

POLYMYOSITIS IN RHEUMATOID ARTHRITIS

BY

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The family of conditions which comprise the polymyositis group have been clarified only in recent years and the syndrome has been extensively reviewed by Walton and Adams (1958), Pearson and Rose (1960), Barwick and Walton (1963), and Pearson (1964). There is now increasing awareness that many cases of polymyositis are to be found in association with diseases of connective tissue. However, the onset of the condition in patients with rheumatoid arthritis, if insidious, may be attributed to simple muscle weakness commonly found in such patients or to a myopathy induced by long-term steroid therapy. If the onset of polymyositis is acute with much systemic upset, the diagnosis may be difficult unless one is familiar with the presenting features of the condition. In order to draw further attention to the association of polymyositis and rheumatoid arthritis, three cases are described below.

Methods

The serum glutamate-oxaloacetate transaminase

(SGOT) and the serum glutamate-pyruvate transaminase (SGPT) were estimated by the methods of Mohan and Cook (1957). The sheep cell agglutination test (SCAT) was performed by the method of Ball (1950). The serum aldolase was measured by the method of Bruns (1954), a modification of the technique of Sibley and Lehninger (1949). The serum creatine kinase was estimated using a commercial kit from Biochemica Boehringer. The upper limits of normal for aldolase and creatine kinase were 10 units and 0.72 units per ml. respectively.

Mean Potential Duration (MPD) was estimated by the technique of Coomes (1965), based on the work of Buchthal and Clemmesen (1941). Briefly this consisted of inserting a concentric needle electrode into the deltoid muscle. The action potentials obtained on minimal volition were displayed electromyographically, under standardized conditions, and photographed. MPD was the mean of the durations of twenty or more such potentials and the reproducibility of successive estimations was up to 8 per cent. The normal range was defined by examining 33 control subjects from a wide age spectrum none of whom had any evidence of muscle disease (Fig. 1).

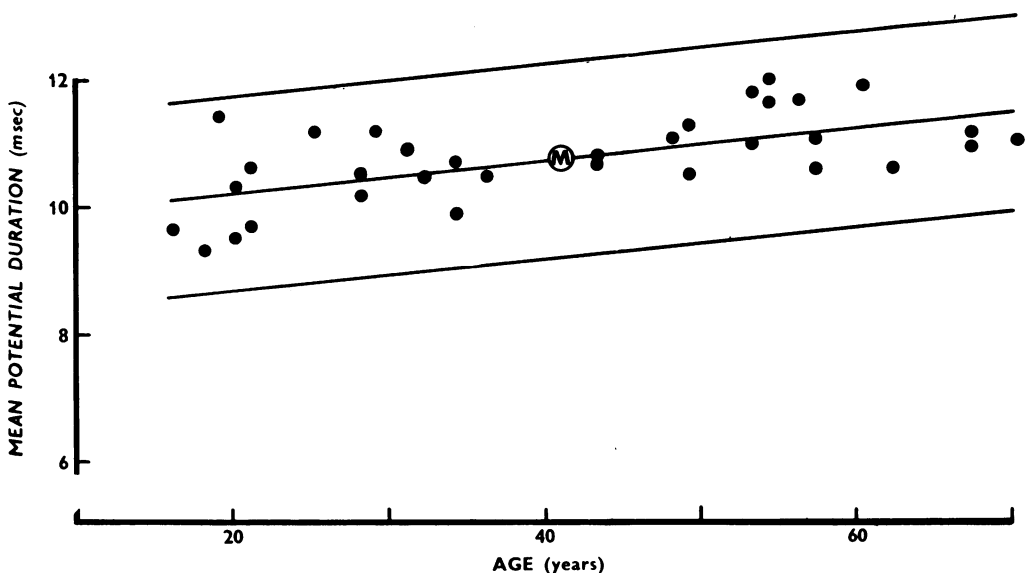


Fig. 1.—Mean potential duration (deltoid) by age in 33 normal persons. Equation of regression line: $MPD \text{ (m.sec.)} = 9.701 + 0.026 \text{ years of age}$. Outer lines are 99 per cent. fiducial limits of deviation from regression (width 1.55 m.sec.). M = group mean.

