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MUSCULAR LESION IN CHRONIC POLYMYOSITIS

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Polymyositis and the sub-group dermatomyositis, are assigned by most authors to the group of collagenous diseases (*Walton & Adams* 1958). Several diseases of this group, e.g. rheumatoid arthritis, may be accompanied by unmistakable clinical signs of myopathy, and in such cases microscopic examination reveals nodular interstitial myositis (*Rossel* 1963).

However, it is particularly the differential diagnosis between progressive muscular dystrophy and chronic polymyositis which has given rise to difficulties after *Keil,* in 1940, described a patient whose condition had been interpreted for many years as muscular dystrophy, but who was actually suffering from chronic polymyositis. *Matthews & Burne* (1953) have reported a similar case. *Zieler & Lilienthal* (1953) pointed out that a few cases of progressive muscular dystrophy might be due to previous polymyositis and described two misinterpreted cases of their own. *Wilson* (1954) stated that in rare cases dermatomyositis may be reminiscent of muscular dystrophy. *Natrass* (1954) tried, both alone and in collaboration with *Walton,* to adduce a proof that certain cases of so-called muscular dystrophy in children are in fact due to polymyositis, but in the absence of muscle biopsies the final proof is lacking.

The significance of muscle biopsies in differentiating between chronic polymyositis and progressive muscular dystrophy has been stressed by several authors. Out of 6 patients with histologically confirmed chronic myositis *Christensen & Levison* (1950) found 3 to have clinical signs reminiscent of progressive muscular dystrophy. In 5 of these patients histological examination revealed changes of the muscle fibres in the form of hypertrophy and atrophy, like those seen in dystrophy. Two of the patients also had interstitial fatty infiltration, socalled pseudohypertrophy. On the basis of the clinical and histological findings in muscle biopsies from patients with polymyositis *Eaton* (1954) emphasized the similarity between the two diseases. He admitted that he himself had

made the incorrect clinical diagnosis of muscular dystrophy in a patient whose muscle biopsy proved to represent chronic interstitial myositis. He states that the degenerative as well as proliferative changes may be seen in muscle biopsies in both conditions.

Furtado & Alwin (1945) have published two cases of the so-called pseudomyopathic form of polymyositis in a 9-year-old child and in a 50-year-old man. In their opinion, these two cases of polymyositis with secondary and progressive wasting of the muscles—clinically similar to dystrophy—belong to an autonomous group of polymyositis. *Greenfield et al.* (1957) found it very difficult to distinguish, histologically as well as clinically, between the various forms of muscular dystrophy and myositis. *Walton & Adams* (1958) point out that an outburnt case of myositis, in which the inflammation cells are absent, may be difficult to distinguish, also histologically, from an advanced case of dystrophy. It may be mentioned, moreover, that *Heathfield & Williams* (1960) reviewed old specimens from two patients with the diagnosis progressive muscular dystrophy owing to an atypical course and on this basis the diagnosis was altered to chronic polymyositis. The difficulty of the clinical differential diagnosis between the various muscle diseases is apparent also from *Christensen & Jedrzejowska*'s analysis (1961) of 174 cases of various forms of histologically confirmed chronic myositis. Here the clinical diagnosis was muscular dystrophy in 28 patients.

PRESENT SERIES

Having 9 patients with various forms of histologically confirmed myositis who have been submitted to muscle biopsy at intervals, we felt that it would be of interest to publish their histories and discuss the value of the biopsy findings in relation to the clinical diagnosis.

The follow-up biopsies were removed from the same muscle as the first ones. The detailed histories of some of these patients have previously been published by *Rossel* (1962), *Kryger & Rossel* (1963), and *Rossel & Bærentsen* (1963). In the present paper the main stress will be laid on the histological findings, and only positive laboratory findings will be mentioned.

Case 1.

A male, born in 1940, who was *admitted in September 1962* because of a suspicion of rheumatic fever. No predisposition to muscular diseases. For six weeks there had been severe stiffness, tenderness and weakness of all muscles and mild articular symptoms.

Obj. findings: All muscles tender to palpation and hard. General condition debilitated.

Laboratory findings: ESR 25 mm. Urine creatinine and serum transaminases elevated. Serum electrophoresis: Elevated α_2. Eosinophils 5825 per cu mm. At the end of 2 weeks on steroid medication 119 per cu mm.

Electromyography revealed signs of severe myogenic lesion and small potentials at rest.

Biopsy from the right forearm (No. 8598–99/62) showed in the interstitial vascular connective tissue some infiltration with lymphocytes and leukocytes, a few of which were eosinophilic. The vessels showed no changes, in partticular no fibrinoid necroses.

H.D.: Focal subacute interstitial myositis (sd. *Bruzelius*).

Discharged on prednisone and was soon improving.

Follow-up in January 1963: Only complaint stiffness of muscles. The steroid is being levelled off.

Obj. findings: Muscles rather stiff and hard.

Muscle biopsy showed no definite abnormalities.

Conclusion: Neither clinical nor histological signs of chronic myositis which might be mistaken for muscular dystrophy were found, but the clinical finding of hard muscles indicated a lesion of the muscles. The first biopsy specimen showed interstitial myositis—which explains the altered consistency of the muscles—although the muscle fibres proper were not involved. The second biopsy, four months later, showed normal interstitial tissue, although the muscles were still stiff and hard. It cannot be ruled out that mild histological changes might have been found if the biopsy specimen had been removed from another muscle, but the improved general condition would seem to indicate that the patient is going to recover on steroid medication.

