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Drug treatment of juvenile dermatomyositis

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SUMMARY A series of 29 children with dermatomyositis has been reviewed and the outcome compared between cases treated by us initially with a low dosage short duration course of corticosteroids, and those referred late and having had various different therapeutic regimens and usually more active and higher dosage drug schedules. There were fewer relapses and less morbidity in the low dosage short term group. It was noted also that there was no relation between the initial mode of onset or severity and the eventual outcome or course of the disease. However, pronounced skin vasculitis appeared to reflect severity of disease.

The clinical features and diagnosis of juvenile dermatomyositis have been described,[1–4] and it is generally accepted that corticosteroid therapy has reduced the morbidity and mortality of the disease[5–7] and that with current treatment techniques the prognosis for life and physical function is favourable.[8 9] There is, however, still inconsistency in the recommendations for treatment as regards the amount and duration of treatment with drugs, and the view is often still held that a high dosage of corticosteroids is more effective than a low dosage and that it is particularly necessary in the more severe cases.

The efficacy of moderate dose steroids used for a short period has been reported previously[10] and it was recommended that a moderate daily dose of prednisolone of about 1 to 1·5 mg/kg a day should be used and as soon as clinical improvement started, generally within 2 weeks, the dosage should be reduced gradually by about 2·5 mg a week. Should any symptoms of regression occur, the previous week's dose should be maintained for a further week. The dose should be sufficient to suppress the disease and, if not effective, further gradual increases may be needed. An improvement is gauged by an increase in muscle strength and general wellbeing.[2 11] Serum enzymes and erythrocyte sedimentation rate can be unreliable when monitoring the disease.[10] They can be normal in the presence of acute and severe disease and, in addition, the resolution of an increased level of creatine phosphokinase may trail behind clinical improvement.

We have found that once lower doses of prednisolone are reached the chance of relapse is less if the dosage is tapered slowly. For example, when a dose of 10 mg/24 hours is reached the prednisolone is then reduced by 1 mg each week, and on reaching 5 mg/24 hours the dose is then reduced by 1 mg on alternate days for one week—that is 5/4 mg for a week, then 4 mg/24 hours for one week, and so on. This regimen does not necessarily need to be slavishly followed and should be flexible. It reflects the need for a gradual but steady tapering of dose allied to close clinical monitoring of the patient so that the schedule can be tailored individually to the course.

We have been able to compare children treated in this way with others whose management has differed and in most of whom treatment had already started before referral to our muscle clinic.

Patients and details of management

Patients were divided into two groups. Group 1 were those referred to us in the acute phase before drug treatment was started and managed exclusively by us (Table 1), and group 2 were those already established on drug treatment before referral (Table 2). Patients in group 2 were subdivided further according to whether they had been referred during the acute phase of the illness (Cases 12–15, Table 2) or later (Cases 16–29).

No clear underlying aetiology was established in any patient except for two who were atypical. One, a boy (Case 10, Table 1), had developed polymyositis as a presumptive chronic graft-versus-host reaction 8 months after successful marrow transplant for acute lymphoblastic leukaemia. The other,

a girl (Case 14, Table 2), had had discoid lupus for the previous 7 years and the lupus rash was active at the time the polymyositis developed.

In group 1 prednisolone was given to all patients, except one (Case 11) who had predominantly skin manifestations and only minimal muscle weakness. All those referred to us late were or had been on steroids.

Tables 1 and 2 summarise the initial presenting features, details of steroid management, and outcome in the two groups. In group 1, initial severity of disease was such that before treatment was started four were initially confined to bed, five had dysphagia, one definite hoarseness, one pulmonary infiltration, and two contractures. Although reporting was probably incomplete in group 2, two initially were confined to bed, three had dysphagia, one arthritis, two ulcers, three contractures, one hoarseness, and one (Case 19) unusual patient presented with ulcerating subcutaneous calcification and only minimal restriction of mobility.

There were some striking differences in details of treatment with prednisolone between the two groups. In group 1 the initial induction dose of prednisolone was 1 mg/kg a day in all cases and the disease was successfully suppressed in all. The dose was reduced once clinical improvement occurred, which was between 1 and 2 weeks in all of them, and the rate of reduction ranged from 1 to 2·5 mg/week in all but one (Case 9) patient. This patient presented some unusual features and difficulties and needed a more prolonged and somewhat different course of management. Relapses were treated with an increase in prednisolone dose adequate to suppress the symptoms and then a gradual reduction again. Seven patients in this group were off treatment within 6 to 9 months.

