Acta neuropath. (Berl.) 31, 297–303 (1975)


# A Myopathy Associated with Myotonia in the Dog

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Received March 22, 1974; Accepted January 10, 1975

*Summary.* The pathology of two cases of a canine myopathy associated with myotonia are presented. The changes were interpreted as dystrophic. The most obvious features were a rounding on cross section and variation in fibre size with numerous internal nuclei, many of which formed chains. Degeneration and regeneration were seen and there was a slight increase in perimysial and endomysial connective tissue. Only one ringed fibre was seen, but no sarcoplasmic masses. Enzyme histochemistry failed to demonstrate any selective Type I fibre atrophy. The peripheral and central nervous systems were normal in both cases.

**Key words:** Canine Myopathy — Associated Myotonia — Varying Fibre Size — Internal Nuclei — Degeneration — Regeneration.

## Introduction

To date, few descriptions of neuromuscular disorders in dogs have appeared in the literature. However, the use of some of the more modern techniques available for investigation of such disorders has shown that diseases of both muscle and nerve do occur frequently in the dog (Griffiths *et al.*, 1973). Reports of myopathies in the dog are few, although a few individual cases have been described (Innes, 1951; Meier, 1958; Whitney, 1958). Two cases, however, will be described which showed evidence of a primary myopathy in associated with myotonia. The clinical and EMG findings in the two dogs have been described elsewhere (Griffiths and Duncan, 1973).

Myotonia has been described in humans, goats (Brown and Harvey, 1939), the horse (Steinberg and Botelho, 1962) and in the dog (Wentink *et al.*, 1972). The pathology of the myopathy found in association with myotonia in the dog (Wentink *et al.*, 1973), varied markedly from that of myotonia dystrophica in man, in which the most common pathological features are sarcoplasmic masses, ringed fibres and internal nuclei, many of which are arranged in chains (Dubowitz and Brooke, 1973). There is also a preferential atrophy of Type I fibres.

## Materials and Methods

Both dogs were young on admission, case 1 being $1^1/_2$ years and case 2 9 months old. Both had a history of limb weakness, stiffness and exercise intolerance, and on EMG examination showed evidence of a myopathy with numerous myotonic discharges (Griffiths and Duncan, 1973).

Table 1

| | Varying fibre size | Degeneration | Regeneration | Hyaline fibres | Split fibres | Internal nuclei | Increased connective tissue | Cellular infiltrate |
|---|---|---|---|---|---|---|---|---|
| Case 1 | | | | | | | | |
| L. Vastus lateralis | ++ | + | 0 | + | + | ++ | ++ | 0 |
| L. Biceps femoris | ++ | + | +++ | ++ | + | + | + | + |
| L. Temporalis | +++ | + | ++ | ++ | + | ++ | ++ | 0 |
| Sternocephalicus | ++ | +++ | +++ | ++ | 0 | + | ++ | 0 |
| L. Long digital extensor | ++ | +++ | ++ | ++ | + | ++ | + | 0 |
| Case 2 | | | | | | | | |
| Vastus lateralis | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Sternohyoideus | +++ | + | + | 0 | 0 | + | + | 0 |
| L. Deltoideus | ++ | + | 0 | 0 | 0 | 0 | 0 | 0 |
| L. Brachycephalicus | +++ | + | + | + | 0 | ++ | ++ | + |

+ = Minimal to mild; ++ = Mild to moderate; +++ = Moderate to marked.

Muscle biopsy was performed on the contralateral side from that of the EMG examination, and samples were taken from the vastus lateralis, biceps femoris and temporalis (case 1), and from the deltoid, sternohyoid and sternocephalicus (case 2) muscles. The muscle biopsy was taken using muscle clamps. Two strips of muscle were removed, the first was frozen directly in liquid nitrogen and the second was formalin fixed for routine paraffin embedding. Cryostat sections were cut at 10 $\mu$ and stained routinely with haemotoxylin and eosin, and a modified trichrome method (Engel and Cunningham, 1963). In addition, the following enzyme histochemical profile was used, myosin ATP-ase (modification of Brooke and Kaiser, 1969), reduced nicotinamide adenine dinucleotide tetrazolium reductase, NADH (Scarpelli *et al.*, 1956), succinic dehydrogenase, SDH (Nachlas *et al.*, 1957) and phosphorylase (Takeuchi and Kuriaki, 1955).

Despite treatment, neither case made any improvement, case 1 dying under anaesthesia during investigation 6 months after first being seen. Case 2 was destroyed by the referring veterinary surgeon and was not available for autopsy. Case 1 was autopsied and various skeletal muscles, as well as oesophagus, cardiac muscle, liver, testis, peripheral nerve, spinal cord and brain, were fixed in 4% buffered neutral formalin.