In May, a positive toxoplasmosis reaction was found.

Case 2.

A male, born in 1912, who was *admitted in June 1961* because of a suspicion of polyneuritis. No inherited predisposition to muscular diseases. Three months prior to admission the patient had developed a short-lasting rash and pain in the left shoulder, followed by such severe, persistent pain in the back and legs that he was admitted.

Obj. examination revealed tenderness of most muscles, slight wasting of the left upper arm and hypothenar, but no definite weakness.

Laboratory findings: ESR 8 mm, BMR + 21 %, + 23 %, + 15 %. Serum electrophoresis: Elevated α_2 and γ.

Electromyegraphy showed a slight loss of motor units and small potentials at rest, but a normal duration of the potentials.

Biopsy from the left deltoid muscle disclosed very large interstitial perivascular infiltrates, consisting predominantly of lymphocytes and plasma cells. There was no involvement of the vessel walls and the muscle fibres, but in the peripheral areas of the lesions homogenization of the muscle fibres was present in a few places.

H.D.: Moderate focal, subacute interstitial myositis.

The patient was not treated with steroid. He recovered spontaneously and went back to his former work.

Follow-up in October 1962: No complaints apart from negligible pain in the shoulder on heavy work.

Obj. examination also showed normal conditions.

Electromyography normal.

Muscle biopsy (5361) showed nowhere any sign of atrophy of the muscle fibres and only small perivascular foci with moderate deposition of lymphocytes and plasma cells. There was no sign of connective-tissue proliferation, vascular changes, or an increase in the mast cell count.

H.D.: Mild focal, interstitial myositis.

Conclusion: In this case, where examination of the first biopsy showed moderately severe, subacute interstitial myositis, the second biopsy—15 months later—showed such slight changes that it seems justified to assume that this patient will recover without any permanent sequelae. This history indicates that spontaneous cure may take place in some cases of myositis.

Case 3.

A male, born in 1899, who was *admitted in November 1960* with a cancer of the rectum. Treated by radical surgery. He had always shown signs of neurasthenia and a psychopathic personality. In June 1960 he had suddenly got a numb feeling and paraesthesiae in the right arm. This gradually increased, and at the same time he developed a sensation of fatigue in the right arm and leg. The subjective muscular complaints continued after the operation.

Admitted in February 1962. Obj. examination showed no abnormalities apart from a mild, diffuse weakness.

Laboratory findings: ESR 62 mm. Serum electrophoresis: Elevated α_2 and γ.

Electromyography indicated myogenic affection in one muscle, while other muscles were normal.

Biopsy from the right anterior tibial muscle showed interstitial oedema in many places, but only in one area a more marked focal perivascular infiltration with lymphocytes and plasma cells. In other parts of the specimen only a trace of perivascular round-cell infiltration. The muscle fibres were normal.

H.D.: Mild, subacute interstitial nodular myositis.

The patient was put on prednisone for 4 months.

Admitted in September 1962. Symptoms almost unchanged, but a little difficult to assess owing to the patient's neurasthenic constitution.

Electromyography indicated myogenic affection.

Muscle biopsy (5327) showed on the whole normal conditions. The muscle fibres had a preserved structure, a uniform diameter and peripheral nuclei. The interstitial connective tissue was on the whole scanty, but there was fairly ample adipose tissue. Only in a very few places slight perivascular infiltration with lymphocytes, but neither mast cells nor histiocytes. Vessels normal throughout.

H.D.: Striated muscle with a trace of interstitial cellular infiltration (but *not* sufficient to justify a diagnosis of myositis).

Conclusions: In this case the clinical as well as histological signs of myositis were mild and not symmetrical. As his muscular symptoms

remained unchanged 15 months after radical operation for cancer of the rectum, it may be discussed whether or not there can have been a question of carcinomatous myopathy. The first biopsy showed only a mild, but nevertheless definite focal interstitial myositis. The nodular lymphocytic infiltration in the latter biopsy must be classified as lymphorrhages to which no importance can be attached, clinically or histologically. The fact that the second muscle biopsy did not show any abnormality, although the patient's complaints were unchanged and the electromyography still indicated a myogenic affection, must be taken to mean that the diagnosis of myositis cannot be rejected by an isolated muscle biopsy.

Case 4.

A female, born in 1900, was *admitted in September 1956* because of a suspicion of polymyositis. Since 1955 there had been febrile periods, diffuse muscle pain, fatigue, and paraesthesiae.

Obj. examination: Muscles tender, pasty and infiltrated; atrophy of the quadriceps on both sides, and mild, diffuse weakness of the legs.

Electromyography normal.

Muscle biopsy from the right lower leg: Normal.

Treated with prednisone for 18 months with a fair effect.

Admitted in May 1958 with largely the same complaints and objective findings.

Laboratory findings: ESR 44 mm, elevated urine creatinine, BMR + 21 % and + 24 %.

Muscle biopsy from the right biceps brachii (6407–58) showed a slight, focal, interstitial, subchronic to chronic myositis (sd.: *Søeborg-Ohlsen*).

Prednisone was continued for some time with some improvement. Admitted in April 1962 with a fracture of the head of the left femur.

At follow-up in October 1962 she complained of mild pain and weakness of the arms and legs, but she was much better, and she could manage her domestic duties.

Obj. examination: Mild atrophy and weakness of the lower limb muscles, in particular both quadriceps muscles.

