Case Letter

Reticular Erythematous Mucinosis

To the Editor:

Cutaneous mucinosis is part of a heterogeneous group of disorders characterized by localized or diffuse dermal mucin deposit. Mucin is a mucopolysaccharide produced by fibroblasts, consisting mainly of hyaluronic acid (HA) bound to heparin and chondroitin sulfate.[1] Reticular erythematous mucinosis (REM) is a rare chronic diffuse form of primary idiopathic mucinosis that was initially described in 1960[2] as plaquelike cutaneous mucinosis.[3] The term *reticular erythematous mucinosis* was introduced by Steigleder et al[4] in 1974. Cutaneous lesions range from erythematous papules and plaques to reticular macular erythema.[3-6] Lesions usually are asymptomatic, though pruritus occurs in up to 30% of patients. Preferentially involved regions are the central chest and back of middle-aged women.[2-5]

A 40-year-old man presented with pruriginous lesions on the torso of 14 months' duration that became exacerbated during the summer months. Erythematous papules and plaques were observed on the chest (Figure 1A) and upper back. He admitted to smoking and occasional use of acetylsalicylic acid and dipyrone. Laboratory tests including rheumatologic screening were within reference range. Imaging studies including chest radiograph and abdominal ultrasonography revealed no abnormalities. Biopsy specimens revealed a normal epidermis, deep and superficial lymphocytic perivascular infiltrate, and dermal mucin (Figures 2 and 3) with hematoxylin and eosin stain and Alcian blue stain, respectively. Reticular erythematous mucinosis was diagnosed and the patient was started on chloroquine diphosphate 250 mg after ophthalmologic tests were performed. There was remarkable improvement of the skin lesions after 6 months (Figure 1B) when the antimalarial dose was slowly tapered.

The etiology of REM is unknown. Several factors such as UV radiation, immunologic diseases, and viral infections could induce the syndrome.[7] Many authors believe this disease could be a subset of lupus erythematosus (LE) because of its clinical presentation and histologic findings. As in LE, REM affects women most often and histologically presents as dermal mucin, with exacerbation from sun exposure and improvement with antimalarial drugs.[8-10] Lupus erythematosus tumidus represents the entity that is most similar to REM.[7] In both diseases, there generally is a perivascular lymphocytic infiltrate, absence of interface dermatitis, dermal mucin deposition, and negative immunofluorescence staining. Neither condition presents with serologic or systemic

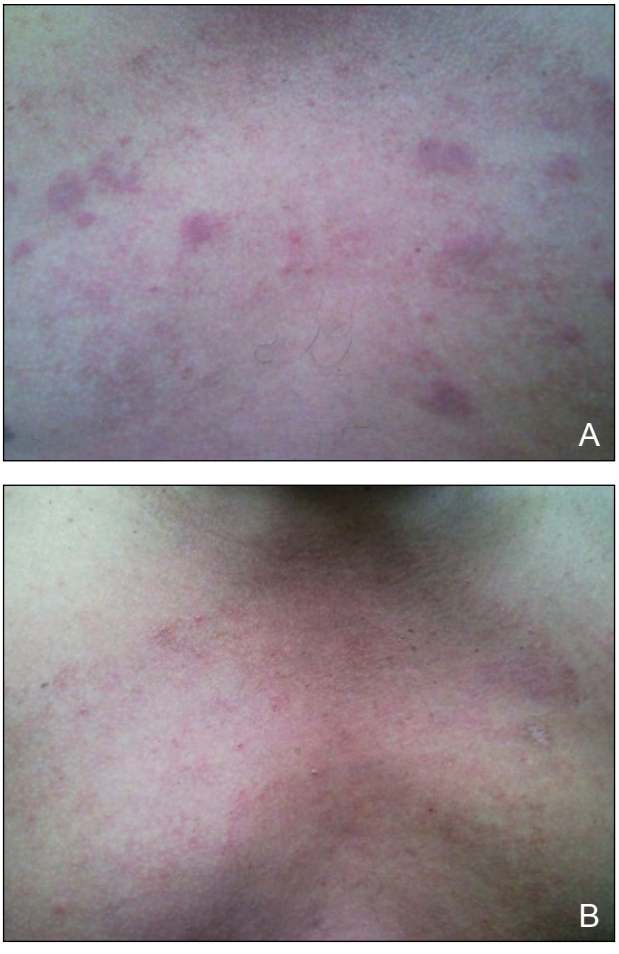

Figure 1. Erythematous papules and plaques on the chest before (A) and 6 months after treatment with chloroquine diphosphate (B).

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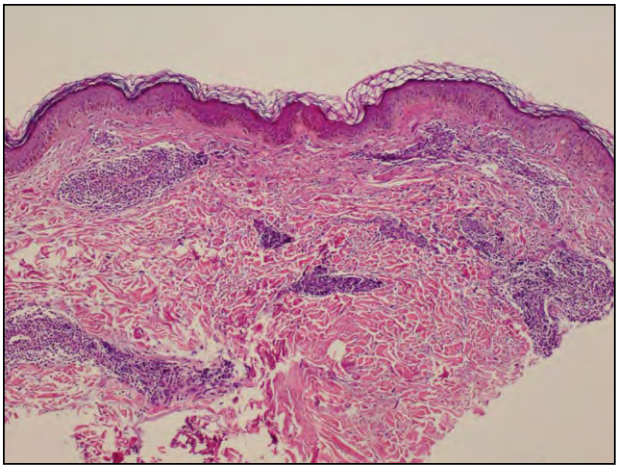

Figure 2. Presence of superficial and deep perivascular lymphocytic infiltrate and interstitial mucinosis (H&E, original magnification ×40).

