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LETTER TO THE EDITOR

Long-term follow-up in a patient with the dermato-neuro syndrome treated with high-dose melphalan, thalidomide, and intravenous immunoglobulins for more than 7 years

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Dear Editor,

Scleromyxedema (SME), a subtype of lichen myxedematosus, is characterized by a generalized sclerodermoid eruption and a monoclonal gammopathy in the absence of thyroid disease. Mucin deposition, fibroblast proliferation, and fibrosis are seen at skin biopsy [1]. The "dermato-neuro syndrome" (DNS) is a rare manifestation of scleromyxedema and only a few cases have been described. It is characterized by a flu-like prodrome, followed by high fever, tonic-clonic convulsions, and coma in the setting of scleromyxedema [2, 3]. We report a case of DNS successfully treated with high-dose melphalan and autologous stem cell transplantation, followed by thalidomide during 1 year and ongoing monthly administration of intravenous immunoglobulins (IVIg).

In December 2005, a 39-year-old Caucasian man was referred to our institute after developing a subacute neurological deterioration (increased confusion, agitation, and visual hallucinations) while being treated for pneumonia. Prior to transfer, he developed generalized tonic-clonic seizures. During the 9-month period, before, the patient had two similar episodes of subacute encephalopathy progressing to status epilepticus and coma. Both were preceded by a flu-like prodrome. Upon admission, the patient was disoriented, agitated, and had fever. Due to progressive loss of consciousness, urgent sedation and mechanical ventilation were mandatory. Serum protein electrophoresis revealed an IgG kappa monoclonal protein (15.9 g/L). The bone marrow plasmocytosis was low (3, 7 %). Electrophoresis of CSF showed a monoclonal protein [4]. High-dose dexamethasone and plasmapheresis were started and neurological, hemodynamic, and respiratory improvement occurred. After 8 weeks, the patient was able to leave the hospital with mild residual cognitive impairment and an M-protein level of 7 g/L. Ten days after discharge, he again developed a flu-like prodrome followed by high fever, confusion, and tonic-clonic convulsions. The M-protein value peaked to 26 g/L in a few days. As a consequence, a relation between the epileptic insult and the rapid increase of paraprotein was suspected. At that time, an erythematous skin induration with longitudinal furrowing of the glabella (leonine facies) was observed (Fig. 1a). The skin biopsy of the glabella showed typical dermal mucin deposition, fibroblast proliferation, and fibrosis, confirming the histological diagnosis of scleromyxedema (Fig. 1c, d). The combination of the dermatologic manifestations, the presence of a monoclonal gammopathy, and the neurologic manifestations led to the diagnosis of DNS [5, 6].

Dexamethasone was resumed in association with IVIg [7]. In February 2006, CAD mobilization chemotherapy (cyclophosphamide 1,000 mg/m2 on day 1; adriamycine 15 mg/m2 on day 1–4; dexamethasone 40 mg on day 1–4) was administered. Three weeks later, high-dose melphalan (200 mg/m^2) was administrated followed by autologous

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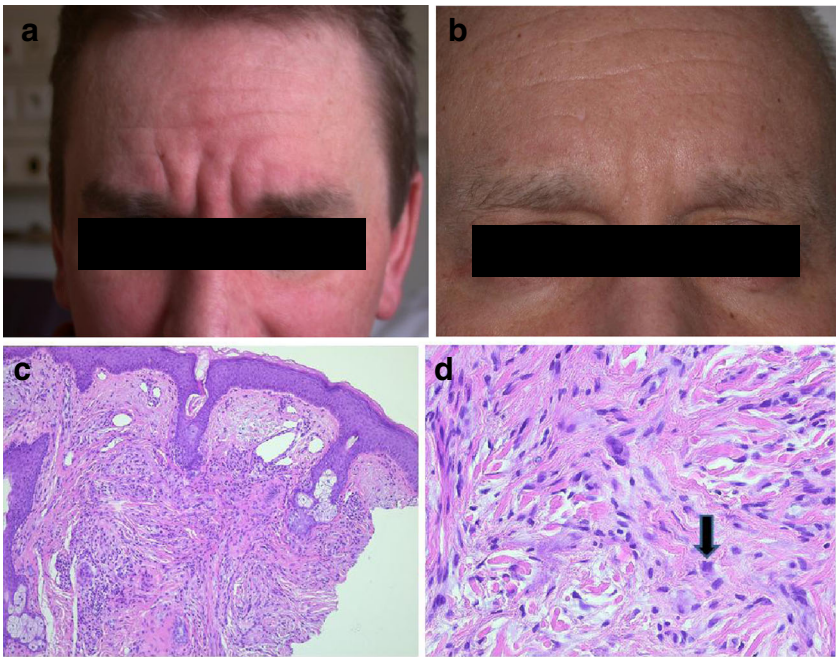

Fig. 1 **a** Skin alterations in the patient with DNS: thickened skin furrows at the glabella at the moment of diagnosis. **b** Disappearance of the deep furrows at 2 months after autologous stem cell transplantation. **c** Skin biopsy revealing scleromyxedema: the upper dermis is lightly stained, due to increased mucin deposition, whereas the reticular dermis shows a marked proliferation of irregularly oriented fibroblasts; a sparse perivascular inflammatory infiltrate is evident. Hematoxylin and eosin staining, original magnification×100. **d** At high power, some of the fibroblasts have a stellate appearance (*arrow*). Haematoxylin and eosin, original magnification×200

stem cell infusion [8]. During the course of transplantation, the patient again developed neurological deterioration, which improved after starting plasmapheresis. Thalidomide 200 mg/d was started at day 14 after transplantation and continued for 12 months in association with low-dose methylprednisolone and monthly administration of IVIg (0.5 g/kg).

During the following years, the patient's condition improved, including substantial recovery of cognitive functions, documented by serial neuropsychological testing. At 7 years post-autologous stem cell transplantation, a complete resolution of cutaneous symptoms is seen (Fig. 1b), no new episodes of encephalopathy or epileptic insults occurred ever since. The paraprotein still remains detectable at very low levels and is stable. Monthly administration of IVIg has never been interrupted.

Conflict of interest The authors declare that they have no conflict of interest.

References

1. Rongioletti F, Rebora A (2001) Updated classification of papular mucinosis, lichen myxedematosus, and scleromyxedema. J Am Acad Dermatol 44:273–281
2. River Y, Levy I, Gilead L et al (1996) Fever, convulsions and coma in scleromyxedema: a "dermato-neuro syndrome". Neurology 46:1778–1779
3. Fleming KE, Virmani D, Sutton E et al (2012) Scleromyxedema and the dermato-neuro syndrome: case report and review of the literature. J Cutan Pathol 39:508–517
4. Johkura K, Susuki K, Hasegawa O et al (1999) Encephalopathy in scleromyxedema. Neurology 53:1138–1140
5. Webster GF, Matsuoka LY, Burchmore D (1993) The association of potentially lethal neurologic syndromes with scleromyxedema (papular mucinosis). J Am Acad Dermatol 28:105–108
6. Berger JR, Dobbs MR, Terhune MH et al (2001) The neurologic complications of scleromyxedema. Medicine 80:313–319
7. Lister RK, Jolles S, Whittaker S et al (2000) Scleromyxedema: response to high-dose intravenous immunoglobulin (hdIVIg). J Am Acad Dermatol 43:403–408
8. Donato ML, Feasel AM, Weber DM, Prieto VG, Giralt S, Champlin RE et al (2006) Scleromyxedema: role of high-dose melphalan with autologous stem cell transplantation. Blood 107:463–466