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Inflammatory Changes in Facioscapulohumeral Muscular Dystrophy

Maria Molnár, Peter Diószeghy, and Ferenc Mechler

Department of Neurology and Psychiatry, University Medical School of Debrecen, Debrecen, Hungary

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Summary. Fifteen patients (10 familial and 5 sporadic cases) with facioscapulohumeral dystrophy were studied with regard to the presence of inflammatory changes. Mononuclear infiltrations were not characteristic of any stage of the disease, but they may be present in differring degrees during the whole course of the process. However, their lack or presence was uniform in the affected families, suggesting that the appearance of infiltrations may be genetically determined. Parallel with the presence of cell infiltrations, the serum creatine kinase (CK) activity was moderately increased and the progress of the disease was slightly accelerated. The relation of these phenomena to polymyositis and the diagnostic difficulties are discussed.

Key words: FSH – Inflammatory infiltration – Serum CK – Diagnostic difficulties

Introduction

The facioscapulohumeral (FSH) syndrome is a group of muscular diseases of various aetiology, with characteristic distribution of muscle involvement. The special nosological entities are identified by detailed clinical investigation, genetic information, electromyography, biochemical studies, muscle histology and histochemistry. Within this group, the FSH muscular dystrophy has maintained a relatively stable nosological position since its original description by Landouzy and Dejerine [6]. However, some confusion has arisen from the presence of inflammatory cell infiltrates in muscle specimens of a few patients with clinically typical FSH [1, 3, 8–10]. This paper reports the findings in patients with FSH muscular dystrophy who were studied with special regard to inflammatory changes in their muscles.

Patients, Methods and Results

Muscle specimens of 15 patients with FSH (10 familial and 5 sporadic) were evaluated. The age of patients ranged from 15 to 56 years. Their clinical features were characteristic of FSH muscular dystrophy. The facial weakness was prominent. Weakness and atrophy were present in the muscles of shoulder girdle, proximal upper extremities, serratus anterior, pectoralis and the anterior tibial muscles were also more or less affected. Electromyography showed a pattern consistent with myopathy. The erythrocyte sedimentation rate (ESR) and the results of other routine laboratory investigations were normal. Serum creatine kinase (CK) activity was moderately elevated or normal. For biopsy, clinically affected but not seriously wasted muscles were chosen. The deltoid, anterior tibial and/or quadriceps muscles were sampled. Fresh frozen cryostat sections were routinely prepared and specimens were stained with a battery of histological and histochemical reactions (Haematoxylin and Eosin, modified Gomory Trichrome, Sudan black, PAS, NADH-TR, Myofibrillar ATPase preincubated at pH 9.4, 4.6 and 4.3).

The histopathological findings consistent with muscle dystrophy were always present: great variability of the calibre of fibres, rounded atrophic fibres affecting both fibre types, internal nuclei, proliferation of connective and fat tissue.

In the first family, four affected members belonging to three successive generations were examined (Fig. 1). At the time of biopsy they were 17, 21, 38 and 56 years

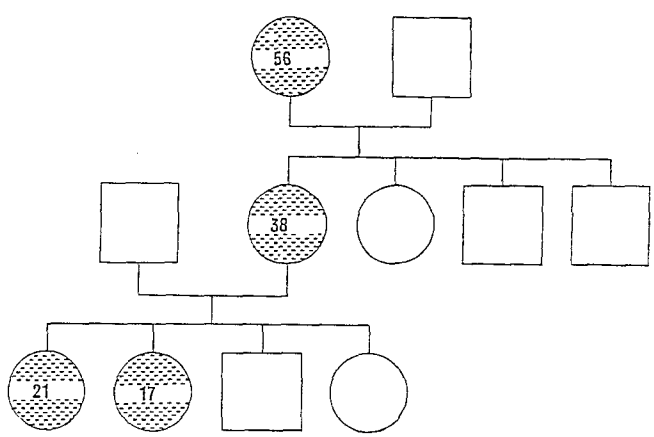

Fig. 1. Pedigree of the first family. Shading denotes the affected members. Numbers represent years

Offprint requests to: F. Mechler, Department of Neurology, University Medical School of Debrecen, H-4012 Debrecen, Hungary

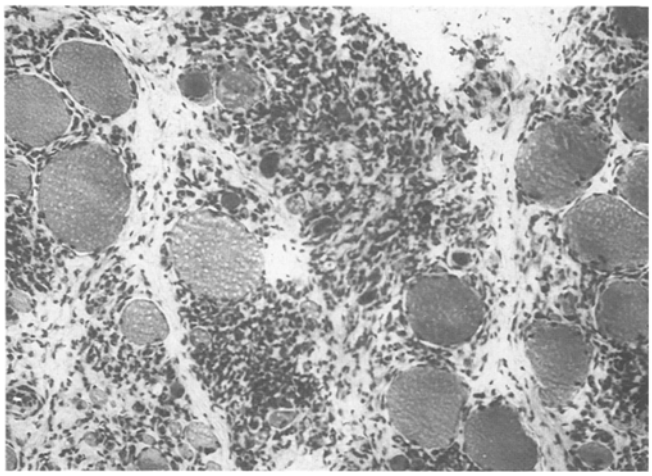

Fig. 2. Anterior tibial muscle biopsy specimen from the third family. Marked variation in muscle fibre size is seen. The degenerating and necrotic fibres are surrounded with dense mononuclear cell infiltration. (*H & E*)

