BRIEF ARTICLES

Reticular Erythematous Mucinosis: Case Report and Review of Literature

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ABSTRACT

Reticular erythematous mucinosis (REM) is a rare disorder that requires both a clinical and a pathological diagnosis. Multiple relevant associations and triggers are known, though exact etiology is unclear. This report aims to demonstrate a classical presentation of REM and available treatment options that have proved efficacious to date.

INTRODUCTION

Reticular erythematous mucinosis (REM) is a disorder of dermal mucin accumulation that has been reported throughout the world. This rarity of the disease prevents many dermatologists from recognizing its hallmark features and treatment options. In the second-largest clinical study to date on REM, the authors diagnosed only 14 patients with REM over a 5 year period, and all of these patients had been referred by primary dermatologists for alternative diagnoses.[1]

While there is ongoing debate regarding the pathogenesis and clinical associations of REM, our case report highlights some its most salient characteristics. Our diagnostic and treatment approach is based on a review of current research, and this report aims to demonstrate a classical presentation of REM and treatment options.

CASE REPORT

A 29-year-old Caucasian female presented with a one-year history of an erythematous, mildly pruritic rash localized bilaterally on the breasts. The patient denied any recent infections, constitutional symptoms, or new medications. She noted a long-standing history of smoking and reported exacerbation of skin lesions with sun exposure. The lesion was unresponsive to several previous antifungal and steroid treatments.

On examination, the patient had erythematous reticulated plaques on the lateral aspects of bilateral breasts, more prominent on the left (Figure 1). There was also slight erythema with scattered papules in the lower sternal region (Figure 2). The initial differential diagnosis included irritant and allergic contact dermatitis, tinea corporis, and interstitial granuloma annulare.

Figure 1: Mildly pruritic, erythematous reticulated plaques on the lateral aspects of the breast

Figure 2: Slight erythema with scattered papules in the lower sternal region.

A 4 mm punch biopsy of the left breast showed a superficial to mid perivascular inflammatory cell infiltrate consisted predominantly of lymphocytes (Figure 3a). The collagen fibers within the reticular dermis were widely separated, and an Alcian blue stain showed deposition of increased dermal mucin within these spaces (Figure 3b).

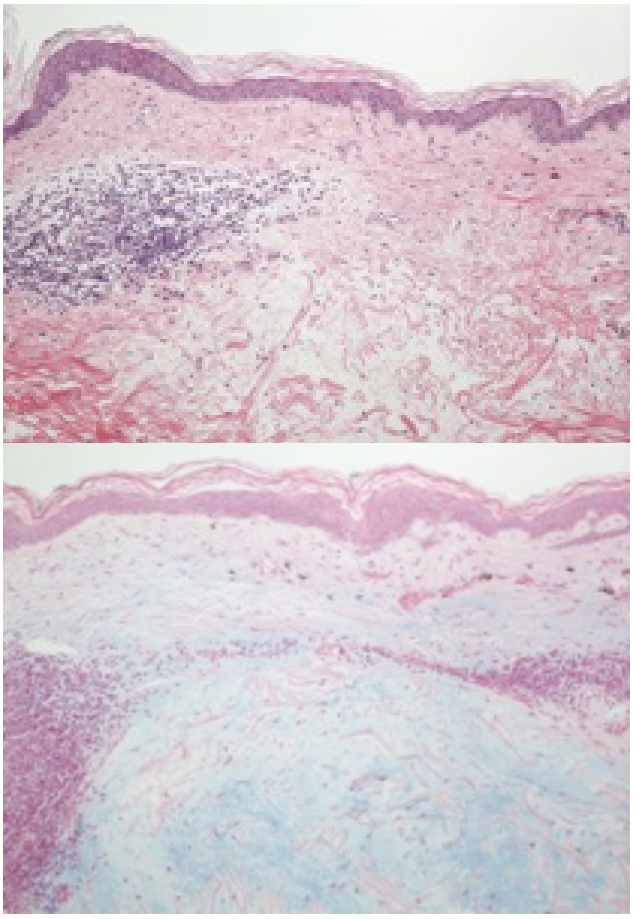
Based on the clinical and histopathological results of the skin biopsy, the patient was diagnosed with reticular erythematous mucinosis. After clearance by an ophthalmologist, the patient was started on 200 mg of hydroxychloroquine daily. Appropriate sun protection of the affected area, as well as smoking cessation, were thoroughly discussed with the patient. She denied symptoms of common comorbidities with REM such as discoid lupus erythematosus (DLE), idiopathic thrombocytopenic purpura (ITP), diabetes mellitus, and thyroid disease. She was instructed to follow-up with her primary care physician for further workup of associated conditions and age-appropriate cancer screening.

