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CASE REPORT

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Development of keloidal morphea after treatment with cyclosporine in a case of recalcitrant generalized morphea

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Abstract

Nodular or keloidal morphea, also known as nodular scleroderma, is a rare form of localized sclerosis (SSc) or morphea. In this paper, we reported a case of this rare entity with a review of the literature.

KEYWORDS

keloidal morphea, localized sclerosis, nodular morphea

1 | INTRODUCTION

Nodular or keloidal morphea, also known as nodular scleroderma, is a rare form of cutaneous sclerosis or morphea.[1] Heretofore, less than 50 cases of keloidal morphea have been described in the literature.[2] The majority of these cases were associated with SSc, and only five cases of NM have been reported in the setting of morphea.[3-6]

Nodular morphea is manifested clinically by single or multiple keloidal nodules or plaques that develop in sclerodermatous areas, most commonly affecting young and middle-aged women.[2] In general, these firm, elevated, nontender lesions have different sizes, ranging from 2 to 3 cm. In this regard, trunk and upper extremities have been reported as the frequently involved sites.[7,8] The histopathology of the lesions can appear as the scleroderma pattern, that is, keloid pattern or mixed type. Treatment is challenging, and several treatment modalities have been reported with unsatisfactory results. According to recent studies, cyclosporine can be effective in the management of hard-to-treat cases of morphea.[9] Herein, we report a case of recalcitrant progressive generalized morphea that responded to treatment with cyclosporine but later complicated with nodular lesions.

2 | CASE

A 54-year-old woman presented with a three-year history of progressive firm skin lesions involving her trunk and thighs. She denied any prior history of trauma to the sites. She did not show any evidence of systemic involvement such as

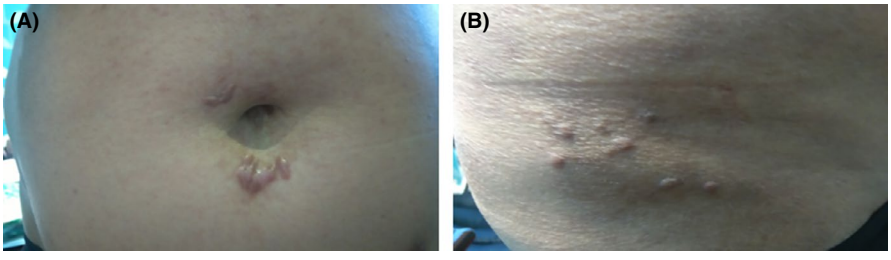

FIGURE 1 Development of keloid lesions after administration of cyclosporin

diarrhea, dysphagia, fatigue, Raynaud's phenomenon, and shortness of breath. Clinical examination revealed symmetrical induration of the skin on her trunk, thighs, and the upper arm. Dermatoscopic evaluation of her proximal nail folds was also normal. Moreover, there was no calcinosis, sclerodactyly, or telangiectasia.

Routine laboratory tests including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP), as well as renal and liver function tests were unremarkable. The patient was referred for rheumatology consultation. Systemic sclerosis was also ruled out.

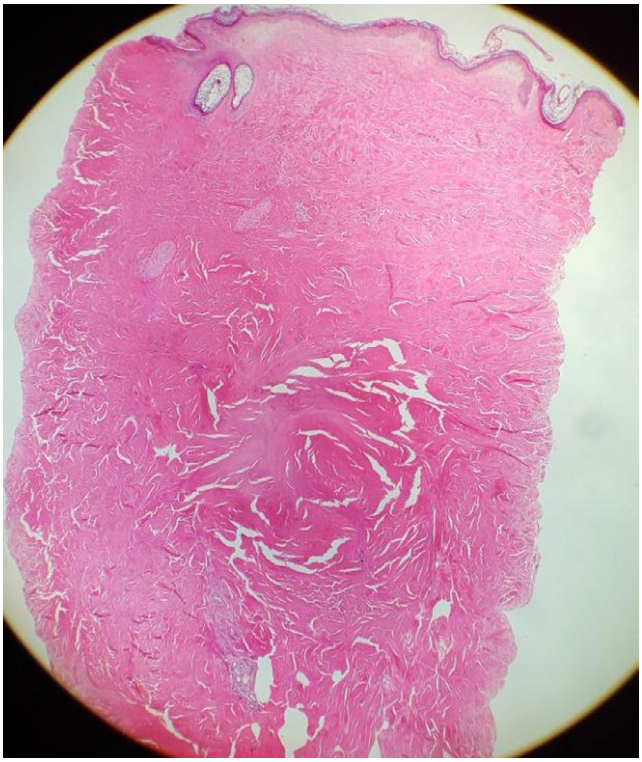

FIGURE 2 Histopathology of nodular lesions demonstrating whorled collagen bundles organized haphazardly throughout the dermis × 40