Since MPD increases with age, individual readings had to be standardized to allow comparison of one patient with another. The standard age chosen was 50 years with an MPD of 11.0 msec. If the slope of the normal regression line is known, it is a simple matter to adjust the readings to 50 years (Fig. 2). For greater clarity in illustration the values have been depicted as percentages of the normal mean at 50 years (Fig. 3, opposite).

Case Reports

Case 1, a 63-year-old woman, developed a polyarthritis in 1950. The disease steadily progressed but she had no treatment other than aspirin. In 1963, one year before she came under observation, she developed weakness of the arms, trunk, and legs. Walking became very difficult and she had fallen many times.

Examination.—There were changes typical of advanced rheumatoid arthritis in many of the peripheral joints. The muscles of the shoulder and pelvic girdles were severely and those of the neck and back muscles moderately wasted and weak. There was also peri-articular weakness and wasting of the muscles of the hands. The patient was unable to rise unaided from a lying position. She walked only with assistance and had a waddling gait of myopathic type. Other features of note were a moderate-sized nodular goitre and conjunctival injection associated with defective lacrimal secretion, the Schirmer test being strongly positive.

Investigations (on admission).—Erythrocyte sedimentation rate 117 mm./hr (Westergren). Serum albumin

3.0 g./100 ml.; serum globulin 5.1 g./100 ml. Electrophoresis showed an increase in gamma globulin. SGO 8.5 units; SGPT 10 units; serum aldolase 6.8 units serum creatine kinase 0.56 units; SCAT positive (1:2048); L.E. cells not seen; anti-nuclear factor strongly positive; serum protein-bound iodine 4.0 g./100 ml. radio-iodine uptake 26 per cent in 2 hours.

The electromyogram (right deltoid) showed fibrillation present at rest with spontaneous high frequency discharges. Volitional pattern was composed almost entirely of low-amplitude short-duration polyphasic potentials. The MPD was 6.6 msec. which is within the myopathic range (normal for age 9.7 to 12.7).

Muscle biopsy (left deltoid) showed severe diffuse infiltration between muscle fibres by plasma cells and lymphocytes with some lymphoid follicle formation.

Treatment and Progress.—The patient was started on a programme of partial rest in bed and exercises with splintage for the hands and wrists. Prednisolone 15 mg. daily was given. There was a slow improvement. After several weeks she was walking unaided although rather unsteadily. A dorso-lumbar corset was provided and this has been invaluable in supporting the weakened back muscles. At present she requires help in rising from bed and in applying the corset; otherwise she is independent of others. Serial estimations of the MPD (right deltoid) (Fig. 3) showed an improvement in the third month after commencing treatment but the last reading almost 6 months from the start of steroid therapy is still well below the normal range.

Comment.—This patient had advanced rheumatoid arthritis and chronic polymyositis. Normal serum enzyme levels contrasted with severe abnormalities in the

