Case report

Scleromyxedema: a rare disorder and its treatment difficulties

Sandra Koleta Koronowska1, Agnieszka Osmola-Mańkowska2, Oliwia Jakubowicz2, Ryszard Żaba2

1Student Scientific Group at Department of Dermatology, Poznan University of Medical Sciences, Poland
Tutor: Agnieszka Osmola-Mańkowska MD, PhD
2Department of Dermatology, Poznan University of Medical Sciences, Poland
Head: Prof. Zygmunt Adamski MD, PhD

Abstract
Scleromyxedema is a rare progressive cutaneous mucinosis, usually associated with a systemic involvement and paraproteinemia. Its aetiology remains unknown. The therapeutic options include numerous treatment modalities, however, no standard treatment exists as the rarity of this disease prevents the execution of controlled therapeutic trials. This paper reports a case of a 38-year-old male with progressive scleromyxedema associated with gammapathy. Initially, the patient was treated with prednisolone and later etretinate was added to the therapeutic schedule with quite good clinical improvement. However, after 6 months of treatment, several adverse effects were observed: hypercholesterolemia, hypertriglyceridaemia and cataract of the right eye. The patient was consulted by dermatologists in Warsaw and Gdansk as well as by a haematologist. The patient was excluded from oncological treatment. Melphalan therapy was not recommended as it is associated with very toxic side effects. IVIG treatment (intravenous immunoglobulin) was not initiated because of financial issues. As the disease progressed, treatment with plasmapheresis was introduced. The patient received 4 cycles of the therapy. It was well-tolerated by the patient and gave satisfactory, but temporary results. In order to obtain long-lasting improvement the patient was treated with IVIG (21.0 g/dose for 5 consecutive days). This treatment modality seems to have resulted in a more stable improvement.

Key words: scleromyxedema, treatment, intravenous Immunoglobulin, plasmapheresis.

Introduction
Scleromyxedema (SM) is a rare progressive cutaneous mucinosis usually associated with a systemic involvement and paraproteinemia. It was first defined by Arndt and Gottron (1954) [1], then redefined by Rongioletti and Rebora (2001), as a disease characterised by a generalised papular and sclerodermoid eruption, monoclonal gammapathy (mostly Ig-λ paraproteinemia) and a triad of histological features: presence of mucin deposition within the upper and mid reticular dermis, fibroblast proliferation and fibrosis with the absence of a thyroid disorder [2] (Figure 1).

Scleromyxedema is a severe disorder that may be fatal. It is characterised by an excessive deposition of mucin in the connective tissue [3]. The deposits may stimulate the synthesis of collagen and glycosaminoglycans [1]. As a result, lichenoid papules are formed which cause thickening and hardening of the tissue [4]. Scleromyxedema has a chronic, disabling course because it is often associated with a systemic involvement of internal organs. Scleromyxedema is thought to have three main clinicopathological subsets: local, generalised and atypical [3]. The generalised form is often referred to as the “generalised lichen myxedematous”, and its course is much more severe than that of the other forms (Figure 2).

The prevalence of SM is equal in men and women. No standard treatment exists as the rarity of the disease has prevented the execution of controlled therapeutic trials. Until 2009, only 150 cases of patients suffering from scleromyxedema were reported [5].

The skin appears to be elephant-like and forms linear folds. The papules tend to group in the neck and forehead area. Histopathological examination reveals numerous mucin deposits in papules and sclerotic malformations,
Mucin deposits may stimulate the synthesis of collagen and glycosaminoglycans
Lichen papules are formed
Thickening and hardening of the tissue occur
Severe internal manifestations are associated
Death

Figure 2. Chronic, potentially fatal course of scleromyxedema

Table 1. Internal manifestations of scleromyxedema

| Type of involvement | Manifestation |
|---------------------|---------------|
| Muscular            | Proximal myopathy, joint contractures, muscle weakness |
| Neurological        | Encephalopathy, peripheral neuropathy, coma |
| Rheumatological     | Joint pain, migrating arthritis, sclerodactyly, seronegative polyarthritis, carpal tunnel syndrome |
| Pulmonary           | Obstructive/restrictive lung disease, pulmonary hypertension |
| Renal               | Renal insufficiency |
| Cardiovascular      | Myocardial infarction, hypertension, atherosclerosis |
| Ophthalmological    | Corneal deposits, thinning of the eyelid, ectropion |

Figure 1. Diagnostic criteria of scleromyxedema

which consist of thickened collagen fibres. The mucin deposits are subtle in these lesions [1].
Numerous internal manifestations may occur in SM [6-8] (Table 1).

Case report

We report a case of a 38-year-old man with a 1.5-year history of scleromyxedema typically associated with light chain \( \lambda \) IgG monoclonal gammopathy. He was first hospitalized in February 2011 due to severe pruritus of his feet and shanks, elbow, and carpal joint pain and sclerodactyly. Simultaneously erythema and small papules appeared on the skin of his face.