Electromyography of the right biceps brachii indicated myogenic lesion.

Muscle biopsy (5329) showed around a few of the vessels and in some of the vessel walls infiltration with lymphocytes, eosinophilic granulocytes, and occasional macrophages, but no mast cells. In other parts of the specimen there was a varying degree of atrophy of the muscle fibres and clumping of the nuclei, but no signs of neurogenic atrophy.

H.D.: Mild, subacute nodular interstitial myositis with secondary muscular dystrophy.

Conclusion: In this case, the condition was diagnosed clinically as polymyositis, although the first muscle biopsy in 1956 showed no abnormality. On the other hand, myositis was found in the second muscle biopsy, in 1958, although the patient had been put on steroid medication, which was then continued. Even in 1962 mild active interstitial inflammatory changes remained, and there was focal wasting of the

muscle fibres corresponding to the clinical finding of mild atrophy and paresis in all muscle groups, but particularly both quadriceps muscles —and it must be mentioned that the biopsy was from the biceps brachii. It is impossible to tell how this patient would have fared without prednisone therapy, but probably she would have developed more severe muscular atrophy.

Case 5.

A girl, born in 1954, was *admitted in December 1961* because of a suspicion of muscular dystrophy. No inherited predisposition to muscular diseases. Within one month, she developed a gait disturbance, pain in the thigh muscles, and general weakness.

Obj. findings: A girl of normal appearance with diffuse muscle weakness and difficulty in raising herself from the horizontal position.

Laboratory findings: ESR 20 mm. serum transaminase and urine creatinine elevated, electrocardiagraphy showed tachycardia, serum electrophoresis elevated α_2.

Electromyography showed unmistakable signs of myogenic lesion. In addition, small potentials at rest.

Muscle biopsy from the right vastus lateralis showed focal, mild to severe infiltration with lymphocytes, plasma cells and granulocytes, many of which were eosinophilic. A small number of the muscle fibres showed signs of degeneration.

H.D.: Subacute focal interstitial myositis (sd.: *Søeborg-Ohlsen*).

Discharged on prednisone and Durabolin.

Follow-up in October 1962. Almost completely symptom-free. She could play normally and attended school. Her muscle strength was found to be normal.

Electromyography showed signs of myogenic affection, but less marked than in December 1961.

Muscle biopsy (5332) showed severe, but mainly focal changes consisting of cellular infiltration and atrophy of muscle fibres as well as interstitial connective-tissue proliferation and development of fat tissue in these areas. Inflammatory infiltration and mild degeneration of the myelin sheaths occurred also in some of the intramuscular nerves. As a whole, however, the appearances were predominated by areas of heterogenous atrophy of the muscle fibres, not by the cellular infiltration.

H.D.: Chronic, nodular interstitial myositis with secondary muscular dystrophy.

Conclusion: Thus, the degeneration of the muscle fibres had progressed during the interval of 10 months between the two biopsies. There were still interstitial inflammatory changes, although the patient was being treated with steroid. The reason for using the term secondary muscular dystrophy as the histological diagnosis in the second biopsy was to emphasize that there was a heterogenous diameter of the muscle fibres in each affected fibre bundle, as seen in true muscular dystrophy.

Case 6.

A male, born in 1887, was *admitted in December 1961* because of a suspicion of humero-scapular periarthritis. During the past 6–12 months he had been complain-

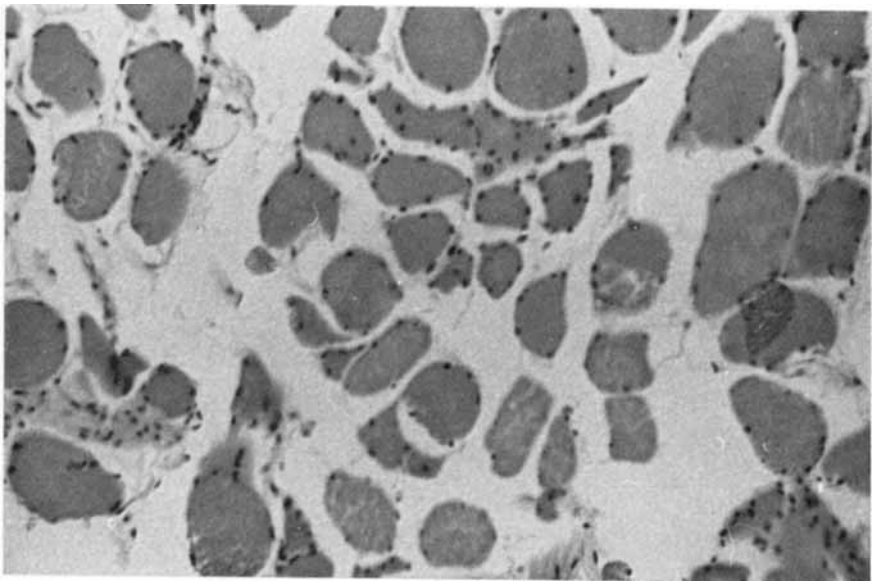

Fig. 1.
Case 6. Small clusters of completely or partially atrophic fibres and mild focal interstitial infiltrations with lymphocytes. (H.E.-stain, × 40).

ing of gradually decreasing strength and pain in the left shoulder. Immediately before admission there had been mild erythema which had subsided in one week.

Obj. examination revealed wasting of the muscles of the shoulder girdle and the upper arm and weakness in these areas.