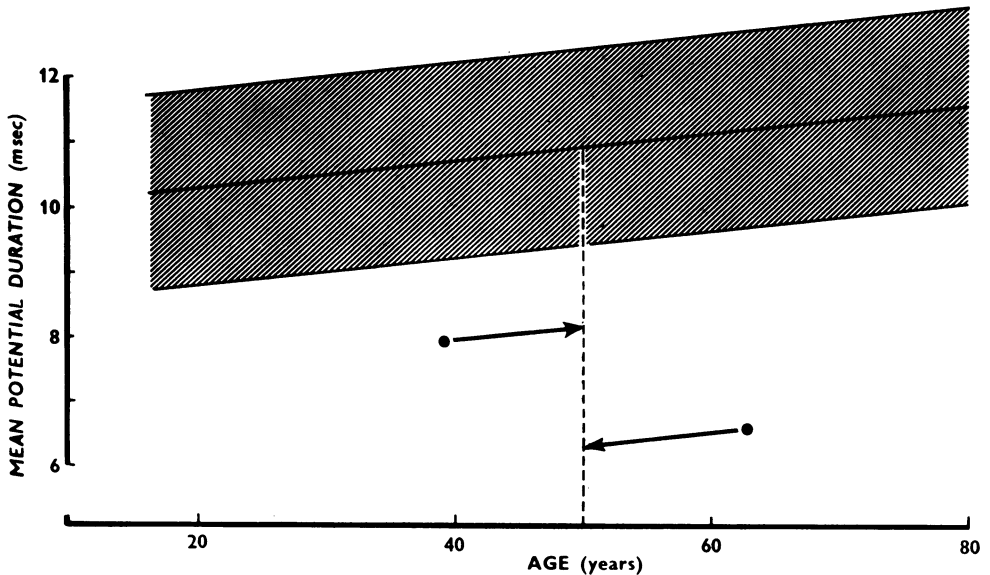
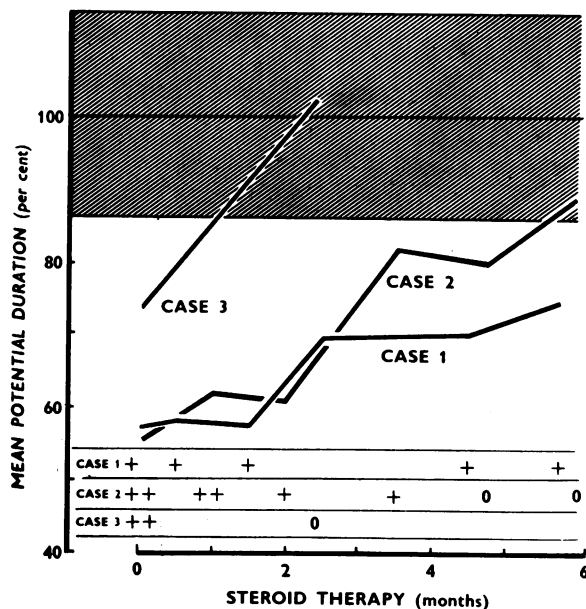


Fig. 2.—Standardization of individual readings to 50 years.

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Fig. 3.—Serial estimations of mean potential duration and fibrillation potentials correlated with duration of steroid therapy. Values for MPD standardized to 50 years and expressed as percentages of the normal mean at that age.



electromyogram and muscle biopsy. Recovery of muscle function has been modest because of the severity of the myositis.

Case 2, a 56-year-old woman, had developed stiffness and weakness of the neck one year previously, and this was followed by weakness of the shoulders, arms, and legs. For 4 months she also had been having pains in many of the peripheral joints and during this period she had deteriorated rapidly. Weakness of the arms and legs had become profound with the result that she spent most of the day in bed. Raynaud's phenomenon had been present for 25 years.

Examination.—There was early active arthritis of the hands, wrist and knees. All the muscles were wasted and weak especially the proximal muscle groups. She was unable to lift the arms above shoulder level and could not raise the extended leg off the bed. There was a dorsal kyphosis and the head was held up with difficulty. Schirmer's test of lacrimal function was negative.

Investigations (on admission):—Erythrocyte sedimentation rate 32 mm./hr (Westergren); serum albumin 2.9 g./100 ml.; serum globulin 3.3 g./100 ml. Electrophoresis showed a small increase in the alpha-2 and gamma globulins. SCAT positive (1 : 512); L.E. cells not seen; anti-nuclear factor negative.

The electromyogram (right deltoid) showed numerous fibrillation potentials at rest; the vast majority of the motor units were polyphasic and of low amplitude. MPD 6.6 msec. (normal for age 9.6 to 12.6).

