CASE STUDIES

Scleromyxedema: Successful treatment with IVIg and lenalidomide

Jyotsna Oak[1], Sandeep Goyale[2], Rupali Mathur[3], Vishal Haripara[3]

[1]Consultant Physician & Rheumatologist, Kokilaben Dhirubhai Ambani Hospital, Mumbai, India
[2]Consultant, Oncologist, Kokilaben Dhirubhai Ambani Hospital, Mumbai, India
[3]Residents, Kokilaben Dhirubhai Ambani Hospital, Mumbai, india

Abstract

Scleromyxedema is a rare progressive disorder associated with severe morbidity due to altered coarse facial features. The disease etiology is unknown. Various therapies have been investigated like the use of corticosteroids, IVIg (intravenous immunoglobulin), plasmapheresis, and thalidomide. The disorder being rare, evidence from controlled therapeutic trials is very limited. This report describes the case of a 37-year-old male with progressive scleromyxedema, without gammopathy. The patient was treated with prednisolone followed by IVIg. He showed remarkable improvement initially. Subsequent treatment with lenalidomide for one year showed complete resolution of the skin lesions with no side effects of the therapy.

Keywords: Scleromyxoedema, intravenous immunoglobulin, IVIg, lenalidomide

Introduction

Scleromyxedema (SM) is a variant of lichen or papular mucinosis in which lichenoid papules are present along with scleroderma like features. It was first described by Arndt and Gottron (1954) and subsequently by Rongioletti and Rebora (2001).[1] It is characterized by scleroderma type increased fibroblast proliferation, sclerodermatoid eruptions and mucin deposition. It is associated with paraproteinemia, mainly of the immunoglobulin G lambda type monoclonal gammopathy, in the absence of thyroid disorder.[2] Patients with scleromyxedema have clinical resemblance to systemic sclerosis and are mistaken due to its multisystemic affection like pulmonary, gastrointestinal, cardiovascular and renal. Scleromyxedema affects both genders at middle age.

SM is one form of lichen myxedematosus that was proposed by Rongioletti in 2006. The different forms of lichen myxedematosus are: (a) generalized papular and sclerodermatoid variant (the only one that should be called SM), (b) localized form, which is further classified as papular, acral persistent papular mucinosis, papular mucinosis of infancy and a nodular form, (c) atypical or intermittent form including SM without monoclonal gammopathy, localized form with monoclonal gammopathy and/or systemic symptoms.[3]

There is no standard treatment for SM, as the disease is rare. Until 2009, only 150 cases of SM were reported.[4] The skin of SM patients may appear elephant like with linear folds. Histological examination has shown the presence of subtle mucin deposits within upper and midreticular dermis and sclerosis in the form of thick collagen fibers. The present study deals with the case of a male patient with SM who showed complete resolution of skin lesions upon treating with intravenous immunoglobulin, corticosteroids and lenalidomide.

Case report

A 37-year-old male was admitted with complaints of swelling of face and 1-2 mm waxy, firm, pink colored globular, papular eruptions over forehead, neck, face and both shoulders, which progressed in 15-20 days. He gradually developed swelling and pain in joints of hands and was unable to do fine movements. He complained of severe periorbital swelling and altered facial features due to thickening of skin over forehead, cheeks and submental swelling. He also had itching of skin. However, he did not

have any history of Raynaud's phenomenon, dysphagia, dyspnea on exertion or chest pain.

On examination, he had coarse features due to severe periorbital swelling (Fig. 1). His pulse rate was 84 per minute, BP was 130/90 and he had no hepatosplenomegaly or lymphadenopathy. His cardiovascular and respiratory systems were normal. He had no muscle weakness.