Laboratory findings: ESR 32 mm. Serum electrophoresis: Slightly elevated α_2.

Electromyography indicated a myogenic affection. At rest small potentials.

Biopsy from the skin (4906) revealed moderate perivascular lymphocytic infiltration in the corium, but no mast-cell infiltration and no involvement of the vessel walls. The corium was slightly oedematous, but not sclerosed. Biopsy from left trapezius muscle showed muscle fibres of a somewhat heterogenous diameter with small clusters of completely or partially atrophic fibres. In addition, in some sites mild interstitial infiltration with lymphocytes (Fig. 1). In other sites incipient degeneration of the muscle fibres with invasion of macrophages and a tendency to central displacement of the nuclei in the degenerated fibres.

H.D.: Mild chronic dermatomyositis. Mild panmyositis with neurogenic involvement.

Treated, with a favourable effect, with prednisone for 6 months, but the strength again decreased when the medication was withdrawn. Nevertheless, he was able to work 6 hours a day.

Follow-up in October 1962: Obj. examination showed some atrophy, especially of the muscles of the shoulder girdle.

Electromyography indicated a myogenic affection. As previously, small potentials at rest.

Muscle biopsy (5326) showed severe changes in the form of proliferation of the interstitial tissue and heterogeneous atrophy and hypertrophy of the muscle fibres

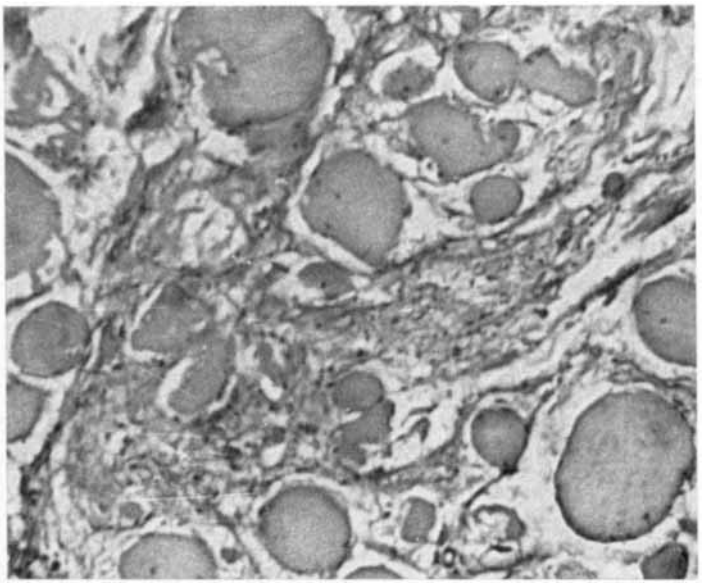

Fig. 2.
Case 6. Follow-up biopsy. Fields of atrophic fibres in between hypertrophic fibres with regenerative changes. Marked proliferation of cellular interstitial tissue. (Van Gieson-stain, × 40).

(Fig. 2). In addition, fields of atrophic fibres in some bundles. In a few places also focal perivascular infiltration with lymphocytes and areas of granulation tissue, in places invading the muscle fibres, could be seen. In a few sites longitudinal splitting of the fibres, interpreted as a sign of regeneration.

Biopsy from the skin was unchanged from first biopsy.

H.D.: Chronic dermatomyositis with severe secondary muscular degeneration and neurogenic involvement.

Conclusion: It will be seen, thus, that the inflammatory lesions had decreased, while the muscle fibre degeneration had progressed in 10 months. Both biopsies showed degeneration in the muscle fibres proper in addition to the atrophy which is interpreted as being secondary to the interstitial inflammation and the consequent connective-tissue proliferation. The second biopsy also showed signs of regenerative processes.

Case 7.

A male, born in 1921, was *admitted in January 1961* because of weight loss and a suspicion of muscular dystrophy. No inherited predisposition to muscular diseases. During the past nine months he had lost nearly 20 kg, and he was complaining of fatigue, muscular weakness, difficulty in carrying his arms up to his head, muscle pain, transitory diplopia, palpitations, and dysphagia.

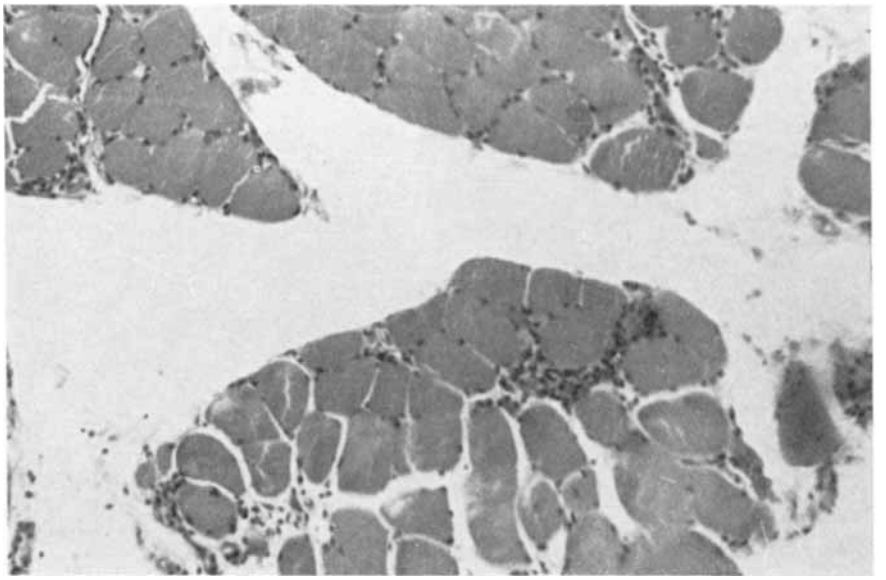

Fig. 3.
Case 7. Focal interstitial infiltration and varying of atrophy of the muscle fibres with slight neurogenic involvement. (H.E.-stain, × 40).