In group 2 the induction dose was generally higher, ranging from 1 to 3 mg/kg a day, and usually given for a longer period ranging from 1 to 15 weeks. Fourteen patients in group 2 were given some form of prolonged maintenance treatment with prednisolone, either daily or on alternate days, and total time on treatment was much longer, ranging from 12 to 84 months.

Additional immunosuppressant therapy as an adjunct to prednisolone was given to only one patient (Case 9) in group 1. In group 2, nine of the 18 patients were treated with immunosuppressants, azathioprine alone in seven, azathioprine with chlorambucil in one, and cyclophosphamide alone in the other. Only one (Case 22) received immunosuppressants (azathioprine 1·5 mg/kg a day) from the outset; the others were started from 3 months to 2 years later when relapse occurred. Of the eight

Table 1 *Presentation, steroid management, and outcome for patients treated entirely by us (group 1)*

Case	*Presenting features*	*Time from onset of symptoms to treatment (months)*	*Prednisolone*			*Relapses*	*Total duration prednisolone (months)*	*Maintenance dose*	*Duration of follow-up after treatment (months)*	*Comment*
			Initial dose (mg/kg/a day)	*Duration (weeks)*	*Initial reduction (mg/week)*					
1	R D*	3	1	2	2·5	0	6	—	12	Recovery. Mild calcinosis
2	F	29	1	2	2·5	0	9	—	36	Complete remission
3	R	8	1	2	1	0	9	—	48	Complete remission
4	R D	3	1	2	2·5	0	6	—	48	Complete remission
5	R D H*	6	1	1	2	1	9	—	30	Complete remission
6	R D C	3	1	1	2·5	0	5	—	24	Complete remission
7	L	24	1	1	2·5	1	8	—	66	Remission. Mild calcinosis
8	D*	2	1	2	2·5	1	8	—		Still on low dose steroids
9	R A*	1	1	1	10	1	12	+		Died. Intestinal haemorrhage
10	C	1	1	2	2·5	1	7	—		Died. Leukaemia
11	R	—	—						12	Complete remission

*Virtually confined to bed. R = rash, C = contractures, D = dysphagia, A = joint pains, H = hoarseness, F = fatiguability and emotional lability, L = pulmonary infiltration on chest x-ray film.

Table 2 *Presentation, steroid management, and outcome for patients referred to us (group 2)*

Case	*Presenting features*	*Time from onset of symptoms to treatment (months)*	*Prednisolone*			*Relapses*	*Total duration prednisolone (months)*	*Maintenance dose*	*Duration of follow-up after treatment (months)*	*Comment*
			Initial dose (mg/kg/a day)	*Duration (weeks)*	*Initial reduction (mg/week)*					
12	R D C	6	2	4	2·5	4	50	+		On steroids. Fair mobility
13	R	1	1	6	1·5	2	12			On steroids
14	C Lupus	2	1·5	2	5	2	8			On steroids
15	R D	2	1·4	3	2	3	45			Fair mobility. On steroids
16	R	6	1·3	1	6–7	3	54	+	24	Disease inactive. Calcinosis and C
17	R U A	1	2	6	12	4	18	+	48	A and calcinosis
18	R U	9	1·75	2	2·5	4	18	+	40	Good mobility. Calcinosis and C
19	Calcinosis	48	1	2	0·25	1	18	+	30	Poor mobility. Calcinosis and C
20	R	8	1·6	2	4–5	5	48	+	65	Recovered. Skin vasculitis
21	R	5	2·5	3	?	2	84	+	—	C. Poor mobility
22	R	7	2	4	5	2	36	+	12	Calcinosis and C. Poor mobility
23	R *	12	2	6	6	3	60	+	18	Recovered. Mild calcinosis
24	R	3	1·6	2	4	4	60	+	24	Recovered. Calcinosis
25	R H	2	1·3	15	5	3	98	+		On steroids. Poor mobility
26	R	4	3	1	15	1	24	+	24	Complete remission
27	R C	6	2	?	3	5	36	+	—	Poor mobility. C
28	R D	6	2·5	4	10	2	12	+	—	Recovered. C
29	R *	1	3	2	10	2	12		—	Died. Duodenal perforation

*Confined to bed. R=rash, C=contractures, D=dysphagia, A=joint pains, U=ulcers, H=hoarseness, Lupus= discoid lupus.

patients who received azathioprine, the drug was introduced by us in five, mainly in an attempt to taper the longstanding prednisolone treatment they were on. The starting dose of azathioprine was 2 mg/kg a day but in two patients (Cases 15 and 28) we increased the dose to 4 mg/kg a day in an attempt to suppress disease.