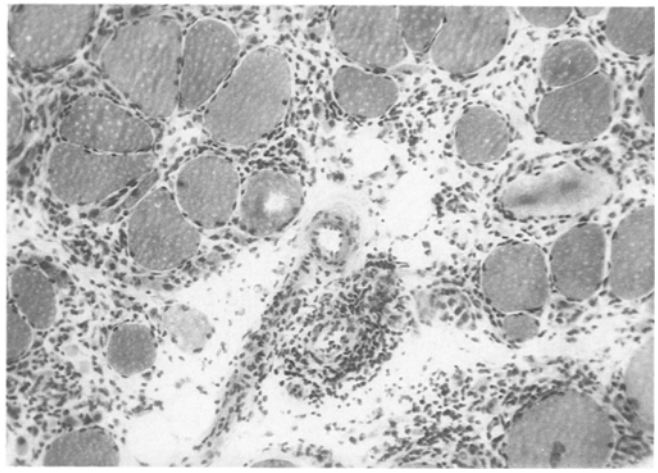

Fig. 3. Anterior tibial muscle biopsy from the third family. Peri- and endomysial inflammatory infiltrations are seen. A nodular dense infiltration is present in the vicinity of a small vessel, but its wall is intact (*H & E*)

old and their complaints had appeared 3–13 years earlier. Serum CK levels were normal in all of the patients. Electromyograms revealed short-duration, low amplitude motor units. In two patients fibrillatory potentials were occasionally present. No inflammatory changes were found in the biopsy specimens.

Two affected members of the second family (35 and 39 year-old females) showed moderate and mild clinical symptoms and histological findings respectively. Neither inflammatory changes in muscle nor increased serum CK levels were observed in these patients. In one of them fibrillations were easily observed.

In two other FSH families, 2–2 patients were investigated. In both families, the affected members showed inflammatory infiltrates in muscle and elevated serum CK activity. In one of these families (3), two brothers (age 15 and 18 years) were affected with a moderate but typical pattern of FSH dystrophy. Their serum CK levels were consistently elevated for years. Electromyography was myopathic. Sporadic fibrillations were present in one of them. Tissue specimens from anterior tibial muscle showed scattered fibres with marked atrophy and degenerative changes, great variation of muscle fibre size, nuclear centralisation and necrosis with phagocytosis. Scattered and dense nodular mononuclear cell infiltrations were observed in many areas both between fibres and between fascicles. Infiltrates were present not only in the vicinity of necrotic fibres but also surrounded small blood vessels (Figs. 2 and 3). In the younger brother, biopsies in deltoid and anterior tibial muscles were carried out at the same time. The histological changes in the two muscles, including the inflammatory infiltrates, were similar, but they proved to be more prominent in the anterior tibial muscle.

In the other family (4), a 21-year-old man and his 25-year-old sister were studied. The biopsy specimen from the anterior tibial muscle of the male patient showed similar pathological changes with marked lymphoplasmocytic infiltrates as in the previous family (3). Biopsy from the affected sister was not available. Serum CK

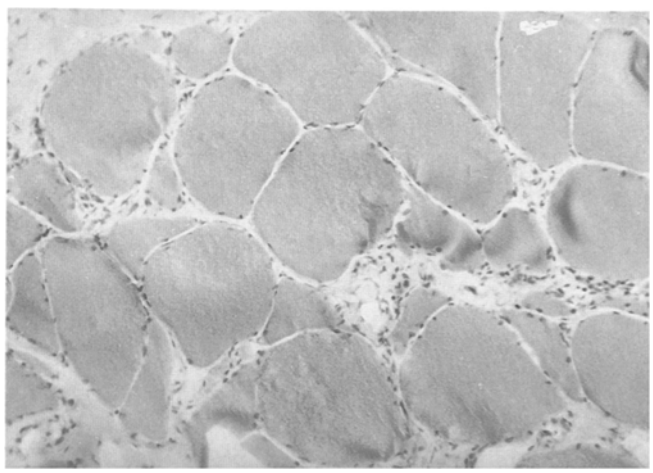

Fig. 4. Quadriceps femoris muscle biopsy specimen from a sporadic case. Small rounded and angular fibres are seen. Slight scattered infiltratory cells are present. (*H & E*)

levels in both patients were repeatedly increased. In the electromyogram of the female patient some fibrillatory potencies were found.