He looked tired and was generally debilitated. Was unable to rise from the horizontal position without first turning over into the prone position. Considerable weakness and wasting of the muscles of the shoulders and arms, less so of the hand muscles, while the leg muscles were normal.

Laboratory findings: ESR 6 mm. Serum transaminase and urine creatinine elevated. BMR: + 30 % + 26 % + 29 %. Electrocardiography: Tachycardia and mild myocarial degeneration. Cineradiography of the oesophagus revealed passage of the bolus into the trachea and retention in the right pyriform recess.

Electromyography indicated myogenic affection. Small potentials at rest.

Muscle biopsy from the right deltoid (4310) showed severe changes consisting of a wax-like or hyaline degeneration of a number of the muscle fibres, varying degree of atrophy of other fibres in some areas, of neurogenic character, and cellular infiltration—interstitial as well as within more or less degenerated muscle fibres. This infiltration consisted of lymphocytes, fibroblasts, occasional granulocytes and macrophages mainly in the degenerated muscle fibres.

H.D.: Severe subchronic panmyositis involving interstitial tissue as well as muscle fibres, with a slight neurogenic involvement (Fig. 3).

The patient was treated with prednisone for eight months until he was re-admitted for follow-up in September 1961. On this medication he improved so much that he went back to work.

Obj. examination showed that he was in good general health. He had mild wasting of the shoulder muscles and slight weakness of the muscles of the shoulders and upper arms, but definitely less than previously. No biopsy was obtained, and the steroid medication was discontinued.

At follow-up in October 1962 there was only a suggestion of weakness in shoulder

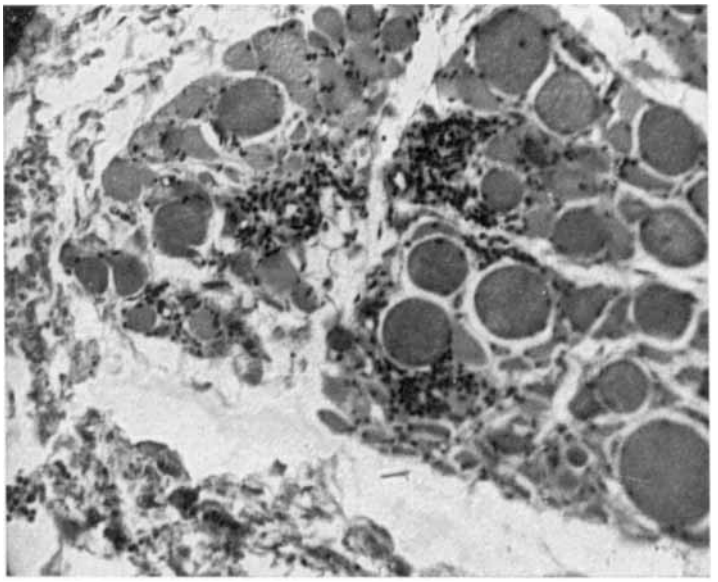

Fig. 4.
Case 7. Follow-up biopsy. Degenerated muscle fibres, both with hypertrophy and fields of uniformly atrophic fibres and in places with macrophages inside the sarcolemma. Marked hypertrophy of interstitial tissue with inflammation. (Van Gieson-stain, × 40).

movements and no visible atrophy. The patient had been working full-time for a year, but tired quickly. Still negligible difficulty in swallowing.

Electromyography indicated myogenic affection.

Muscle biopsy (5342) showed very severe changes with hypertrophy of the interstitial connective tissue and focal, especially perivascular infiltration with lymphocytes, fibroblasts, and occasional mast cells, but no eosinophils. Only a very few vessel walls were infiltrated with lymphocytes. The muscle fibres showed atrophy in many places, to a lesser extent hypertrophy and swelling and more or less blurring of the structure. In a few sites also degeneration of the fibres, there being fibre remnants and granulation tissue within the sarcolemma. The field-shaped atrophy was more distinct than at the first biopsy.

H.D.: Severe chronic panmyositis with secondary muscle fibre degeneration and a neurogenic involvement (Fig. 4).

Conclusion: Comparison with the first biopsy showed that now there was less active inflammation, but more connective tissue proliferation and more degeneration of the muscle fibres. The explanation of the field-shaped atrophy may be assumed to be affection of the peripheral nerve ends. However, the final proof cannot be advanced, as the biopsy had not been removed from the site of the nerve branching.

Case 8.

A female, born in 1905, was *admitted in June 1958* with polyneuritis. She had been suffering from psoriasis from childhood and from rheumatoid arthritis from 1946. From 1952 paraesthesia and increasing weakness of the lower limbs. Treated with cortisone from 1955.

Obj. findings: Moderate rheumatoid changes of the joints and severe paresis of the dorsal flexors of the feet.

Electromyography indicated a mixture of neurogenic and myogenic affection.