The following pathological changes were graded on an 0 to +++ basis by each of the authors independently (Table 1); varying fibre size, muscle degeneration, regeneration, hyaline fibres, split fibres, internal nuclei and increased connective tissue (either perimysial or endomysial). Regeneration was judged by the presence of basophilic sarcoplasm with vesicular nuclei containing prominent nucleoli. Where both cryostat and paraffin sections were available, it was often necessary to refer to the latter in order to obtain accurate sarcolemmal nuclear detail.

## Results

The histopathological changes seen in both cases were similar but not identical (Table 1).

### *1. Routine Tissue Stains*

In case 1 abnormalities were present in all the striated muscles examined including the oesophagus, but in case 2 the vastus lateralis was normal. Table 1

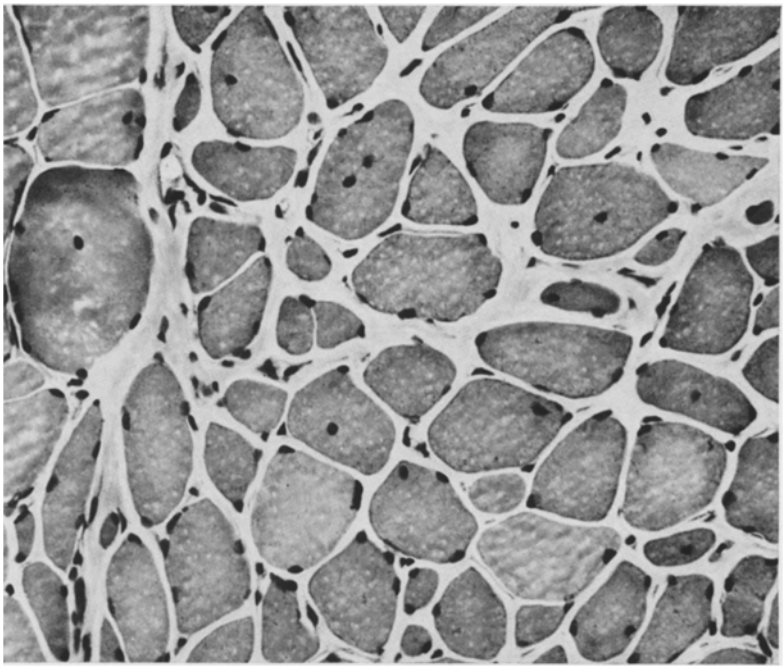

Fig. 1. Cryostat section showing variation in fibre size, internal nuclei and increase in endomysial connective tissue. Case 1. H.-E. × 450

shows there was no selective involvement of any muscle group in either case, although distal limb muscles were not sampled in case 2.

The changes in all the muscles were essentially the same, varying only in degree. These changes included fibre hypertrophy with a marked variation in fibre size (Fig. 1), fibre splitting (Fig. 2) and internal nuclei. Nuclear chains were commonly seen and were either internal or sub-sarcolemmal (Fig. 3a and b).

Fibre necrosis and regeneration was frequently seen but the latter change was more marked in case 1. Only one ringed fibre was found in the sternocephalicus muscle of case 1. No evidence of sarcoplasmic masses was found in either case. There was endomysial and perimysial fibrosis but this was slight. Intramuscular arteries, veins, muscle spindles and nerve bundles were all normal. There were no histological abnormalities in the peripheral and central nervous systems, and all other tissues examined histologically were normal.

### *2. Enzyme Histochemistry*

The fibre type distribution was normal in all muscles except the vastus lateralis in case 1 where a minor degree of type grouping was present. This feature was confirmed by all the enzyme methods. Whole fascicles were of predominantly one type with only an occasional fibre of a different type. (The normal canine vastus lateralis shows a mosaic pattern on enzyme histochemistry.)