Muscle biopsy (left deltoid) showed severe diffuse non-

specific chronic inflammatory cell infiltration with occasional focal collections of lymphocytes and degeneration and atrophy of muscle cells.

Radiographs showed early erosive changes in the hands and erosions and sclerosis of the sacro-iliac joints.

Treatment and Progress.—She was treated with a standard programme of conservative treatment for the arthritis. A cardboard collar was applied to stabilize the head as initially she was thought to be suffering from atlanto-axial subluxation. Prednisolone 15 mg. daily was commenced and she was mobilized as soon as muscle power had started to improve.

The improvement was steady, the change in the posture and muscle power was striking, and eventually the latter was restored to a level acceptable as normal for a woman of her age and build.

Serial MPD studies showed a substantial improvement after 3 months of treatment and after 6 months the reading had reached the lower limit of normal (Fig. 3).

Comment.—This patient had early rheumatoid arthritis preceded by severe polymyositis. A feature was the presence of sacro-iliac joint changes of a degree unusual in rheumatoid disease. One of the main points of interest was the profound weakness of the neck muscles which allowed the head to fall forwards giving the appearance of severe atlanto-axial subluxation.

Case 3, a 39-year-old woman, had a history of severe polyarthritis of 18 years' duration. In 1951, an arthrodesis of the left knee was performed and 6 months later

a Judet prosthesis was inserted into the left hip. Steroid therapy was started during the same year. In 1956 a prosthesis was inserted into the right hip, but the following year the prosthesis in the left hip broke and was removed. She remained ambulant until September, 1964, when she became acutely ill with fever, sore throat, and generalized aching. The muscles were painful and tender and she had dysphagia for solids. She came under observation of our department in April, 1965, at which time she was taking 12 mg. prednisolone daily.

Examination.—She was thin and febrile. There were no signs of hypercorticism. Many joints showed rheumatoid changes and were much limited in movement. The trunk, neck, and limb muscles were severely wasted and weak. She could not lift her head off the pillow nor raise the extended leg off the bed. The thyroid gland was symmetrically enlarged. Schirmer's test of lacrimal function was negative.

Investigation.—Erythrocyte sedimentation rate 30 mm./hr (Westergren). Serum albumin 2.8 g./100 ml. serum globulin 2.7 g./100 ml.; SGOT 10 units; SGPT 11 units; serum aldolase 21.5 units; serum creatine kinase 2.25 units; SCAT positive (512); L.E. cells not seen; anti-nuclear factor negative. Serum protein-bound iodine 4.4 g./100 ml., radio-iodine uptake 22 per cent. at 2 hours. Tanned cell agglutinating antithyroglobulin titre positive (1 in 10³).

The electromyogram (right deltoid) showed fibrillation at rest with many polyphasic low amplitude motor units on volition. The MPD was 7.9 msec. (normal for age 9.2 to 12.2).

Muscle biopsy (left deltoid) showed focal interstitial chronic inflammatory cell infiltration mainly situated perivascularly. Occasional muscle fibres showed vacuolar or granular degeneration with macrophagic reaction.

Treatment and Progress.—The dose of prednisolone was increased until the patient was afebrile and the Erythrocyte Sedimentation Rate normal, which did not occur until she was taking 150 mg. daily. Over the next 2 months there was a gradual improvement in the power of the trunk, neck, and arm muscles. Unfortunately, several weeks after admission she developed extensive deep vein thrombosis in the legs with gross oedema and these did not resolve despite anticoagulant therapy. The lower limbs remain almost powerless because of the combination of joint immobility, severe oedema, and muscle wasting. Serial electromyogram studies were not considered advisable owing to the institution of anticoagulant therapy, although two MPD readings were obtained, the first just before she was started on anticoagulants and the second 11 weeks later, immediately after the anticoagulants were discontinued. Fig. 3 shows that the second reading had returned to the normal range. Serial serum enzyme estimations performed while anticoagulants were being taken showed a steady fall in values when the dose of prednisolone was raised sufficiently (Fig. 4).