Results

Group 1. Of the ten treated patients in group 1, six made uncomplicated recoveries. One (Case 5) had a mild relapse while steroids were being withdrawn which was treated with a temporary increase in dose. The seventh patient had a more complicated illness with a relapse 6 months after he had successfully stopped steroids necessitating a second course of treatment. His total time on steroids was 8 months. His illness was complicated by respiratory involvement, sclerodermatous skin changes, joint contractures, and mild calcinosis. One other patient (Case 1) developed mild calcinosis 5 months after the steroids had been stopped.

Of the remaining three patients, one (Case 8) is still on steroids which are being tailed off. The other two (Cases 9 and 10) died, both being somewhat atypical. Case 9 presented with very severe general symptoms, was extremely 'toxaemic' and bed-bound, and had a generalised muscle weakness and marked tenderness to touch. He responded strikingly to prednisolone within 2 days and it was considered reasonable to reduce the dose from 50 mg by 5 mg decrements at half-weekly intervals to 40 mg, and after a further week to 35 mg. He relapsed after that and subsequently had extensive vasculitis affecting the skin as well as the bowel with multiple ulcers and recurrent haemorrhage. He was unresponsive to plasma exchanges and intravenous cyclophosphamide but responded temporarily to high dosage (2mg/kg) prednisolone and during one crisis to additional treatment with intravenous infusion of hydrocortisone. He died at home some 12 months later of gastrointestinal haemorrhage complicated by an Addisonian crisis and pneumonia. Case 10, whose polymyositis was a manifestation of graft-versus-host disease after bone marrow transplant, was recovering from his polymyositis when he developed a large mediastinal mass, possibly due to reactivation of leukaemia.

Group 2. All four patients (Cases 12–15) referred during the acute phase of the illness are still on steroids. One (Case 14) with the discoid lupus relapsed after having been successfully tailed off steroids for 2 months. Case 12 had a high induction dose of prednisolone of 2 mg/kg a day, Case 13 had an induction dose of 1 mg/kg a day but for a long period of 6 weeks, and Case 15 had an induction dose of 1·4 mg/kg a day for 3 weeks. All three managed successfully to reduce the dose to below 10 mg/day and then all relapsed. Cases 12 and 15 reduced the prednisolone in 2·5 mg steps below 10 mg/day and this was probably too rapid a rate and contributed to the relapse.

Of the remaining 14 patients, 11 were still on steroids at the time of referral and difficulty with drug management had been a specific problem in all. We managed to stop the drug successfully in all but one (Case 25) patient. The other three were already off steroids at the time of referral. Case 24 had stopped shortly before and had just relapsed. The other two (Cases 19 and 27) had been off for some time and their main problem was a need for rehabilitation; Case 19 had severe foot deformity, limited mobility, and extensive calcinosis, and Case 27 was virtually confined to a wheelchair with severe hip and knee contractures.

Only one patient (Case 26) in group 2 made an uncomplicated recovery. She was on prednisolone for 2 years. The five (Cases 12–15 and Case 25) still on steroids are mobile but one (Case 25) has extensive calcinosis. Of the remainder most have problems with contractures and calcinosis and in four (Cases 19, 21, 22, and 27) mobility is very limited as a result.

Case 17 has some residual arthritis and mild calcinosis but reasonable mobility. Case 18 has extensive subcutaneous calcinosis with numerous discharging sinuses but is mobile. Case 20 has residual skin vasculitis but is otherwise fairly mobile. Case 23 has troublesome calcinosis but good mobility. Case 24 has problems with contractures which have improved with active physiotherapy. Case 28 came from abroad and was seen only once and painful joint contractures were one of her major difficulties.

