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http://dx.doi.org/10.1016/j.jaad.2014.06.034

Atypical scleromyxedema with prominent nodular lesions associated with immune thrombocytopenia: An unusual presentation

To the Editor: Scleromyxedema (SM) is a rare cutaneous mucinosis that usually occurs with monoclonal gammopathy (>83.2%), predominantly an IgG lambda subtype.[1,2] SM may show a great variety of extracutaneous manifestations (gastrointestinal, musculoskeletal, neurologic, pulmonary, cardiac, and renal involvement) leading to significant morbidity and mortality.[1,2] We report a case of SM with prominent scalp involvement, presence of nodular lesions, and immune thrombocytopenia.

A 69-year-old woman presented with a 2-week history of facial edema and progressive eruption. The patient also reported severe scalp pruritus and increased hair loss.

On physical examination, skin-colored firm papules, nodules, and edema of the face and both hands were observed. The papules were initially located on the scalp, neck, and back of the auricular area, then gradually involved upper aspect of the trunk and the surrounding skin showed scleroderma-like induration in these areas. Several nodules, 4 to 10 mm in size, were present on the scalp, forehead (Fig 1), and side portions of the chin.

Pathological examination of biopsy specimens from a nodular scalp lesion and of a neck papule (Fig 2) revealed an increase in fibroblasts, collagen, and deposits of mucin in the papillary and midreticular dermis. Laboratory analysis showed a progressive low platelet count (60-10 $10^3/\mu$L, normal range 150-400 $10^3/\mu$L, platelet count within normal limits 6 months earlier), with a normal peripheral blood smear result and a normocellular bone marrow with trilineage hematopoiesis. Serum protein electrophoresis, immunofixation electrophoresis of serum and urine, and immunoglobulin free light chain assays did not show paraproteinemia. Other laboratory examination findings including thyroid function were within normal limits and autoantibody screening produced negative results. Computed tomographic scans of the chest, abdomen, and pelvis showed no relevant abnormalities. Electromyography detected signs consistent with a right carpal tunnel syndrome and peripheral sensory and motor neuropathy. Based on clinical manifestations, and histopathological and laboratory data, the diagnosis of SM with a secondary immune thrombocytopenia was made. The patient was treated with 3 methylprednisolone pulses of 1 g, followed by 1 mg/kg/d of prednisone for 1 month, and intravenous immunoglobulins (2 g/kg per cycle). Administration of a second course of intravenous immunoglobulins, delivered after 4 weeks, dramatically improved skin manifestations; however persistence of low platelet count prompted the addition of romiplostim, a thrombopoietin-receptor agonist. The prescribed corticosteroids were gradually tapered off and romiplostim was withdrawn. After 12 months of follow-up, she remains asymptomatic and platelet count was within normal limits

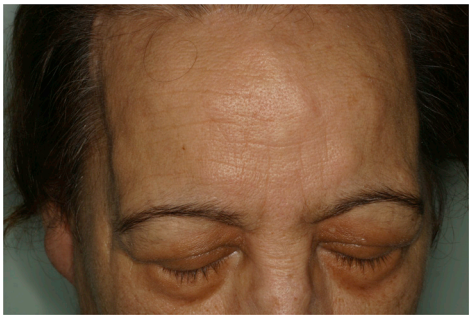

Fig 1. Scleromyxedema. Skin-colored subcutaneous nodules on the forehead and eyelid edema.