Muscle biopsy from the right anterior tibial muscle (2993) showed muscle fibres of varying diameter, there being both atrophic, a few normal, and many swollen and hyalinized in a mixture without a demonstrable field-shaped arrangement. Some fibres showed degeneration, there being an empty sarcolemma sheath or macrophages within the sarcolemma. The interstitial connective tissue showed proliferation and massive inflammatory infiltration, in places involving the muscle fibres. There were lymphocytes, eosinophilic granulocytes, as well as a few groups of plasma cells. Only in a very few places did there seem to be inflammatory infiltration in the vessel walls.

H.D.: Severe subchronic panmyositis with secondary degeneration of muscle fibres.

During the subsequent years the patient was treated periodically with prednisone.

Admitted in January 1962. At that time the joint symptom had almost disappeared, while the pareses in the lower limbs had become more pronounced.

Obj. examination: Pronounced paresis af the dorsal flexors of the feet, very moderate articular changes, and signs of Sjögren's syndrome.

Laboratory findings: ESR 35 mm. RA test positive, serum transaminase and alkaline phosphatases elevated, serum electrophoresis: Elevated α^2 and γ.

Electromyography showed signs of myogenic affection as well as small potentials at rest.

Muscle biopsy (4936) revealed a very marked increase in interstitial connective tissue and heterogeneous atrophy and hypertrophy of the muscle fibres within the same bundle. No inflammatory changes, neither in the interstitial connective tissue nor in the vessel walls could be seen.

H.D.: Sequelae of myositis.

Striated muscles with very severe degeneration of muscle fibres and hypertrophy of the interstitial tissue.

Conclusion: The histological appearance of the second biopsy reminds very closely of myogenic dystrophy, but there was unusually pronounced proliferation of the interstitial connective tissue. When considering the previous biopsy, a primary muscular dystrophy can be definitely excluded.

Case 9.

A female, born in 1887, was *admitted in January 1959* because of a suspicion of amyotrophic lateral sclerosis. No inherited predisposition to muscular diseases. For 10 years the strength of her limbs had been slowly decreasing, and she had distal paraesthesiae, first of the hands and then of the feet.

Obj. examination: Diffuse muscular atrophy, especially in the upper limbs.

Biopsy from the right biceps brachii showed normal muscle fibres but acute and chronic interstitial myositis (sd.: *Søeborg-Ohlsen*).

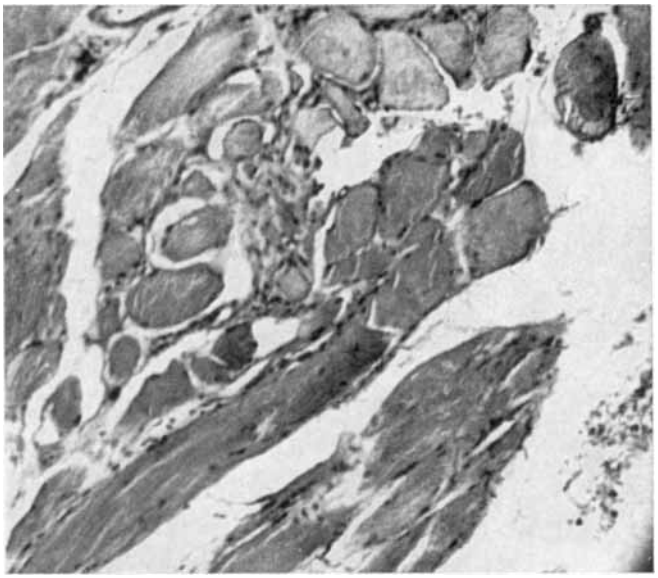

Fig. 5.
Case 9. Atrophic and hypertrophic muscle fibres in the same fiber bundle with proliferation of interstitial tissue. (Van Gieson-stain, × 40).

Treated with triamcinolone for 5 months.

Admitted in June 1959 for follow-up.

Obj. examination showed wasting and weakness of the limbs, especially distally on the upper limbs. All laboratory tests gave normal results.

Electromyography indicated myogenic affection.

Biopsy from the left hypothenar eminence (3530) revealed very marked changes in the form of heterogeneous shrinkage of many muscle fibres within the same bundle, hypertrophy of occasional fibres, longitudinal splitting and ring formation in others. A few fibres had completely degenerated, leaving in their place granulation tissue. The interstitial tissue showed severe hypertrophy, in places with development of fatty tissue. Apart from the named cellular infiltrations at the sites of degenerated muscle fibres, there were no signs of inflammation.

H.D.: Muscular dystrophy of myogenic origin (Fig. 5).

During the subsequent 3 years there was some aggravation of the condition, the strength in the hands being further reduced so that the patient could no longer attend to her domestic duties.

At follow-up in October 1962 she was found to have a considerable weakness and slight contracture of the muscles of the hands.

Electromyography indicated a severe myogenic affection. In addition, small potentials at rest.