Cutaneous examination revealed small, symmetric, disseminated papules (of 1 mm in diameter). Waxy and firm papules were localised mainly on both arms. The patient also presented excessive and diffuse thickening of the skin on the face, especially surrounding the lips, which later led to facial expression impairment.

Radiological and ultrasonographic examinations were also performed to exclude any systemic involvement of the disease (chest X-ray, USG of abdomen). In laboratory investigation complete blood count was normal. Serum analysis indicated hyperproteinemia: IgG monoclonal gammopathy with \( \lambda \) light chains were present. Bence-Jones protein was detected, however, further investigations excluded haematological disorders. Urine analysis was normal. Based on clinical manifestations, and histopathological and laboratory data, the diagnosis of scleromyxedema with associated IgG-\( \lambda \) was obtained.

As scleromyxedema leads to systemic involvement, the patient was consulted by several specialists: a haematologist, cardiologist, neurologist, ophthalmologist, internal medicine doctor and several dermatologists. The haematologist disqualified the patient from treatment with mel-

Scleromyxedema: a rare disorder and its treatment difficulties
phalan. Therapy before hospitalisation included oral prednisolone, oral antihistaminic drugs and topical steroids but remained ineffective. Treatment was started with hydrocortisone i.v. 2 × 200 mg/3 consecutive days, afterwards 1 × 200 mg/6 days which resulted in a short-term improvement.

Acitretin 75 mg daily and methylprednisolone: 2 doses in an alternating manner: 48 mg or 32 mg daily were administered – hypercholesterolemia, hypertriglyceridaemia and a mere hyperglycaemia occurred.

Doses were lowered to: acitretin 50 mg daily, methylprednisolone 16/8 mg and later 16/24 mg but this led to another relapse of SM.

IVIG treatment, 3 cycles of Ig (21 g/day for 5 days in each cycle).

Four cycles of plasmapheresis – a short-term clinical improvement was obtained – the cutaneous manifestation each time became less severe.

Table 2. Treatment modalities of scleromyxedema

| Treatment modality                        | References |
|-------------------------------------------|------------|
| Systemic corticosteroids                  | [10]       |
| Cyclophosphamide                          | [11, 12]   |
| Melphalan                                 | [15]       |
| Interferon α                              | [16]       |
| Cyclosporine A                            | [17, 18]   |
| Plasmapheresis                            | [19, 20]   |
| Methotrexate                              | [21]       |
| Chlorambucil joined with PUVA             | [22]       |
| Surgical intervention                     | [23]       |
| 2-chlorodeoxyadenosine                    | [24]       |
| Retinoids                                 | [25]       |
| Mucopolysaccharides (thiomucase)          | [26]       |
| Thalidomide                               | [7, 14]    |
| Immunoglobulins                           | [6, 27-30] |
| Autologous stem cell transplantation      | [13, 31, 32]|
| Biological treatment – bortezomib         | [13, 14]   |

Hydrocortisone i.v. 2 × 200 mg/3 consecutive days, afterwards 1 × 200 mg/6 days, which resulted in a slight improvement – erythema started to fade. After a relapse of the disease several weeks later, we introduced a combination of oral acitretin 75 mg daily and methylprednisolone: 2 doses in an alternating manner 48 mg or 32 mg daily were administered. This stopped the progression of the disease. However, as a result of steroid and retinoid administration, the patient presented hypercholesterolemia, hypertriglyceridaemia and mere hyperglycaemia. This is why the doses were lowered to: acitretin 50 mg daily, methylprednisolone 16/8 mg and later 16/24 mg, but this led to another relapse of clinical symptoms. Then, plasmapheresis was started. The patient received a total of 4 cycles of plasmapheresis. Each cycle consisted of 4-5 procedures of plasmapheresis. Every course resulted in short-term clinical improvement – cutaneous manifestation each time became less severe. In order to attempt to achieve remission, IVIG treatment was started (Figures 3 and 4).

Discussion

Causal treatment of scleromyxedema is unavailable, as the aetiology is still unclear [9]. The severe course of the disease requires very aggressive treatment and long-term maintenance therapy is necessary in most cases [7].

According to the literature, a successful therapy with relatively long-term effects and few side effects involves the use of IVIG [28, 29]. It is considered to be the best ther-
apeutic option as it is associated with relatively few side effects [27]. Plasmapheresis remains effective only in a short-time perspective and leads to relapses. For this reason we started IVIG treatment. We received a relatively good and longer lasting response to this treatment modality: the papules and generalised sclerodermoid eruption became less visible. The progression of the disease was stopped. However, from a financial aspect, this treatment modality may be challenging.

The chronic course of this disease affects the patient mentally, thus psychological or psychiatric therapy may also be introduced in order to improve the results of systemic treatment.