The therapeutic value of azathioprine was difficult to assess. Use of azathioprine from the start in Case 22 did not prevent relapse. She was maintained on daily steroids over a 9-month period reducing from an induction dose of 2 to 0·5 mg/kg a day and then changed over to alternate-day steroids (0·5 mg/kg on alternate-days). She relapsed at this point and lost the ability to walk. In the others, three (Cases 12, 15, and 25) of the five patients were started on azathioprine 12 months, 6 months, and 2 years after starting steroids and are still on steroids 38, 39, and 24 months later. Case 14 was started on azathioprine during her second relapse and is now reducing her steroids successfully. Case 18 was given azathioprine one year after starting steroids and was able to stop steroids 6 months later.

No serious complications such as bone marrow suppression or hepatic toxicity were seen with the use of azathioprine. Increased susceptibility to infection may have occurred. Case 12 had an extensive and persistent perianal abscess due to anaerobic organisms aggravated by delay in surgical treatment in her own country. Case 25 had a severe and intractable cellulitis of the thigh in association with a sinus discharging calcium.

Discussion

Juvenile dermatomyositis has a characteristic clinical presentation but the onset, course, and duration may vary in relation to severity of disease and duration. Spontaneous exacerbations and remissions are well known to occur and without specific treatment about one-third of children were estimated to recover, usually within one year of onset, but death occurred in a further one-third, generally within the first 2 years, and significant morbidity in the remaining one-third from muscle atrophy, contractures, and calcinosis.[12] Before the widespread use of treatment with corticosteroids there was a significant mortality and morbidity.[13]

Although the use of steroids is undoubtedly beneficial, there is always a risk inherent in chronic steroid administration, and of the many secondary complications that of steroid myopathy may make interpretation of weakness difficult. It is also possible that the risk of steroid-induced gastrointestinal ulceration and perforation may be greater in dermatomyositis,[14] even though gastrointestinal involvement was already documented before the use of steroids. It would therefore seem prudent to use the lowest dose of steroid which produces a good response and to reduce this dose and stop it when it is no longer necessary. However, several recent publications still advocate either high dose steroids or a prolonged maintenance dose.[4 15 16]

Comparison of the two groups of patients in this present series shows striking differences in the drug treatment and the final outcome. Those in group 1 had a lower induction dose of prednisolone which was reduced sooner and yet more gradually. The result was that total time spent on steroids was shorter. Six of the 10 patients in group 1 made an uncomplicated recovery and have now remained off prednisolone for at least a year, while only one of the 18 patients in group 2 did as well. Of the 12 in group 2 who have now stopped steroids there have been more serious problems with calcinosis and contractures and four are severely incapacitated and have little mobility.

It may be argued that this series may be biased as those who were referred late were perhaps selectively referred because of difficulties in their course or management. However, looking back on the case histories of the patients on the high dosage regimens who did badly, there did not seem to be any difference in clinical severity, initial response, or the presence of complications such as bulbar, respiratory, or myocardial involvement in comparison with the series which we treated *ab initio*.

Our present data certainly suggest that the method of management with prednisolone may be critical in determining final outcome. Use of a high induction dose (greater than 1 mg/kg a day) and maintaining it beyond the time that remission has started to occur will inevitably lead to a more prolonged course of treatment. This in itself may induce a certain chronicity in the disease and lead to development of complications such as severe weakness, contractures, calcinosis, and vasculitis apart from the usual side effects of steroid therapy. Calcinosis in particular is thought to relate to the duration of the disease[17 18] but may perhaps be induced or aggravated by long-term steroid therapy.

Once remission is induced prednisolone should be reduced gradually but steadily. Too rapid reduction may precipitate relapse which can be difficult to control. It is also important that relapses are supported with an adequate but temporary increase in prednisolone, as failure to do so may lead to a progressively downhill course.

Fatal gastrointestinal complications seen in this series probably related both to the steroids and the disease. Similar fatalities have been reported by others.[8 16] Severe spinal osteoporosis is probably a specifically steroid-related complication. It occurred in the boy (Case 9) in group 1 while on a very high prednisolone dosage (2 mg/kg a day).

Other immunosuppressive agents had been used in a few patients before referral. This usually reflected difficulty with management. Although their efficacy and steroid-sparing effect has been documented previously,[19 20] we have not been convinced that they have made much difference in individual cases. We have favoured the use of azathioprine as it seems to have the least toxicity, and have used it to achieve a reduction in steroid dosage only if there is steroid dependency or unacceptable steroid toxicity. Our experience with other immunosuppressive drugs—such as cyclophosphamide and methotrexate—is limited.

