Letters to the Editor

Interstitial lung disease due to polymyositis or dermatomyositis: Effect of a 6-month course of i.v. pulse cyclophosphamide

Sirs,

Interstitial lung disease (ILD) is a well-recognized manifestation of polymyositis (PM) or dermatomyositis (DM), with a 5% to 65% occurrence rate (1-2). A minority of patients with ILD and PM/DM fail to respond to glucocorticoid therapy (3). In this situation, a few uncontrolled open-label studies found that cyclosporine (4) or cyclophosphamide as oral or intravenous (IV) pulses (5-6) was effective. The objective of the present study was to evaluate the effectiveness of IV pulse cyclophosphamide in the treatment of ILD related to PM/DM in 7 patients with a previous inadequate response to oral high-dose glucocorticoid therapy.

We undertook a retrospective non-randomised, non-blinded study to examine the effectiveness of treatment for 6 months with prednisone (1 mg/kg/d) for at least 1 month tapered to 0.5 mg/kg/d for the next 2 months, then to 0.2 mg/kg/d), and 6 monthly IV cyclophosphamide pulses (15 mg/kg of body weight per pulse). All patients met the criteria for PM/DM developed by Peter and Bohan (7), had evidence of ILD by lung function testing (LFT) and high-resolution computed tomography (HRCT) of the lungs and failed to respond to corticosteroid therapy as the first-line treatment. Five were females, 2 males; mean age at PM/DM onset: 45± 14.6 years (median 37); mean duration of ILD at cyclophosphamide treatment: 3.8 ± 3.5 years (median 4). There were 6 PM/ 1 DM; anti-JO1 was present in 5; anti-PM Scl in 1 and in 2 cases SSA/Ro antibodies were associated with anti-J01. In one case homogenous ANA were present without myositis specific autoantibodies.

To evaluate the ILD, the following data were collected before and after the 6-month treatment period: clinical manifestations, chest radiographs, LFTs, and HRCTwith 1-mm to 1.5-mm slices scored on a 0-to-5 scale for ground-glass attenuation honeycomb septal thickening and reticulation (Kazerooni score) (8). Improvement was the primary end-point and was defined as an at least 10% amelioration (compared to the predicted value) in forced vital capacity (FVC), total pulmonary capacity (TPC), or DLCO, expressed as the percentages of the predicted values. Worsening was defined as an at least 10% deterioration in the same variables. The HRCTscores for fibrosis and inflammation were the secondary end-points. In the overall group of 7 patients, comparisons of pre-treatment and post-treatment LFT results (Table I) showed no statistically significant differences in median DLCO, FVC, or TPC (primary end-point). However, three patients (cases 2, 3, 6) had an at least 10% DLCO improvement after treatment. HRCT scores before and after cyclophosphamide therapy did not differ significantly . The mean ground-glass score decreased from 2.23 to 1.93 and the mean fibrosis score from 1.5 to 1.43. The total score also improved from 3.73 to 3.36. The ground-glass score decreased in 2 of 6 patients (patients 3 and 7).

Table I. Serial lung function test results in cyclophosphamide-treated patients (primary end-point).

	FVC		TPC		DLCO	
Patients	Pre	Post	Pre	Post	Pre	Post
1	71	71	69	59	79	53
2	82	87	66	61	36	68
3	71	67	75	66	63	97
4/1	48	41	43	36	36	44
4/2*	43	46	34	40	36	( ) NA
5	82	55	79	50	70	( ) NA
6	74	94	78	94	63	86
7	47	50	58	67	72	75
Median	71	67	69	61	63	68
Mean	68.8	66.4	66.8	61.8	59.8	63.3
P *value*	< 0.07		<0.34		< 0.69	

FVC: functional vital capacity; TPC: total pulmonary capacity; DLCO: diffusing capacity of the lung for carbon monoxide. Results are expressed as percentages of predicted values. NA: not applicable.
* Patient 4 had 2 six month courses of IVcyclophosphamide.

Overall, LFT results improved in 3 patients (cases 2, 3 and 6) and stabilized in one (case 7). Of these 4 patients, 2 had improvements in their HRCTscores (cases 3 and 7), 1 had no change (case 2), and 1 did not undergo HRCT(case 6). The 4 responders had a significantly shorter mean duration of lung symptoms at cyclophosphamide initiation (0.75 ± 0.29 years), as compared to the 3 non-responders (3.67 ± 1.53) (p = 0.01). Mean follow-up was 4.0 ± 3.9 (median, 3.1 years; range, 9-139 months). One patient died (case 4). Two patients (cases 1 and 5) required permanent oxygen therapy. IV pulse cyclophosphamide therapy was well tolerated, with no serious adverse event.

Identification of predictive factors associated with a response to cyclophosphamide in patients with ILD and PM/DM would be of considerable assistance in selecting patients for cyclophosphamide therapy. Three factors can be considered.

Anti-Jo1 antibody is associated with ILD but does not predict the response to glucocorticoids or immunosuppressants (1, 4, 9). Of our 5 patients with PM and anti-Jo1 antibodies, 3 responded and 1 was stabilized after IV pulse cyclophosphamide therapy.

Amyopathic DM is believed to carry a poor prognosis with a high mortality rate (1). Recent data have highlighted the poor prognosis of ILD in DM versus PM (10).

Finally, in our series, earlier initiation of cyclophosphamide was significantly associated with a response.

These data suggest that early administration of a 6-month course of IV pulse cyclophosphamide in combination with oral high-dose prednisone therapy may be useful in 40% of PM/DM patients with corticosteroid resistant ILD.

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