Clinical investigations revealed Hb 15.7 gm/dl, WBC 17000/cmm and platelet count 3.8 lakh/cmm. His liver and renal functions were normal (serum AST 11.7U/L, ALT 26.6U/l, creatinine 0.74 mg/dl). Thyroid profile (Total T3 75.09 ng/dl, T4 3.77 mcg/dl, TSH 3.75 microIU/ml) and urine examination were within normal limit. The serum protein electrophoresis was normal and no M band was observed. Anti-nuclear antibodies and anti Scl-70 antibody were negative. CPK was 32.8 U/l (10 to 171 U/L)

Radiological and ultrasonographic examinations were performed to exclude any systemic involvement of the disease, but they were normal. Skin biopsy showed increased fibroblast and increased space between collagen bundles due to mucin deposition (Fig. 2). Based

Fig. 1: Coarse facial features due to severe periorbital swelling

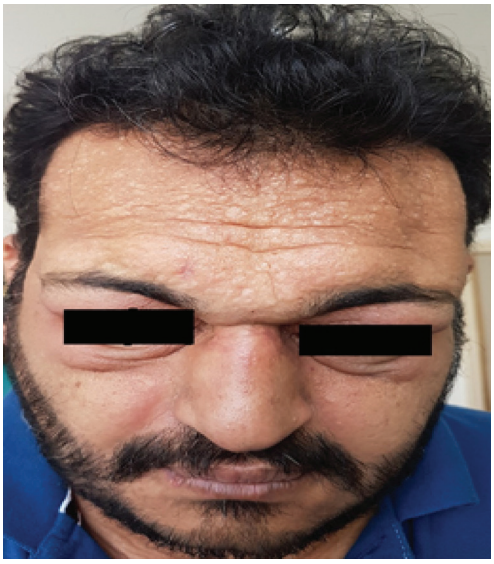


Fig. 2: Skin biopsies showing increased fibroblast and increased space between collagen bundles due to mucin deposition

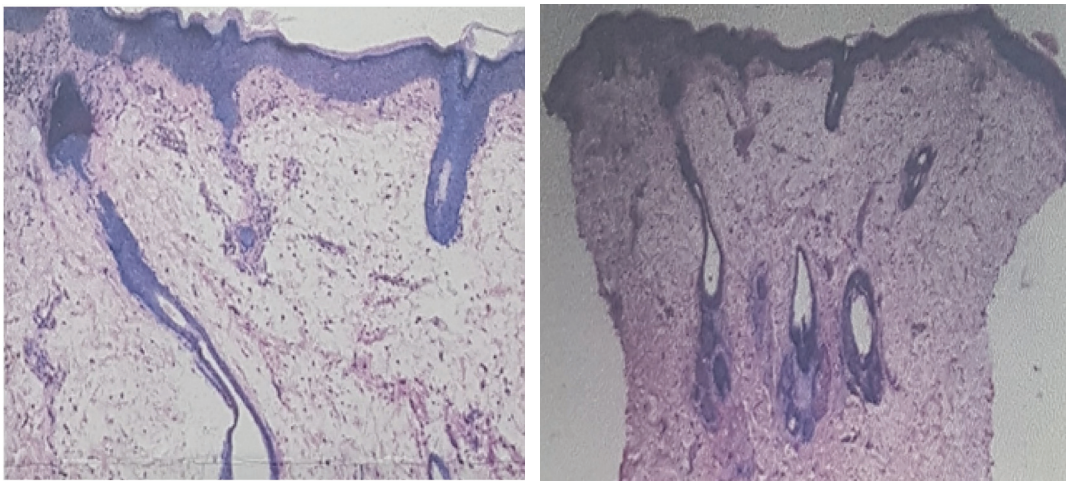
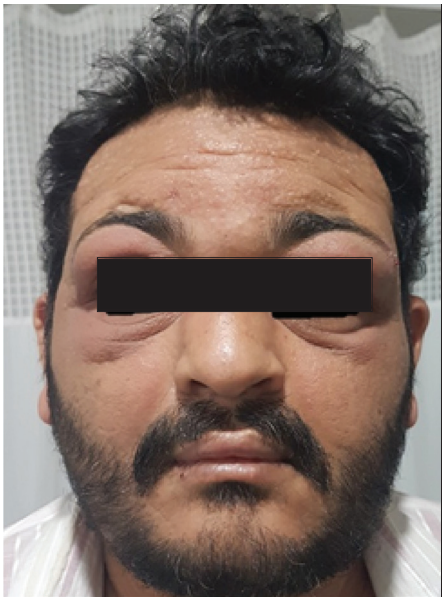


Fig. 3: improvement in facial features after IVIg and lenalidomide treatment



on clinical features, histopathological and laboratory data, the diagnosis of scleromyxedema without paraproteinemia was concluded.