As in other diseases which affect the neuromuscular system and in which contractures occur, supportive therapy in addition to drug treatment is of major importance to the outcome and an intensive physiotherapy programme should form part of the management in all cases. Our programme has included passive movements when the child is

too ill, miserable, or weak to undertake active movements, followed by active movements as soon as the child is fit enough, and mobilisation as soon as he is able to cope. Our general philosophy has been towards early mobilisation and rehabilitation. In children who feel well enough to remain ambulant in the acute phase we do not recommend any immobilisation at all. Contractures can occur early and even in the acute stage one frequently sees a 20 or 30° limited extension of joints such as elbows. This usually resolves rapidly with the general response to drug therapy and may be further helped by physiotherapy. Once fixed contractures are allowed to occur in the chronic phase of the disease they may result in longstanding disability and prevent the patient walking again even though the power of the muscles has returned sufficiently. This was the case in several of the late referral patients, whose myositis was already burnt out.

References

1 Banker BQ, Victor M. Dermatomyositis (system angiopathy) of childhood. *Medicine (Baltimore)* 1966; **45:** 161–89.

2 Dubowitz V. *Muscle disorders in childhood.* Philadelphia: Saunders, 1978; 202–18.

3 Pachman LM, Cooke N. Juvenile dermatomyositis: a clinical and immunologic study. *J Pediatr* 1980; **96:** 226–34.

4 Malleson P. Juvenile dermatomyositis: a review. *J R Soc Med* 1982; **75:** 33–7.

5 Rose AL. Childhood polymyositis: a follow-up study with special reference to treatment with corticosteroids. *Am J Dis Child* 1974; **127:** 518–22.

6 Sullivan DB, Cassidy JT, Petty RE, Burt A. Prognosis in childhood dermatomyositis. *J Pediatr* 1972; **80:** 555–63.

7 Medzger TA, Jr, Robinson H, Msai AT. Factors affecting survivorship in polymyositis. *Arthritis Rheum* 1971; **14:** 249–58.

8 Coleman WP III, Coleman WP, Derbes VJ, Jolly HW, Jr, Nesbitt LT, Jr. Collagen disease in children: a review of 71 cases. *JAMA* 1977; **237:** 1095–100.

9 Chalmers A, Sayson R, Walters K. Juvenile dermatomyositis: medical, social, and economic status in adulthood. *Can Med Assoc J* 1982; **126:** 31–3.

10 Dubowitz V. Treatment of dermatomyositis in childhood. *Arch Dis Child* 1976; **51:** 494–500.

11 Resnick JS, Mammel M, Mundale MO, Kottke FJ. Muscular strength as an index of response to therapy in childhood dermatomyositis. *Arch Phys Med Rehabil* 1981; **62:** 12–9.

12 Bitnum S, Daeschner CW, Jr, Travis LB, Dodge WF, Hopps HC. Dermatomyositis. *J Pediatr* 1964; **64:** 101–31.

13 Wedgewood RJP, Cook CD, Cohen J. Dermatomyositis: report of 26 cases in children with discussion of endocrine therapy in 13. *Pediatrics* 1953; **12:** 447–66.

14 Rowland LP, Clark C, Olarte M. Therapy for dermatomyositis and polymyositis. *Adv Neurol* 1977; **17:** 63–97.
Dis Child 1979; **133:** 386–9.

15 Day RO, Pearson CM. Primary inflammatory muscle diseases. *Compr Ther* 1981; **7:** 22–30.

16 Lell ME, Swendlow ML. Dermatomyositis of childhood. *Pediatr Ann* 1977; **6:** 203–12.

17 Ansell BM. Dermatomyositis and polymyositis. In: Scott JT, ed, *Copeman's textbook of rheumatic diseases.* Edinburgh: Churchill Livingstone, 1978: 926–34.

18 Sewell JR, Liyanance B, Ansell BM. Calcinosis in juvenile dermatomyositis. *Skeletal Radiol* 1978; **3:** 137–43.

19 Metzger AL, Bohan A, Goldberg LS, Bluestone R, Pearson CM. Polymyositis and dermatomyositis: combined methotrexate and corticosteroid therapy. *Ann Intern Med* 1974; **81:** 182–9.

20 Fischer TJ, Rachelefsky GS, Klein RB, Paulus HE, Stiehm ER. Childhood dermatomyositis and polymyositis: treatment with methotrexate and prednisone. *Am J*

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