Arndt–Gottron scleromyxoedema: successful therapy with intravenous immunoglobulins

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Sir, Arndt–Gottron scleromyxoedema is a rare fibromucinous disorder regarded as a variant of the lichen myxoedematous. The diagnostic criteria are a generalized papular and sclerodermoid eruption, a microscopic triad of mucin deposition, fibroblast proliferation and fibrosis, a monoclonal gammopathy (mostly IgG-κ paraproteinaemia) and the absence of a thyroid disorder. This disease initially presents with sclerosis of the skin and clusters of small lichenoid papules with a predilection for the face, neck and the forearm. Progressively, the skin lesions can become more widespread and the induration of skin can result in a scleroderma-like condition with sclerodactyly and microstomia, reduced mobility and disability. Systemic involvement is common, e.g. upper gastrointestinal dysmotility, proximal myopathy, joint contractures, neurological complications such as psychic disturbances and encephalopathy, obstructive/restrictive lung disease, as well as renal and cardiovascular involvement. Numerous treatment options have been described in the literature. These include corticosteroids, retinoids, thalidomide, extracorporeal photopheresis (ECP), psoralen plus ultraviolet A radiation, ciclosporin, cyclophosphamide, melphalan or autologous stem cell transplantation.

In September 1999, a 48-year-old white female first noticed an erythematous induration with a lichenoid papular eruption on her forehead. Three months later the lesions became more widespread including her face (Fig. 1a), neck, shoulders, forearms (Fig. 2a) and legs. When the patient first presented in our department in June 2000, she had problems opening her mouth fully as well as clenching both hands or moving her wrist. The histological examination of the skin biopsy was highly characteristic of Arndt–Gottron scleromyxoedema. Full blood count, blood morphology, bone marrow biopsy, bone scintigraphy and thyroid function tests were normal. Serum immunoelectrophoresis revealed an IgG-κ paraproteinaemia. Urinary Bence-Jones proteins were negative. No systemic involvement was disclosed.

We initiated ECP therapy in August 2000, initially at 2-week intervals (later monthly) on two succeeding days. When there was no improvement after 3 months, we also administered cyclophosphamide (Endoxana®; Baxter Healthcare Ltd, Newbury, U.K.) at a daily dose of 100 mg with mesna 400 mg (Uromitexan®; Baxter) prophylaxis. The response to this therapy was rather moderate.

In February 2003 the patient developed a change of personality and loss of orientation and was admitted to hospital. The extensive neurological, radiological and microbiological diagnostics were unremarkable at that time. A few hours later the patient had seizures and was put on artificial ventilation in an intensive care unit. The patient was comatose for several days. A repeated magnetic resonance imaging scan was still normal, but the cerebrospinal fluid tap showed a dysfunction of the blood–cerebrospinal fluid barrier. A bilateral loss of somatosensory evoked potentials was noticeable. The neurological symptoms were classified as a ‘dermatoneuro’ syndrome, a rare extracutaneous manifestation of scleromyxoedema. After initiation of treatment with methylprednisolone (Urbason®; Aventis, Frankfurt, Germany) the neurological situation normalized in the following 2 weeks. No further medical treatment was necessary.

In April 2003 therapy options were re-evaluated and the patient was started and maintained on a 7-day course of melphalan 7.5 mg daily (Alkeran®; GlaxoSmithKline, Uxbridge, U.K.) in combination with prednisolone 40 mg daily (Decortin H®; Merck, Darmstadt, Germany) every 6 weeks. This treat-
ment was well tolerated, but after an initial softening of the skin in the first five cycles, no further improvement occurred.

In April 2005 we decided to change to an intravenous immunoglobulin (IVIg) therapy. A total of 160 g (2 g kg⁻¹ bodyweight) immunoglobulins (Intratect®; Biotest, Dreieich, Germany) was infused every 4 weeks on two succeeding days. Prednisolone at a dose of 10 mg daily was also administered. The first course was well tolerated and after 1 month the patient again noticed a softening of the skin in the region of the wrist with a subsequent improvement of the motility of the joints. After the third course, opening of the mouth improved markedly, so that she could eat a banana without cutting it lengthwise into halves. Also sensorimotor sensitivity in both hands disappeared and motility improved, so that she could perform delicate tasks, e.g. opening a bottle of water or clenching both hands. Over the following months the skin softened continuously and a reduction of induration and lichenoid papular eruption occurred (Figs 1b, 2b). The thickening of the skin decreased, so that a recently acquired ring was now loose fitting. After 12 cycles we stretched the intervals to 5 weeks. In November 2006, after 20 courses of IVIg therapy, we could still see a sustained response to the treatment.