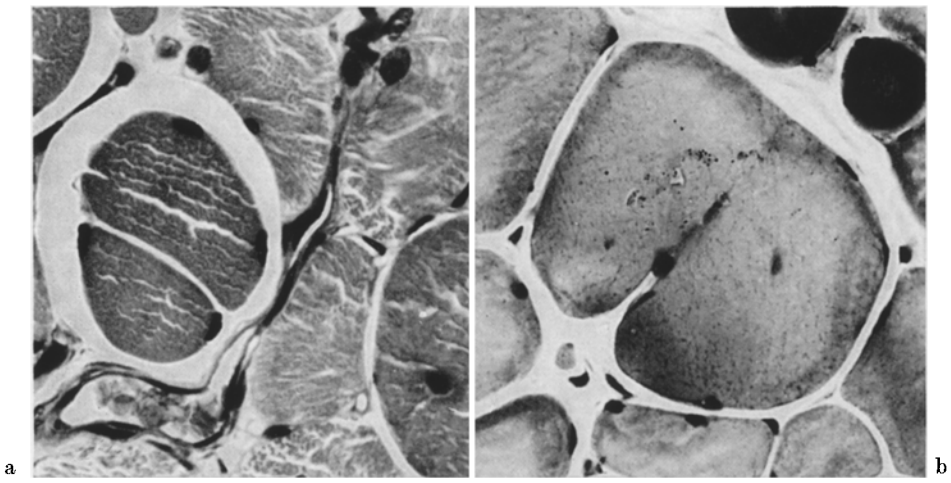


Fig. 2a and b. Muscle fibres at different stages of splitting. H.-E. × 640

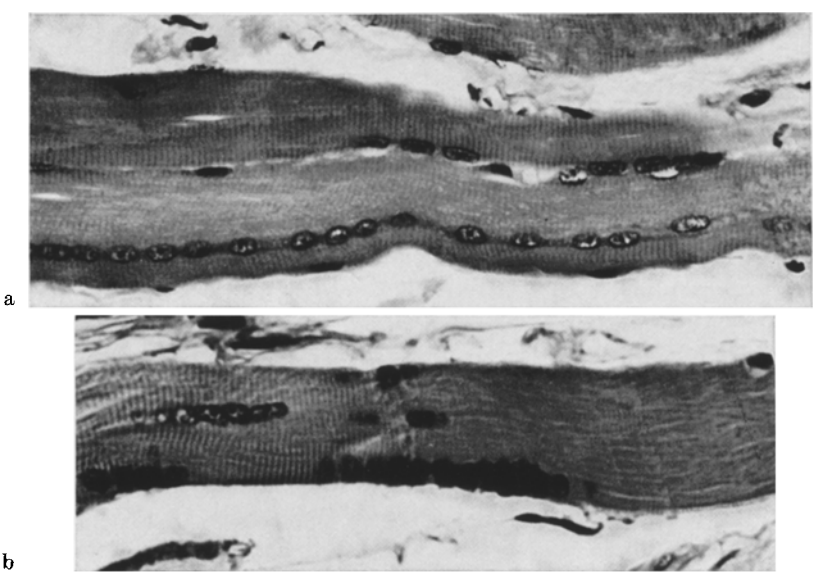


Fig. 3. (a) Internal nuclear chains. (b) Muscle fibre with both internal and sub-sarcolemmal nuclear chains. H.-E. ×500

In both cases the pathologically large and small fibres were of both types but the largest fibres tended to be of Type II. This feature was most obvious in case 2 (Fig. 4).

The rounded, hyalinised fibres seen in case 1 stained strongly for A.T.Pase, N.A.D.H., S.D.H. and glycogen (Fig. 4). In some of these fibres there was an increased zone of N.A.D.H. and S.D.H. activity in the sub-sarcolemmal region.

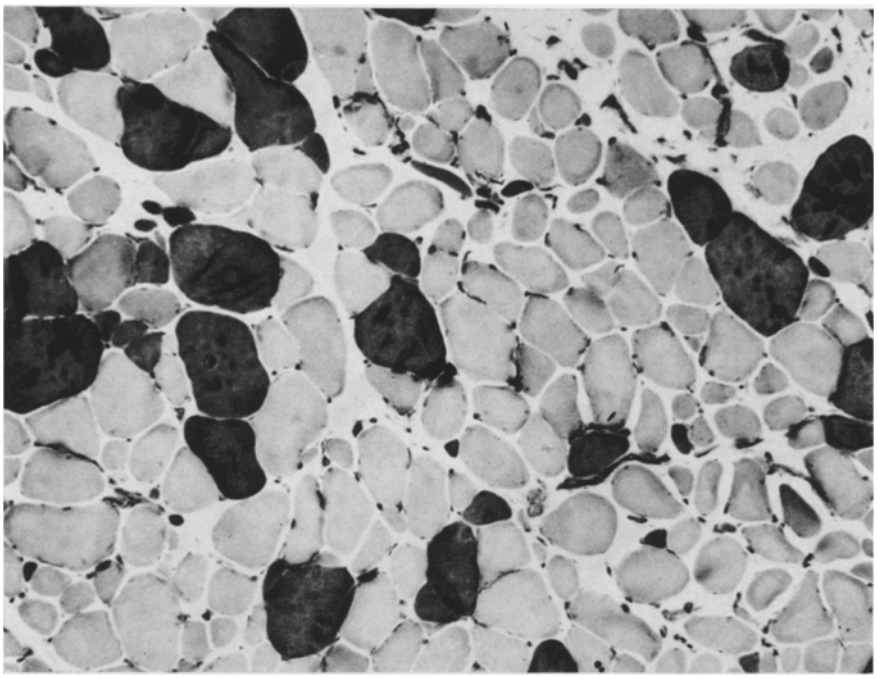

Fig. 4. Cryostat section of the sternohyoideus muscle. Case 2. Myosin A.T.Pase × 99

## Discussion

Because of the present dearth of knowledge on canine muscle disease it is difficult to classify with certainty the pathological changes described. However, the biopsy and post-mortem findings suggest a primary myopathy in which the principal abnormalities are: 1) marked rounding of fibres on cross section and variation in fibre size; 2) internal nuclei (with tendency to chain formation in case 1); 3) hyalinised fibres, myonecrosis and myophagia; 4) regeneration; 5) increase in connective tissue.

