoin, though used here for the control of seizures, has since been tried in the therapy of myotonia (Munsat, 1967). Hence it is possible that it may have masked clinical myotonia in our patient. The raised spinal fluid protein and the neuropathy also raised the question of Landry-Guillain-Barré-Strohl syndrome with reactive myotonia (Worster-Drought and Sargent, 1952). This was unlikely in our case because of the history, clinical picture, and biopsy findings.

Multisystem involvement is known in myotonic dystrophy and there have been reports of associated hereditary neuropathy (Ziegler and Rogoff, 1956), as well as of Charcot-Marie-Tooth disease (Wald *et al.*, 1962) and of Friedreich's ataxia (Chaco and Taustein, 1969). In all of these cases there was a strong family history. However, in our patient, the gene may have been recessive and pleomorphic, transmitting both the myotonic dystrophy and the neuropathy, without similar manifestations in other members of the family.

Epilepsy has not (as far as we are aware) been previously described as occurring in myotonic dystrophy, though non-specific changes in the EEG have been seen (Barwick *et al.*, 1965; Watters and Williams, 1967). Central nervous system involvement in myotonic dystrophy usually takes the form of dementia and cerebral atrophy (Refsum *et al.*, 1967). In our case the epilepsy may be coincidental.

In conclusion, we think our patient manifested early onset myotonic dystrophy with associated neuropathy.

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