Due to the disease severity, aggressive treatment and long-term maintenance therapy are essential in most of the cases. Our patient was initially treated with intravenous corticosteroids, followed by immunoglobulin, and then maintained on oral regime of lenalidomide. The treatment with IVIg 20 gm/ day was started and was given for 5 days along with systemic corticosteroids.

He showed a remarkable improvement after IVIg (Fig. 3). The swelling of fingers and cutaneous eruptions as well as periorbital edema showed regression.

Discussion

The pathogenesis of scleromyxedema is uncertain. Majority of the patients with SM have concomitant monoclonal gammopathy of unknown significance. The serum of these patients has been shown to produce fibroblast proliferation *in vitro* as well as an increased production of hyaluronic acid and prostaglandin E. However, the immunoglobulins alone do not reduce these effects. SM typically presents with symmetric sheets of linearly arranged 2-3 mm waxy, firm flesh colored papules, most commonly involving face, neck, forearms and dorsum of hands.[1] SM, a rare cutaneous disorder with unknown etiology, is characterized by progressive cutaneous mucinosis. Since the disease is rare, evidence from therapeutic trials and research is scarce. SM can be associated with paraproteinemia and other systemic disorders. But in the current patient, there was no evidence of gammopathy and his serum protein electrophoresis was normal.

IVIg is considered as the best therapeutic option for SM, as it has fewer side effects.[5] Plasmapheresis has short-term efficacy and often leads to relapse. Following IVIg treatment, the patient's skin eruptions and sclerodermoid lesions had become less visible. In a therapeutic study involving 30 patients, it was observed that the mean age of diagnosis was 59 years and monoclonal gammopathy was detected in 27 patients.[6] IVIg had induced a complete remission in 4 and partial remission in 9 patients with treatment duration of 2 years. Twenty-one patients were followed for 33.5 months and they were subsequently maintained on lenalidomide.[6] A few case reports are available with long-term efficacy of lenalidomide, which is an oral immunomodulatory agent showing positive response in patients with multiple myeloma. This drug is an analogue of thalidomide with better tolerability profile, less somnolence, constipation and neuropathy, thus allowing long-term administration.[7] Lenalidomide has immunomodulatory effect due to stimulation of NK cell activity and the increased IL-2 production, which enhances cell activity. These properties make lenalidomide a good maintenance treatment, even though the side effects such as cytopenia and thromboembolic events have been

reported.[7]

SM being a chronic progressive disease associated with high morbidity and mortality, a number of other therapies have been reported having varying success, including high doses of steroids, plasmapheresis, IVIg, melphalan, cyclosporin, and autologous stem cell transplant (ASCT), after conditioning with melphalan and thalidomide.[8,9,10] Combination of thalidomide and IVIg has been used most frequently.[9,11]

The recently introduced highly effective anti-plasma cell therapy such as bortezomib, thalidomide and lenalidomide has been shown to provide a higher likelihood of achieving a complete response. The favorable toxicity profile of these agents makes it a more reasonable treatment, even in patients without manifestations of multiple myeloma.

Thus, scleromyxedema is a chronic, unpredictable disease with severe manifestations and guarded prognosis. No specific or definite treatment is available. IVIg is effective and safe. As the response may not be permanent, maintenance infusions are required. The present patient demonstrated a long-acting response with lenalidomide. The chronic course and altered facial features due to scleromyxedema had affected the patient mentally and he required psychological support throughout the therapy. During the prolonged therapy for one year with lenalidomide, the patient did not have any relapses and side effects of the drug, thus proving it to be a safe alternative to ASCT.

Competing interests
The authors declare that they have no competing interests.

Citation
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*Correspondence: Dr.Jyotsna Oak
jyotsnaoak@gmail.com

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