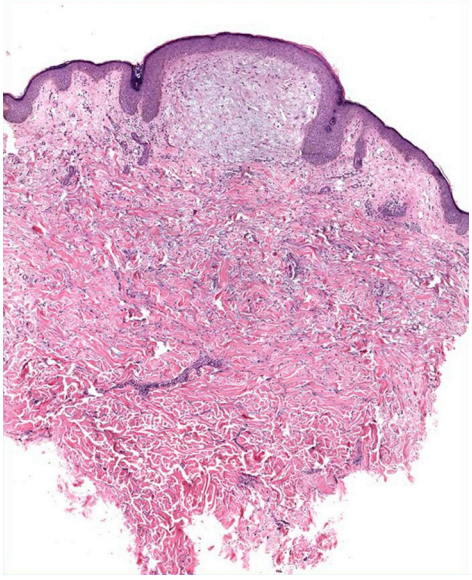

Fig 2. Scleromyxedema. Photomicrograph of skin biopsy specimen, showing pronounced deposit of mucin associated with increase in fibroblasts and collagen. (Hematoxylin-eosin stain; original magnification: ×40.)

with a maintenance therapy of intravenous immunoglobulins every 2 months.

The characteristic cutaneous manifestations in SM, also known as generalized lichen myxedematosus,[1] is a widespread eruption of 2- to 3-mm, firm, waxy papules, often in linear arrays, and the sclerodermoid induration of the skin. These characteristic skin findings were observed concomitantly with other unusual clinical findings in this patient. Nodular eruption[3,4] and scalp involvement leading to alopecia have been reported only sporadically.[3] Interestingly, the recently reported cases, with a prominent nodular eruption, presented in absence of underlying paraproteinemia.[3,4] Associated hematologic diseases in SM include Waldenström macroglobulinemia, Hodgkin lymphoma, and non-Hodgkin lymphoma, particularly after chemotherapy with melphalan.[1] To our knowledge, immune thrombocytopenia has not been reported previously in SM. Based on the current classification,[1] a final diagnosis of atypical form was made (SM without monoclonal gammopathy). Long-term follow-up to further characterize the natural course and prognosis in these patients is required.

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Funding sources: None.

Conflicts of interest: None declared.

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http://dx.doi.org/10.1016/j.jaad.2014.07.004

Lupus erythematosus–like skin eruption after vemurafenib therapy

To the Editor: Vemurafenib (PLX4032, Zelboraf, Roche Registration Ltd, Welwyn Garden City, UK) is a selective inhibitor of the oncogenic BRAF kinase activity.[1] The BRAFV600 mutation is the most common protein kinase mutation reported in melanoma with a frequency of 40% to 50%.[2,3] BRAF is a member of the RAF kinase family, which acts in the ERK/MAP kinase pathway, a signaling cascade regulating cellular proliferation, differentiation, and survival.[3] Vemurafenib treatment of patients with metastatic melanoma carrying the BRAFV600E mutation results in partial or complete tumor regression in the majority of patients and increases overall survival time.[4,5]

Common adverse events during vemurafenib therapy include photosensitivity, fatigue, rash, and arthralgia.[4,5] Furthermore, approximately one third of the patients develop epithelial tumors of the skin such as warts, squamous cell carcinomas, and keratoacanthomas.[1,4,5]

Hereby, we wish to report a case of lupus erythematosus–like skin eruption after vemurafenib therapy in a 70-year-old woman with stage IIIc progressive metastatic melanoma (pT4bN3M0). After excision of a 8-mm thick primary tumor on the left upper aspect of her back and lymph node dissection of the left axilla (7 metastatic of 19 lymph nodes), the tumor reoccurred within 26 months. Because the melanoma cells were found to have the BRAFV600E mutation, vemurafenib therapy was started at the regular daily dosage of 1920 mg. The treatment was well tolerated for a total of 4 months but then needed to be paused for 4 months because of fatigue and nausea. Vemurafenib was reinitiated at a total dose of 960 mg daily for 2 months and then increased to 1920 mg twice daily for another 2 months. Because of gastrointestinal discomfort and flareup of a rash the treatment was aborted. The rash started with erythematous macules on the face and subsequently over the next 2 to 4 weeks progressed into demarcated, infiltrated, scaly plaques that were symmetrically distributed over all sun-exposed body areas, particularly the face, décolleté, and upper aspect of the back (Fig 1, *A*). Histopathology revealed interface dermatitis with follicular plugging and dermal mucin deposition consistent with a lupus