References
1. Brown-Falco O, Burgdorf WHC, Wolff HH, Landthaaler M. Dermatology. Czelej, Lublin 2011; 1289-90.
2. Rongioletti F, Rebora A. Updated classification of papular mucinosis, lichen myxodematosus and scleromyxedema. J Am Acad Dermatol 2001; 44: 273-81.
3. Serdar ZA, Yasar SP, Erfan GT, Gunes P. Generalized papular sclerodermoid eruption: scleromyxedema. Indian J Dermatol Venereol Leprol 2010; 76: 592-2.
4. Binitha MP, Nandakumar G, Thomas D. Suspected cardiac toxicity to intravenous immunoglobulin used for treatment of scleromyxedema. Indian J Dermatol Venerol Leprol 2010; 76: 592-2.
5. Mehta V, Balachandran C, Raghavendra R. Arndt Gottron Scleromyxedema: successful response to treatment with steroid minipulse and methotrexate. Indian J Dermatol 2009; 54: 193-5.
6. Manousaridis I, Loeser C, Goerd T, Hassel JC. Managing scleromyxedema with intravenous immunoglobulin: acute worsening of scleromyxedema with biclonal gammopathy. Acta Dermatoven APA 2010; 19: 15-9.

7. Laimer M, Namberger K, Massone C, et al. Vincristine, dexamethasone and thalidomide in scleromyxedema. Acta Derm Venereol 2009; 89: 631-5.

8. Maciejewska-Radomska A, Sokolowska-Wojdyto M, Wilkowska A, et al. Scleromyxedema in a 70-year-old woman: case report and review of the literature. Postep Derm Aler gol 2011; 28: 63-6.

9. Kuldeep CM, Mittal AK, Gupta LK, et al. Successful treatment of scleromyxedema with dexamethasone cyclophosphamide pulse therapy. Indian J Dermatol Venereol Leprol 2005; 71: 44-5.

10. Rayson D, Lust JA, Duncan A, Su WP. Scleromyxedema: a complete response to prednisone. Mayo Clin Proc 1999; 74: 481-4.

11. Aberer W, Wolff K. Scleromyxedema: immunosuppressive therapy with cyclophosphamide. Hautarzt 1988; 39: 277-80.

12. Kuldeep CM, Mittal AK, Gupta LK, et al. Successful treatment of scleromyxedema with dexamethasone cyclophosphamide pulse therapy. Indian J Dermatol Venereol Leprol 2005; 71: 44-5.

13. Migkou M, Gkotzamanidou M, Terpos E, et al. Response to bortezomib of a patient with scleromyxedema refractory to other therapies. Leuk Res 2011; 35: 209-11.

14. Cañueto J, Labrador J, Román C, et al. The combination of bortezomib and dexamethasone is an efficient therapy for relapsed/refractory scleromyxedema: a rare disease with new clinical insights. Eur J Haematol 2012; 88: 450-4.

15. Dinneen AM, Dicken CH. Scleromyxedema. J Am Acad Dermatol 1995; 33: 37-43.

16. Tschen JA, Chang JR. Scleromyxedema: treatment with interferon alfa. J Am Acad Dermatol 1999; 40: 303-7.

17. Krajnc I. Arndt-Gottron scleromyxedema. Summary of 2 years treatment. Wien Klin Wochenschr 1997; 109: 960-3.

18. Saigoh S, Tashiro A, Fujita S, Matsui M. Successful treatment of intractable scleromyxedema with cyclosporin A. Dermatology 2003; 207: 410-1.

19. Westheim AI, Lookingbill DP. Plasmapheresis in a patient with scleromyxedema. Arch Dermatol 1987; 123: 786-9.

20. Keong CH, Asaka Y, Fukuro S, et al. Successful treatment of scleromyxedema with plasmapheresis and immunosuppression. J Am Acad Dermatol 1990; 22: 842-4.

21. Mehta V, Balachandran C, Rao R. Arndt Gottron scleromyxedema: successful response to treatment with steroid mini pulse and methotrexate. Indian J Dermatol 2009; 54: 193-5.

22. Schirren CG, Betke M, Eckert F, Przybilla B. Arndt-Gottron scleromyxedema. Case report and review of therapeutic possibilities. Hautarzt 1992; 43: 152-7.

23. Ackerl C, Karagöz H, Kucukodaci Z. Surgical treatment of facial disfigurement due to lichen myxedematous. Dermatol Surg 2009; 35: 875-7.

24. Davis LS, Sanal S, Sangueza OP. Treatment of scleromyxedema with 2-chlorodeoxyadenosine. J Am Acad Dermatol 1996; 35: 288-90.

25. Milam CP, Cohen LE, Frenske NA, Ling NS. Scleromyxedema: therapeutic response to isotretinoin in three patients. J Am Acad Dermatol 1988; 19: 469-77.

26. Cosgarrea R, Cosgarrea M, Turcu T. Scleromyxedema with laryngeal changes. Beneficial results of the treatment with mucopolysaccharidases. Ann Dermatol Venereol 1994; 121: 159-61.