Comment.—This patient with advanced rheumatoid arthritis developed acute polymyositis while on steroid

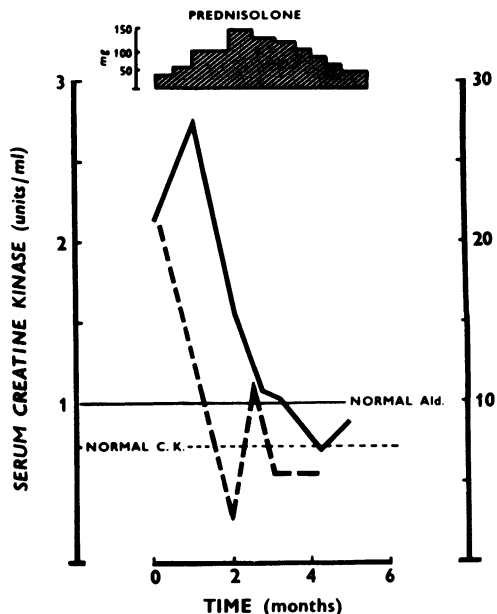


Fig. 4.—Serial serum enzyme estimations in Case 3, showing return to normal range when prednisolone dosage was sufficiently raised

therapy. Partly because of established deformities and partly because of the development of deep vein thrombosis the patient has not yet become ambulant. Serial enzyme studies have shown the effect of steroid therapy in adequate dosage on the myositis.

Discussion

The association of inflammatory polyarthritis and polymyositis has been described by several authors. Most of these studies do not distinguish between polymyositis with and without skin involvement when discussing articular manifestations. Eaton (1954) reported joint symptoms in twelve of 40 patients. Walton and Adams (1958), in a series of forty patients, described similar features in ten, five of whom were considered to have rheumatoid arthritis. Barwick and Walton (1963) had twelve patients with articular symptoms in a series of 50 with polymyositis. Pearson (1959) described 10 further eight patients with joint symptoms in a series of seventeen; five of these eight patients had no skin involvement, and one of the five had intermittent symptoms and signs of rheumatoid arthritis for several years before the onset of muscle weakness, whereas the other four developed rheumatic symptoms after the insidious development of muscle weakness. Lastly, Pearson (1964), in a further

review of the polymyositis group of conditions, stated that symptoms and signs of joint involvement occurred in one-third to one-half of all cases, but that residual articular deformities had been seen in only two patients of his series.

The three patients described in the present study had undoubted erosive rheumatoid arthritis, and the particular interest of the physician involved must predetermine in large part the type of case seen. That polymyositis may precede or follow the development of rheumatoid arthritis is clear from this and previous work.

The first patient draws attention to the important point that polymyositis may develop insidiously in a patient who already has weakness of the limbs due to advanced rheumatoid disease. Accordingly, polymyositis should be borne in mind when a patient with rheumatoid arthritis deteriorates without evidence of increase of disease activity in the joints. Case 1 also had an incomplete Sjogren's syndrome, and it may be noted that Bunim (1961), in a comprehensive review of the syndrome, described four cases associated with myopathy; Pearson (1964), in his series of patients with polymyositis observed two similar cases.

Considerable improvement in muscle function in polymyositis as a result of steroid therapy has been reported by many workers, notably Walton and Adams (1958), Eaton (1954), van Bogaert, Radermecker, Löwenthal, and Ketelaer (1955), Shy and McEachern (1951), Barwick and Walton (1963), and Pearson (1964). We have also been impressed by the effectiveness of steroids, but would stress that a very high dosage may be required initially to suppress the inflammatory process in the muscles—as in our third patient. The severity of muscle damage before treatment is started must predetermine the final result. This is further complicated in patients such as ours by the degree of joint disability. Whereas Case 2 has virtually returned to pre-disease functional capacity, Case 1, because of widespread irreversible muscle changes, has improved only moderately, and Case 3, who has regained normal muscle power in the upper limbs, has not yet become ambulant because of severe joint disease, muscle wasting, and a complicating deep venous thrombosis in the legs.