As of today the pathogenesis of scleromyxoedema is unknown. In approximately 80% of cases the disease is associated with a gammopathy, usually IgG-κ. Many authors propose that the paraproteins might be autoantibodies that stimulate fibroblast proliferation and dermal mucin deposition. Others speculate that the paraprotein represents a response of a B-cell clone to the primary mucin deposition.

The effectiveness of IVIg treatment in dermatological diseases is well documented. Although the precise mechanism of action of IVIg is not known, many hypotheses have been proposed.

Several authors describe successful treatment of scleromyxoedema with IVIg. In our extensively pretreated patient the IVIg therapy induced a sustained improvement of scleromyxoedema. Our experience with IVIg treatment of scleromyxoedema together with all the other published reports suggest, that IVIg is an excellent therapeutic option for scleromyxoedema through its high effectiveness and excellent safety profile.

References


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Concordant lymphoma of cutaneous anaplastic large cell lymphoma and systemic B-cell leukaemia

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Sir, The coexistence of different types of lymphoma falls into two categories, concordant lymphoma and composite lymphoma. Concordant lymphomas are defined by the coexistence of two histologically distinguishable lymphomas involving different anatomical sites, whereas composite lymphomas are two different types of lymphoma within a single organ or tissue.1 Both types are very rare. We experienced a concordant cutaneous anaplastic large cell lymphoma (ALCL) and systemic B-cell chronic lymphocytic leukaemia (B-CLL). To our knowledge, this is the first case of concordant ALCL and B-CLL.

A 58-year-old man presented with a 4-month history of five red nodules which measured 15 × 20 mm in the largest diameter and were distributed on the face, chest and left arm (Fig. 1). Skin biopsy showed massive and nodular infiltration of atypical lymphocytes in the entire dermis and upper subcutaneous tissue (Fig. 2a). The atypical lymphocytes possessed large irregular nuclei and abundant cytoplasm (Fig. 2b). Most (> 75%) cells expressed CD3 and CD30, and were also immunopositive for CD8 but not for CD4, CD19, CD20 or CD56. Clonal rearrangement of T-cell receptor (TCR) γ chain gene was detected by Southern blot analysis. Extensive evaluation did not detect nodal involvement. Although the peripheral blood cell count was within normal range at that time, bone marrow aspirates showed medium-sized abnormal cells, most of which expressed CD5, CD19, CD20 and CD79a but not CD30. Molecular analysis of the bone marrow lymphocytes revealed a monoclonal immunoglobulin heavy chain gene rearrangement but not a TCR gene rearrangement. There were no laboratory data to indicate infection with human immunodeficiency virus, Epstein–Barr virus or human T-cell lymphotropic virus type 1. The patient was diagnosed as having concordant cutaneous CD30+ ALCL and systemic B-CLL.

He was treated with chemotherapy protocols such as CHOP, FND and ESHAP as his condition gradually worsened. During the course of his disease the cutaneous lesions subsided owing to the effect of chemotherapy; however, they sometimes relapsed and showed similar histological results with the ALCL phenotype and clonal TCR gene rearrangement. The patient died 4 years and 9 months after the diagnosis of the concordant lymphoma.

ALCL is defined phenotypically by CD30 expression of at least 75% of the anaplastic large lymphoid cells.2,3 It generally displays an activated T-cell phenotype to a variable extent and

Fig 1. Clinical appearance of skin lesion: red nodule measuring 15 × 20 mm on the upper left arm.

Fig 2. Histology of a skin lesion from the upper left arm. (a) Diffuse infiltration of atypical lymphocytes in the entire dermis and upper subcutaneous tissue. (b) The atypical lymphocytes showed large irregular nuclei and abundant cytoplasm. Haematoxylin and eosin: (a) low-power magnification; (b) high-power magnification.


Key words: dermatoneuro syndrome, hd IVIg, high-dose intravenous immunoglobulin, monoclonal gammopathy, scleromyxedema

Conflicts of interest: none declared.