One other noticeable feature was the general lack of inflammatory cell infiltration. The degree of change varied from muscle to muscle and was clearly more marked in case 1; it could be argued that this was due to the age difference. It was noticeable however, that the changes in case 1 appeared to be no more severe at post-mortem examination than they had been 8 months previously, when first biopsied.

The muscles have been classified as dystrophic on a histopathological basis. Walton (1969) defines muscular dystrophy as a "progressive genetically determined primary degenerative myopathy". The two cases described here fit this definition apart from the inability to determine any hereditary basis, as clinical details of parents and sibs were not available.

Myotonic dystrophy in man is a diffuse disorder combining myotonia and dystrophic features together with cataract, alopecia, gonadal atrophy and often endocrine and immunoglobulin disturbances. The pathology of infantile myotonic

dystrophy, IMD (Karpati *et al.*, 1973), varies from that seen in the later stages of the disease. In IMD the changes are less severe and there is no evidence of degeneration or pyknotic nuclei. Areas of high acid phosphatase activity are seen in the majority of extrafusal and intrafusal muscle fibres. Wolfhart (1951) described the earliest changes as central nuclear chain formation and fibre splitting. Later, sarcoplasmic masses and ringed fibres may be present although it must be emphasised that these are not considered pathognomonic of myotonic dystrophy (Dubowitz and Brooke, 1973).

The possibility of a neurogenic origin in the aetiology of myotonic dystrophy has been advanced (McComas and Sica, 1970; Engel, 1971). The only possible evidence of neural involvement in our cases could be the finding of pyknotic nuclei, and occasional tigroid nuclei which are more commonly associated with the neuropathies, although they have been seen in myotonic dystrophy in man (Dubowitz and Brooke, 1973).

In a previous description of myotonia in the dog (Wentink *et al.*, 1972), recessive X-linked inheritance was strongly suggested by the family history. Indeed, of the litter of eight Irish Terriers described, five of the pups were affected, all males, with two males and one female unaffected. Identical signs were described, by the owner, in the bitch's two previous litters. The pathology of the condition was different from that seen in our cases, although some features were common to both. As in our cases, degeneration, regeneration and internal nuclei were seen, varying in degree from muscle to muscle. However, in their cases there was no increase in connective tissue but there was a marked cellular infiltration with the presence of multinucleate giant cells. Histochemically the main findings were a lack of differentiation of Type I and Type II fibres in affected areas, the fibres in these areas having lost phosphorylase activity and containing little or no glycogen.

McGavin and Baynes (1969) reported a muscular dystrophy in lambs, associated with internal nuclear chain formation and numerous sarcoplasmic masses, but no ringed fibres were described. Although these lambs showed stiffness of gait, the stiffness increases with exercise, and it is doubtful therefore that myotonia was present, as stiffness in myotonic dogs decreases with exercise.

In the equines in which myotonia was demonstrated (Botelho and Steinberg, 1962), the main pathological changes were a slowly progressive myofibre necrosis, perimysial fibrosis and compensatory myofibre hypertrophy (Kelly, 1973). No ringed fibres nor sarcoplasmic masses were seen and enzyme histochemistry demonstrated fibre type grouping in affected muscles. It is obvious therefore that the structural lesions, associated with the diverse myotonic syndromes described in the horse and dog, vary in type and extent.

While our cases showed electromyographic features very similar to those seen in true myotonia in man, none of the other signs of myotonia dystrophica (cataract, alopecia etc.) was present. The pathological changes were not identical with those seen in man, the main difference being the absence of ringed fibres and sarcoplasmic masses. Neither is the histology similar to that described by Innes (1951) and Whitney (1958) in case reports of muscular dystrophy in the dog nor to the familial canine myopathy described by Wentink *et al.* (1972). Until more is known about canine muscle disease, particularly concerning its genetic aspects, it is

probably wise to refer to these two cases as "myopathies associated with myotonia".

*Acknowledgements.* We wish to thank Miss C. Quirk and Miss R. Miller for their skilful technical assistance and Mr. A. Finnie for the photography.

One of us (I. D. Duncan) gratefully acknowledges support from the Horserace Betting Levy Board.

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