DISCUSSION

Reticular erythematous mucinosis was initially classified in 1974, though similar clinical and histological descriptions of plaque-like cutaneous mucinosis date back to 1960.[2,3,4,5] REM typically affects middle-aged females with a female: male ratio of 2:1.[5,6] Its hallmark features of are erythematous macules and papules that coalesce into a reticulated pattern, favoring the midline chest and mid-back.[5, 6,7] The macules and papules may be indurated but lack scale or other surface changes, and may also be less commonly found on the neck, face, upper abdomen, and limbs.[1,5,7]Most patients show no associated clinical symptoms, though 20-30% of patients report pruritus or a slight burning sensation.[1,5,6]

REM is a subtype of cutaneous mucinoses that often requires histologic assessment for diagnosis, demonstrating an accumulation of dermal-type mucin in the upper and mid dermis, which is predominantly composed of hyaluronic acid and other glycasimoglycans.

Figure 3: A) Moderately dense superficial to mid perivascular lymphocytic infiltrate with separation of reticular dermal collagen. (H and E stain, original magnification 100X). B) Increased dermal mucin within reticular dermis. (Alcian blue stain, original magnification 100X)



Alcian blue or colloidal iron staining shows this dermal mucin to be prominent around a perivascular and perifollicular lymphocytic infiltrate.[5, 7,9] This excessive mucin accumulation leads to marked separation of dermal collagen bundles, which is a hallmark of REM.[7] The epidermis is usually unaffected in REM, with only focal spongiosis and lichenoid inflammation when the epidermis is involved.[2,6,7,9]

In the 2 largest clinical reports on REM in publication, 20% and 54% of patients reported photosensitivity leading to REM exacerbations.[1,5] Only 1 of these patients from both studies showed clinically reproducible REM lesions following UVA and UVB photo-provocation tests, though smaller studies have demonstrated histological (without clinical) REM exacerbation with photo-provocation.[12]Among reports of REM exacerbated with photo-provocation testing, some patients required up to a 4 week interval to display REM symptoms after testing, making it difficult to demonstrate a causal link between photosensitivity and REM.[11,13] Smoking appears to be another important risk factor associated with REM, as studies have shown up to 91% concurrence rate.[1,10]

REM can be comorbid with several medical conditions, including thyroid disease and internal malignancies of the lung, breast, and colon.[1,5] Less substantiated associations with REM include oral contraceptives, ITP, DLE, diabetes mellitus, hypertension, HIV, and monoclonal gammopathy.[5,7,11,14]

Currently, hypotheses regarding REM pathophysiology are centered around mucin synthesis, which is modulated by TGF-β, interleukins, TNF-α, and interferons.[6] This theory is supported by the association of REM with lung, breast, and colon carcinomas, as mucinogens are produced in these cancerous states and can reach the cutaneous lymphovascular structures as seen on histology.[6,7] Furthermore, mucin-producing Mucin1 and Mucin4 genes are up-regulated in lung carcinomas.[7] Dermal fibroblasts have an abnormal response to IL-1β, resulting in excessive hyaluronic acid production and causing the dermal mucin accumulation seen in REM.[6,7,9,10]

The differential diagnosis for REM includes lupus erythematous tumidus, and there has been considerable debate regarding the relationship and distinction of these two

entities. There are subtle clinical and histologic differences between these two entities; perhaps the most distinct is the typical midline location and lack of basement membrane thickening in REM.[9] Jessner's lymphocytic infiltrate can be nearly impossible to differentiate clinically and histologically when it presents with increased mucin.[5] Other cutaneous mucinoses to consider include papular mucinosis, acral persistent papular mucinosis, dermatomyositis, Degos disease, and granuloma annulare.[7]

First-line therapy for REM is antimalarials, including hydroxychloroquine and chloroquine diphosphate.[1, 2,5,9,15] These drugs can inhibit the release of IL-2 from CD4+ T cells and inhibit major histocompatibility complex expression by macrophages.[6] Most patients found resolution of REM symptoms in 1-2 months following anti-malarial therapy.[1,5] Patients on these medications should be monitored for side effects such as irreversible ophthalmologic manifestations, gastrointestinal upset, and neurologic symptoms.[1,5,6,9,15]

In recalcitrant cases of REM, light therapies have shown some efficacy. Pulsed Dye Laser (PDL) therapy reduces the mucin and lymphocytic infiltrate of REM, with a lower rate of recurrence compared to hydroxychloroquine treatment.[16] Other light therapies with promising results for treatment of REM include UVA and UVB phototherapy.[2, 14,16] 2 case reports have demonstrated partial treatment of REM with UVB therapy with no appreciable adverse side effects.[14,17] Animal models suggest that UVB decreases hyaluronic acid synthase activity by decreasing expression of the TGF-β receptor and decreasing production of hyaluronic acid synthase mRNA from murine papillary dermis.[14] UVA, particularly UVA-1, penetrates deeper into the dermis and has demonstrated efficacy as monotherapy in REM treatment in 2 reported cases.[2,16] UVA-1can induce proteoglycanase in dermal fibroblasts and induce formation of dermal reactive oxygen species, which may degrade hyaluronic acid depositions.[2, 18]

CONCLUSION

Reticular erythematous mucinosis can be recognized by clinical and histological findings. Studies have demonstrated REM to be associated with sun exposure and smoking.[1,10] The best studied and first line drugs of choice for REM include hydroxychloroquine and chloroquine.[1,2,5,9,15] UVA and UVB therapies may also be useful in treating this relapsing disease in recalcitrant cases.

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