Pearson (1964) stressed the value of serial enzyme estimations, particularly of serum aldolase, in assessing recovery, and the results obtained in our Case 3 confirms his findings. Coomes (1965) has followed up patients with steroid and metabolic myopathies using serial MPD determinations to show the rate of recovery, and has demonstrated the usefulness of this parameter to assess muscle power

in the presence of widespread joint disease. Another point brought out in this investigation is the gradual diminution of fibrillation potentials as the disease came under control, especially in Cases 2 and 3.

Patients with rheumatoid arthritis and profound iatrogenic hypercorticism (Coomes, 1965) had certain features in common with the present group—namely widespread joint disease and muscle weakness. Clinically, it is the presence of advanced hypercorticism which distinguishes steroid myopathy from polymyositis. Case 3 illustrates this point well. On the other hand, electromyogram studies can differentiate these two conditions. In our opinion electromyogram studies are of great value in the investigation and diagnosis of muscle weakness associated with rheumatoid disease. Therapeutically, the management of steroid myopathy and polymyositis are diametrically opposed: in the former, steroid dosage must be reduced to control the hypercorticism; in the latter, steroid dosage must be increased—sometimes substantially. Particular care has been taken to prevent the development of severe prolonged hypercorticism in the patients described in this study as this could only reverse the beneficial effects obtained.

Summary

Three patients with polymyositis and rheumatoid arthritis have been reported and the literature relating to the association of the two conditions has been reviewed. The beneficial effects of steroid therapy on the myositis are described and the value of serial electromyographic studies, particularly determinations of the mean potential duration have been shown in two patients. In the third patient serial enzyme estimations were carried out and recovery was seen to occur as the serum enzyme levels fell. Lastly, the importance is stressed of differentiating between steroid myopathy and polymyositis developing in patients with rheumatoid arthritis.

We wish to thank Prof. J. H. Kellgren for permission to publish case reports of these three patients, all of whom were under his care, and we are grateful to him for advice in the preparation of this paper. Our thanks are due to the Biochemistry Department, in particular to Miss Venize Hewitt, for carrying out the serum enzyme estimations, and to the Department of Medical Illustration for technical assistance.

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La polymyosite dans l'arthrite rhumatismale

RÉSUMÉ

On rapporte sur trois malades atteints de polymyosite et d'arthrite rhumatismale et on passe en revue la littérature

concernant l'association de ces deux affections. On décrit les effets favorables de la thérapie stéroïde sur la myosite et on montre la valeur des études électromyographiques en série et surtout des déterminations de la durée moyenne du potentiel chez deux malades. Chez le troisième malade on a titré régulièrement les enzymes et on a noté son rétablissement lors de la chute du niveau des enzymes sériques. Finalement, on souligne qu'il est important de différencier entre la myopathie stéroïde et la polymyosite survenant chez des malades atteints d'arthrite rhumatismale.

La polimiositis en la arteritis reumatoide

SUMARIO

Se relatan los casos de tres enfermos con polimiositis con artritis reumatoide y se pasa revista a la literatura respecto a la asociacion de estas dos condiciones. Se describen los efectos favorables de la terapia esteroides sobre la miositis y se muestra el valor de los estudios electromiograficos seriados y, particularmente, de las determinaciones de la duracion media del potencial en dos enfermos. En el tercer enfermo se hicieron estimaciones seriadas de las encimas y se notó su restablecimiento al bajar el nivel de las encimas séricas. Finalmente, se subraya la importancia de diferenciar entre la miopatía esteroide y la polimiositis en enfermos con artritis reumatoide.