Biopsy from the right biceps brachii (5316) showed rather marked, but focal changes, partly in the interstitial tissue and partly in the muscle fibres. Interstitially, there was in particular perivascular deposition of lymphocytes, histiocytes, and macrophages, but no definite proliferation. In the muscle fibres there was in most places a preserved transverse and longitudinal striation, while in a few areas the

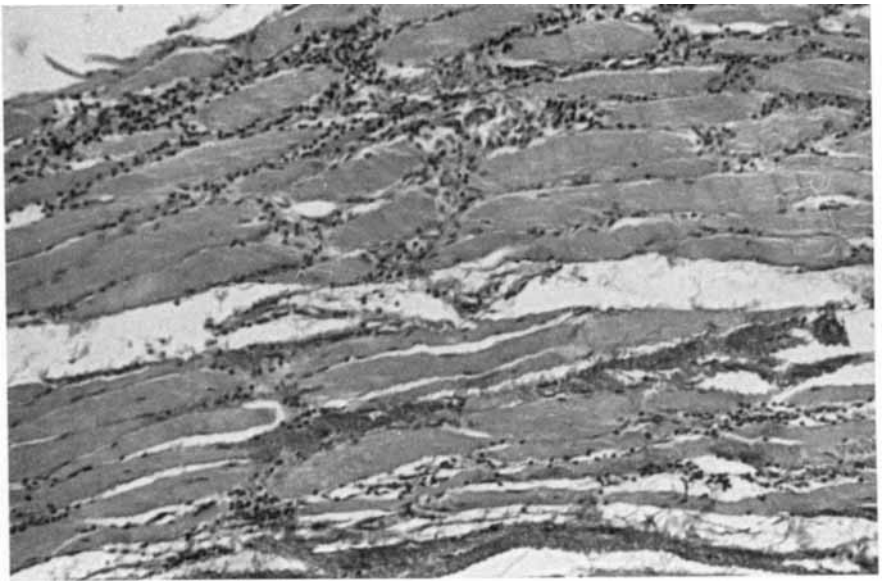

Fig. 6.
Case 9. Follow-up-biopsy. Focal interstital infiltration with lymphocytes, histiocytes and macrophages; in places degeneration of the muscle fibres. (H.E.-stain, × 40).

fibres were swollen and showed a somewhat blurred structure. In other places they were shrunken.

H.D.: Focal, subacute myositis, predominantly interstitial (Fig. 6).

Conclusion: This case history, with 3 muscle biopsy findings in the course of 3 years, is the most instructive one of the whole series. On the basis of the second biopsy finding, the diagnosis of myositis was abandoned, and steroid medication was discontinued.

At the time when the second biopsy was studied, it was not known that a biopsy from the patient had previously been investigated and that myositis had been demonstrated at the time. If this had been known, the pathologist would have considered the possibility that the degenerative muscular changes might represent the sequelae of myositis.

The first and third biopsy specimens were removed from the right biceps brachii at an interval of three years. During this period there had been a marked alteration in the appearances, the third biopsy showing some atrophy of the muscle fibres, but both revealing inflammatory lesions. The second biopsy was from the hypothenar and was removed 6 months after the first biopsy from the biceps. At that time the patient had a 10-year history of progressing pareses and wasting of the hands.

The divergent histological findings from the two muscles show—not surprisingly—that myositis may be in different phases in the individual muscles, depending upon whether in the muscle concerned the process is in an active, progressive phase, is burnt-out, or shows signs of regenerative processes as in the biopsy from the hypothenar eminence.

DISCUSSION

As is apparent from the histological descriptions of the muscle biopsies from these nine patients, they represent different clinical and histological varieties and degrees of myositis whose duration ranged from six weeks to ten years before the first biopsy was obtained. There are patients who were cured, clinically as well as histologically, and there are patients having varying degrees of irreversible changes in the muscles and consequently permanent symptoms.

In Case 1, a 21-year-old man who had had symptoms of myopathy for only six weeks, the first biopsy showed focal, subacute, interstitial myositis. The clinical symptoms and signs subsided on prednisone medication, and a new biopsy from the same muscle four months later showed completely normal appearances.

Case 2, a 50-year-old man, had had symptoms interpreted as polyneuritis for three months prior to the first biopsy. In this case the first biopsy revealed moderate, subacute, focal interstitial myositis. His condition improved spontaneously, and accordingly the second biopsy, five months later, showed only very mild changes. His history illustrates that myositis may subside without treatment. It is important to know this in assessing the value of steroid therapy.

Case 3 is more difficult to evaluate owing to his mental abnormality. From the histological point of view, he had only mild myositis at the time of the first biopsy. His muscular complaints remained unchanged, but the second biopsy from the same muscle 9 months later showed normal appearances. It is a matter of discussion whether the main stress is to be laid on the histological findings or on the patient's subjective complaints. Since, however, other objective findings were unchanged at follow-up, it must be concluded that normal histological findings in a muscle biopsy cannot disprove a clinical diagnosis of polymyositis. This accords with the fact that different muscles may show a different degree of involvement and that in mild degrees of focal interstitial myositis there may be large normal areas in a muscle. It has been mentioned above that in this case there may have been a question of carcinomatous myopathy, but as the symptoms persisted 15 months after radical surgery, this is not likely.

Cases 4 and 5 had clinical symptoms and signs of polymyositis and focal interstitial myositis at the time of the first biopsy. They were treated with prednisone and improved. Although the course was more protracted in Case 4 than in Case 5, the second muscle biopsies—4 years and 10 months respectively after the first—showed that both had degeneration of muscle fibres. This was interpreted as being secondary to the interstitial inflammatory process.

Cases 6, 7, and 8 had clinical symptoms and signs of polymyositis, Case 6 in the form of dermatomyositis, and Case 8 also showed signs of polyneuritis and rheumatoid arthritis. The histological findings in the first muscle biopsies from these three patients showed, apart from the interstitial inflammatory infiltration, also primary involvement of the muscle fibres— so-called panmyositis. All three were treated with steroid. Their clinical condition improved, but the muscular atrophy progressed, the second biopsies showing, in addition to varying degrees of myositis, also secondary degeneration of muscle fibres.

