Dear Editors,

Dermatomyositis (DM) is a chronic inflammatory disease characterized by progressive muscle weakness combined with typical skin lesions. Treatment includes immunosuppressive drugs and intravenous immunoglobulin (IVIG) therapy. However, long-term data reporting on the therapeutic effects of immunosuppressants and IVIG in DM patients are sparse. Weak evidence supports improved muscle strength [1–3] and bettering of dermatological symptoms with IVIGs [4–6].

In the present study, we evaluate data from 15 DM patients treated with immunosuppressants and IVIG and report their long-term follow-up data on muscular and skin symptoms using standardized assessment tools. Investigated parameters include physician’s global assessment for muscle strength (PGAstrength) and skin symptoms (PGAskin), as well as clinical characteristics and biomarkers, which were collected routinely during every patient visit. Serum creatine kinase (CK) was chosen as a surrogate marker of myositis activity. For objective evaluation of skin involvement, the Cutaneous Dermatomyositis Area and Severity Index (CDASI) was used. CDASI scores were calculated in all patients with whole-body images (n = 7) by three independent dermatologists. None of our patients experienced joint involvement [7], hence this was not a subject of the present study.

The final study cohort consisted of eleven patients with classic DM (c-DM, 74 %) and two patients with DM-scleroderma-overlap-syndrome (13 %). These patients showed discrete scleroderma-like skin symptoms in addition to the typical skin lesions of DM. Two additional patients were diagnosed with paraneoplastic DM (13 %). All patients received immunosuppressive and IVIG combination therapy. IVIG was administered at a dosage of 2 g/kg bodyweight given monthly over three consecutive days. The mean number of IVIG cycles per patient was 27.9 (range 1–89). Therapy was well tolerated by all patients, with 62.5 % of patients (n = 12) reporting no adverse events. All patients initially received co-medication with either glucocorticoids (GC; n = 5, 33 %) or glucocorticoids plus immunosuppressive drugs including azathioprine 100 mg (AZA; n = 8, 53 %) and mycophenolate-mofetil 1000–2000 mg (MMF; n = 2, 13 %). The mean GC dose within the first four cycles was 65.8 mg per day (range 5–160). 71.4 % of patients were able to discontinue GC therapy, consistent with earlier studies suggesting that IVIG therapy might help to reduce long-term systemic GC administration [8, 9].

Since one patient with paraneoplastic DM died from his underlying disease after receiving only one course of IVIG, 14 patients were available for assessment at the 4th IVIG cycle. Analyses of muscular symptoms revealed that eleven patients (73.3 %) experienced at least moderate improvement of their muscular strength after only one IVIG cycle (t = 4 weeks). Concomitantly, creatine kinase (CK) levels reached normal values after four treatment cycles (t = 16 weeks) in the majority of patients: Initial mean CK levels were 1,723 U/l before initiation of therapy and decreased to 116 U/l (P = 0.024) after four treatment cycles (Figure 1a). Additionally, muscle strength as measured by PGAstrength recovered.

In contrast to the rapid response of muscular symptoms, skin manifestations were recalcitrant: Four patients (27 %) showed a moderate improvement of their dermatological symptoms after the first cycle. Six patients (40 %) reported no changes and one patient even reported a worsening of symptoms (n = 1; 7 %). After four combined IVIG and immunosuppressive treatment cycles, eight patients (28.6 %) showed at least moderate improvement of their skin lesions. One patient (7.1 %) experienced complete relief and three (21.4 %) showed a marked improvement of the skin manifestations. In 14.3 % skin symptoms were refractory to therapy (Figure 2b, Table 1).

All patients were assessed for long-term efficacy (> 4 cycles). The mean follow-up period was 7.6 years (range 0.8–17.3). IVIG therapy was discontinued in seven patients (50 %). In three patients (21.4 %) IVIG was stopped due to a significant improvement of the disease. Two patients (14.3 %) switched to subcutaneous administration at much lower dosages. In one case IVIG was discontinued due to inefficacy after 25 cycles. Another patient with paraneoplastic DM stopped IVIG due to progressive malignant disease after 10 cycles.

Long-term results indicate that all patients continue to benefit from receiving IVIG after four treatment cycles: Muscular strength increased and dermatological symptoms improved in 85.7 % (n = 6) and 57.1 % (n = 4) of cases at the last follow-up visit, respectively. Dermatological symptoms relapsed throughout the course of the disease (follow-up) in 42.9 % of patients (n = 3) (Figure 2a). However, overall skin lesions improved significantly compared to findings at the time of initial diagnosis: Mean CDASI activity scores (0–100) were 17.4 (range 10.3–25) at diagnosis and decreased to 5.1 at the last follow-up visit (range 0.5–18; P = 0.001) (Figure 1b). The damage score did not change significantly (0–32, Mean diagnosis 2.0, Mean follow-up 1.4; P = 0.536).
Even though our cohort is small, this report highlights the long-term safety and efficacy of combined immunosuppressive and immunomodulatory treatment in DM patients. Since skin manifestations of DM have a major impact on a patient’s quality of life (QoL) [10], therapeutic success must include the evaluation of cutaneous DM symptoms. We used high-quality photos and multi-observer evaluations to calculate robust CDASI scores for an objective assessment of skin lesions, which is a strength of this study. Yet, it must be kept in mind that the CDASI is not validated for retrospective assessment. We demonstrate significant differences in the response patterns of dermatological and muscular symptoms: 73% (n = 11) of patients already experienced a moderate improvement of their muscular strength after the first treatment cycle. In contrast, dermatological symptoms are often refractory to treatment, require long-term treatment, and do not necessarily correlate with the improvement in muscular strength.

**Figure 1** Creatine kinase levels significantly drop after four cycles of combined IVIG and immunosuppressive therapy (a). Box-plot of the CDASI Activity and Damage Score at diagnosis (Baseline) and at the last follow-up (b).

**Figure 2** Spider plot of muscular and dermatological symptoms after IVIG and immunosuppressive therapy (a). Recalcitrant skin manifestations in one representative DM patient (b).
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Table 1 Response patterns of DM patients receiving IVIG and immunosuppressive treatment at cycle 1, cycle 4 and follow-up.

| Response of symptoms       | Muscular strength               | Dermatological symptoms          |
|----------------------------|---------------------------------|----------------------------------|
|                            | Cycle 1 n (%) | Cycle 4 n (%) | Follow-up n (%) | Cycle 1 n (%) | Cycle 4 n (%) | Follow-up n (%) |
| Complete relief            | 1 (6.7)        | 1 (7.2)        | 2 (28.6)        | 0 (0)          | 1 (7.2)        | 1 (14.2)        |
| Marked improvement         | 5 (33.3)       | 8 (57)         | 3 (42.9)        | 0 (0)          | 3 (21.4)       | 0 (0)           |
| Moderate improvement       | 5 (33.3)       | 3 (21.4)       | 1 (14.2)        | 4 (26.7)       | 4 (28.5)       | 3 (42.9)        |
| Slight improvement         | 3 (20)         | 1 (7.2)        | 0 (0)           | 4 (26.7)       | 3 (21.4)       | 0 (0)           |
| No change                  | 1 (6.7)        | 0 (0)          | 0 (0)           | 6 (39.9)       | 2 (14.3)       | 0 (0)           |
| Worsening                  | 0 (0)          | 1 (7.2)        | 1 (14.2)        | 1 (6.7)        | 1 (7.2)        | 3 (42.9)        |
| Total                      | 15 (100)       | 14 (100)       | 7 (100)         | 15 (100)       | 14 (100)       | 7 (100)         |

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