In five patients, the inheritance could not be proved. The clinical and histological pictures were characteristic in all of these sporadic cases. Infiltrates were found in the biopsy specimens of three patients (Fig. 4) while in the remaining two they were absent. The patients with inflammatory changes in the muscle had elevated serum CK, while the others without infiltrates had normal CK levels. In one patient without mononuclear infiltrations and with normal serum CK level and in three cases with inflammatory changes and elevated CK activity, fibrillations were occasionally observed in addition to myopathic findings in electromyography.

Showing the relationship between serum CK activity and inflammatory changes, the CK values were plotted in the group of patients with and without mononuclear infiltrates (Fig. 5).

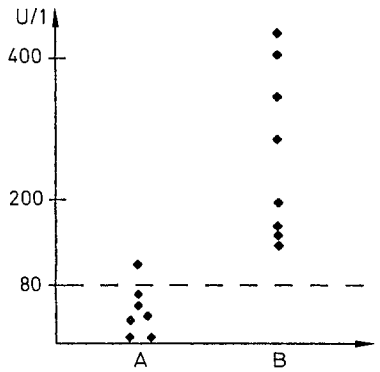

Fig. 5. Serum CK activities of patients with mononuclear cell infiltrations (**A**) and without infiltrations (**B**). The *dotted line* represents the upper normal level

Discussion

Inflammatory changes have been relatively often observed in hereditary myopathies, including facioscapulohumeral muscular dystrophy [1, 3, 8, 9]. However, the significance of mononuclear cell infiltrations in muscular dystrophy is unclear. Several questions can be asked. Are these infiltrations present only temporarily at a given stage (mostly in the early stage of the disease) or permanently during its whole course? Do these patients represent restricted forms of polymyositis or unrelated processes? Is there any correlation between the presence of inflammatory infiltrations and the level of serum CK?

In our study, we could not find any relation between age, duration of symptoms and the presence of infiltrations in muscle. The age of our patients with inflammatory changes and the length of their illness varied quite considerably. Their age at the time of biopsy was between 18 and 32 years. This is consistent with the finding of others [4, 13]. There was a similar dispersion regarding the age of our patients without infiltrations (17–56 years). According to our observations, inflammatory changes are not characteristic of any stage of FSH dystrophy. In certain families they are possibly present to a lesser or greater degree during the whole course of the disease.

In our first family with four patients representing different stages of the disease, mononuclear infiltrations could not be shown. On the other hand, inflammatory changes of varied severity were found in three cases belonging to two other families (3. and 4.). It is of interest that the histological changes in the affected members of a given family are almost identical. This suggests that the presence of inflammatory infiltrations in FSH muscle is genetically determined. We cannot exclude that immunological factors may be involved in their appearance. Inherited autoimmunity against striated muscles may be the basis of inflammatory changes in the hereditary myopathies. Although the immunocytochemical characteristics of these infiltrations are similar to those in myositis [5], their significance in the pathomechanism and in clinical manifestation differs considerably in the two pathological processes. However, immunological analysis of such cases has to be carried out.

A relationship was observed between the serum CK activity and the inflammatory changes in muscle. Parallel with the findings of infiltrations we measured slight but constent increase of serum CK levels. This could be the result of a more prominent fibre necrosis in these patients compared with those without infiltrations, where the CK concentrations were in the normal range. As was predicted, the progression of the disease was accelerated and the course was worse in the patients with infiltrations and elevated serum CK level.

In clinical practice, difficulties may arise with regard to differentiating between sporadic cases of FSH muscular dystrophy and polymyositis. A special form of polymyositis with predominant facioscapulohumeral distribution has been reported [2, 11, 12]. The polymyositis may be localized to certain muscle groups and may also progress very slowly [4]. In polymyositis the facial involvement is slight, the muscle involvement is usually symmetrical and the weakness is more prominent than the atrophy. On the other hand, in FSH dystrophy, the early and predominant facial muscle involvement is characteristic, the weakness may be asymmetrical and is less marked than expected from the amount of atrophy. The hereditary transmission and the lack of serological abnormalities but moderately elevated CK level may help to exclude polymyositis. In 8 of our 15 patients, the electromyogram revealed sporadic fibrillations, which has been observed by others [4, 8]. However, it is also characteristic in polymyositis [7]. We could not find a correlation between fibrillatory activity and the presence of mononuclear cell infiltrations in muscle. Therefore, the presence or lack of fibrillations does not help to distinguish between FSH dystrophy and polymyositis. When inflammatory cells are present, histopathology can not contribute to the exact diagnosis in sporadic cases. The infiltrations are indistinguishable from those found in polymyositis and can be the source of diagnostic difficulties.

There have been studies suggesting the efficiency of corticosteroid treatment even in muscular dystrophies in which inflammatory infiltrations are present [1, 8]. Relying upon the similarities in histological changes with polymyositis, steroid therapy is worth considering. We did not give corticosteroids in our cases, but a fully controlled study would be advisable.

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