Cases 6 and 7 also had field-shaped atrophy, interpreted as a sign of involvement of terminal nerve endings, while no histological signs of neurogenic muscular atrophy were found in Case 8 who presented clinical signs of polyneuritis. This explains the denervation potentials found on electromyography in Cases 6 and 7. The fact that the other patients having potentials at rest did not exhibit field-shaped atrophy may be due to the electromyography and the biopsy not having been done in the same site or on the same muscle.

Case 9 had been suffering, for several years, from a progressive muscular disease which was first presumed to be amyotrophic lateral sclerosis. The diagnosis of myositis was based on a muscle biopsy from the biceps brachii. After periodical steroid medication for 3 years, a new biopsy from the same muscle still showed some myositis, but also secondary degeneration of the muscle fibres. In the meantime, a biopsy had been obtained from the hypothenar muscles, where there was such severe muscular degeneration that the histological diagnosis was muscular dystrophy of myogenic origin. The explanation must be that the inflammatory lesion in the hypothenar muscles had subsided at the time of the biopsy. At least, this is in keeping with the outstanding areas of atrophy.

Regenerative changes were demonstrated only in Cases 6 and 9, both of whom had co-existing, severe degeneration of the muscle fibres.

As may be seen from the histological descriptions, the appearances were predominated in the last 6 cases by degenerative changes of the muscle fibres and hypertrophy of the interstitial connective tissue. In Case 9 the second biopsy from the hypothenar eminence showed no in-

flammatory processes, and since at the time the pathologist was not aware of the patient's history of interstitial myositis, the histological diagnosis was muscular dystrophy of myogenic origin. The third biopsy 3 years later, again showed histological signs of myositis in the biceps brachii. This clearly illustrates the difficulty of differentiating between progressive muscular dystrophy and chronic myositis with secondary degeneration of the muscle fibres exclusively on the basis of the muscle biopsy. However, it was because of the repeated muscle biopsies that we were in a position to decide in several cases whether the patients had chronic polymyositis or muscular dystrophy (e.g. Cases 8 and 9). The explanation why the authors cited above have been unable to confirm their suspicion in this respect is that often no biopsy was obtained, and in no case were biopsies repeated in the course of the disease.

The quoted literature is intended to show the difficulties of differentiating between chronic myositis and muscular dystrophy merely on the basis of clinical findings. As is evident from the present study, muscle biopsy is a valuable aid. Probably a number of patients whose condition has been diagnosed as progressive muscular dystrophy have in fact been suffering from polymyositis. The clinical appearances may be very much alike, both involving progressing paresis and atrophy proximally in the limb muscles, and pseudohypertrophy may develop in the course of polymyositis. This was not pronounced in any of our cases, but a number of the cases reported previously by others have shown clinical signs of pseudohypertrophy. If a muscle biopsy is removed at a late stage of the course, it may—as exemplified by the present study—show an appearance resembling muscular dystrophy. Our material distinctly demonstrates the alteration in the histological picture towards dystrophy the more chronic or "burn-out" the myositis is. In such instances a single muscle biopsy at a late stage of the course will point towards muscular dystrophy, but if the history is not typical of muscular dystrophy, the diagnosis as well as the clinical and biopsy findings should be re-evaluated. In that event, it may be discovered at times that the patient has been suffering from a non-diagnosed myositis. As is evident from the history of Case 9, biopsy from several different muscles may be helpful, as the disease may be in different phases in the different muscles, ranging from active myositis to a burnt-out case having only degenerative changes. It is important, therefore, to obtain muscle biopsy while the disease is in an active phase.

Since so far there is no available treatment of progressive muscular dystrophy, and since steroids are valuable in the treatment of myositis, when administered in the right way, we feel that it is important to differentiate between these two conditions. This may be aided by the

muscle biopsies, but the biopsy findings have to be compared with the clinical appearances, the laboratory findings, and electromyography.

SUMMARY

The literature on the differential diagnosis between progressive muscular dystrophy and polymyositis is briefly reviewed. 9 cases of polymyositis are reported. In all cases the diagnosis had been based on muscle biopsy which was then repeated after intervals ranging from 4 months to 4 years.

Three patients had fairly mild interstitial myositis which was cured, and another two showed only mild degenerative changes at the time of the second biopsy. Three patients showed in the first biopsy panmyositis and in the second severe secondary muscular dystrophy. In the last patient the first biopsy from the biceps showed severe myositis, while the second one, from the hypothenar eminence, showed muscular dystrophy. A third biopsy, from the biceps, again showed myositis, but with a muscular degeneration more pronounced than in the first biopsy.

It is concluded that the more chronic and burnt-out a myositis becomes, the more is the histological appearance apt to resemble muscular dystrophy. Moreover, the changes may be more avanced in one muscle than in another. In a few cases the changes are so marked that even on histological examination a diagnosis of progressive muscular dystrophy will be made if only one biopsy is obtained.

There is little doubt that a number of patients whose condition has been diagnosed as muscular dystrophy are in fact suffering from the sequlae of myositis, all the more so as late stages of chronic polymyositis are clinically very similar to progressive muscular dystrophy. The importance of early muscle biopsy is emphasized, int. al. because polymyositis ought to be treated by steroid medication.

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