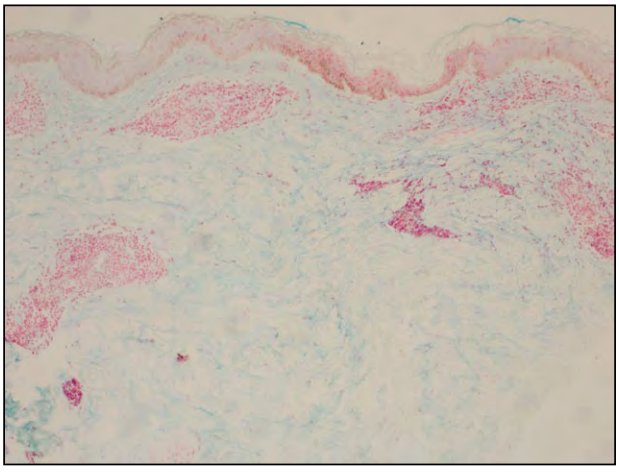

Figure 3. Presence of interstitial mucin stained in blue (Alcian blue, original magnification ×100).

abnormalities. Direct immunofluorescence of REM lesions could reveal granular deposition of IgM in the dermoepidermal junction in up to 20% of cases.[11,12] Nevertheless, immunoglobulin deposition also can be found on direct immunofluorescence of sun-exposed skin of healthy individuals.[13]

The mechanism by which glycosaminoglycans deposition occurs, particularly HA, is still undefined. It is postulated that there could be an altered fibroblast response to some cytokines, especially to IL-1β.[14] In up to 20% of patients, REM may be associated with a variety of systemic disorders, particularly autoimmune disturbances such as LE, idiopathic thrombocytopenic purpura, and diabetes mellitus. Other associated diseases include paraproteinemia, neoplasms, thyroid disease, arthritis, and uveitis.[12,15-20]

Menstruation, pregnancy, heat exposure, and radiotherapy have been cited as exacerbating factors.[20] In many patients, sunlight exposure has been reported to induce new lesions or to aggravate the condition, though the majority of clinical studies failed to reproduce the eruption by UVA and UVB irradiation. In 1988, McFadden and Larsen[21] described a case of induction of histologic but not clinical disease by photoprovocation testing. Morison et al[22] described histologically confirmed REM 28 days following UVB and UVC irradiation. Adamski et al[8] reported 3 cases of REM with positive photobiologic investigation. In this study, UVA1 total-body irradiation reproduced REM clinically and histologically, yet phototesting with UVA and UVB did not produce lesions. Therefore, the authors suggested that other factors could be associated with skin lesion genesis, such as heat and perspiration.[8]

Prominent histologic features include a perivascular lymphocytic infiltrate and mucin deposition among dermal collagen fibers. Dermal vascular ectasia can be found, though clinical presentation of telangiectasia is rare and has been associated with pulmonary carcinoma and thrombocytosis.[23,24]

Reticular erythematous mucinosis responds better to treatment compared to other forms of mucinosis. Because REM is a rare disease, few randomized controlled studies have been reported. Antimalarial agents are considered first-line treatment. In 2011, Kreuter et al[7] published a case series of 11 REM patients who were treated with either chloroquine or hydroxychloroquine. The median age of patients was 44 years, and the majority were smokers (91% [10/11]) and had autoimmune illnesses (55% [6/11]), specifically thyroid disease. Statistically significant improvement was noted after 3 and 12 months of treatment ($P<.001$).[7]

Other treatments include topical and systemic corticosteroids, cyclosporine, calcineurin inhibitors, colchicine, pulsed dye laser, and 308-nm excimer laser, as well as UVA and UVB phototherapy.[25-32] Cyclosporine was not effective in the treatment of a 48-year-old patient,[25] and tacrolimus showed partial resolution of REM lesions in 2 case reports.[26,27] Mansouri et al[28] compared pimecrolimus and pulsed dye laser therapy. Twice-daily pimecrolimus for 5 months and two 585-nm pulsed dye laser sessions showed equivalent therapeutic efficacy.[28] In another report, pulsed dye laser was used to treat 2 female REM patients, with nearly complete remission and only a few side effects, including local hypopigmentation.[29]

Furthermore, paradoxical improvement of REM lesions with solar irradiation or phototherapy has been described. One patient who was treated with UVB phototherapy and occlusive corticosteroid tape showed good therapeutic response.[30] UVB irradiation

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with a 308-nm excimer laser also demonstrated favorable results.[31]

In REM skin lesions, mucin deposits consist mainly of HA, as demonstrated by analysis of the glycosaminoglycan content.[32] UVA1, directly or indirectly, through induction of proinflammatory cytokines such as IL-1 can induce matrix-degrading enzymes such as proteoglycans in dermal fibroblasts, which may lead to increased degradation of HA deposition. These cytokines can lead to a decreased HA production by fibroblasts in REM syndrome. Moreover, reactive oxygen species, such as singlet oxygen, superoxide anion, and the hydroxyl radical produced by UV irradiation, especially UVA, can lead to fragmentation of HA.[32] In 2004, Meewes et al[32] described a case of a middle-aged woman whose lesions had completely cleared following 18 UVA1 irradiations and a cumulative dose of 1210 J/cm^2.

In our patient, there was no relationship between REM, systemic disorders, and sun exposure. Our patient was a smoker, similar to the majority of cases reported by Kreuter et al.[7] More studies are needed regarding the inclusion of REM in the spectrum of LE because there are similarities between this disease and lupus erythematosus tumidus. Our case demonstrates a possible relationship between REM and smoking as well as an excellent therapeutic response to antimalarial agents.

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