Owing to the progressive course of the disease, pulsed intravenous high-dose methylprednisolone (1000 mg; three consecutive days monthly for six months) combined with oral methotrexate (15 mg; weekly) was administrated. Six months after the end of the treatment, the patient showed only mild improvements in skin induration. Therefore, 300 mg of cyclosporine was used daily, resulting in a marked improvement of skin induration. Continuing the cyclosporine treatment led to gradual healing of the lesions. Several months later, the patient presented with asymptomatic nodular lesions within the area of sclerosis on both arms flunks and periumbilical area, without an obvious trigger (Figure 1). Microscopic examination revealed an increased deposition of bundles of collagen extending from the midreticular dermis to the dermal-subcutaneous junction. The papillary dermis was also spared, and there were no pathologic changes in the epidermis. In addition, the collagen bundles replaced adipocytes around the eccrine glands ("trapped" eccrine glands) (Figure 2). Despite this, therapy with cyclosporine was continued. We also administrated intralesional triamcinolone; however, no satisfactory results were obtained.

3 | DISCUSSION

''Nodular scleroderma'' (NS) and ''keloid morphea'' (KM) have been used interchangeably to illustrate the formation of a nodular lesion in the setting of cutaneous sclerosis. The first clinical description was in 1854 by Thomas Addison, who described it as "untrue keloid".[10] Although the cutaneous manifestations may vary clinically, there is a histopathological pattern of both morphea/scleroderma and keloid.[11] The proposed classifications of keloid-like lesion in the setting of

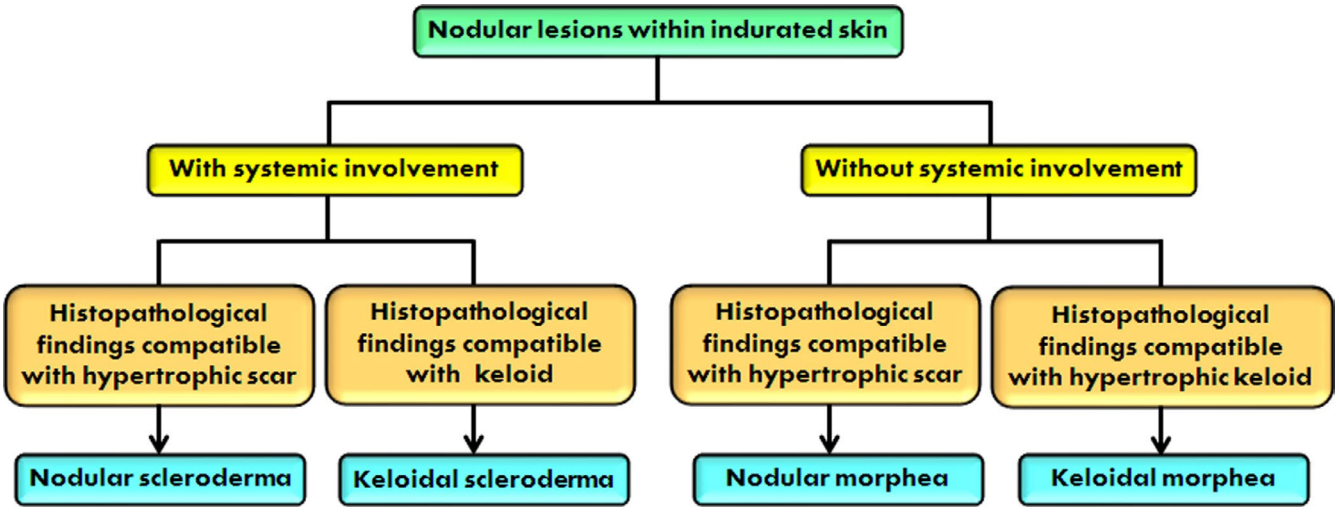

FIGURE 3 The proposed classifications of keloid-like lesion in the setting of cutaneous sclerosis based on the clinical and histopathological findings

cutaneous sclerosis based on the clinical and histopathological findings in depicted in Figure 3.

Evidence abounds in literature that nodular scleroderma lesions are as a result of a keloidal reaction of inflamed skin, involving in an active fibrotic process inherent to localized or systemic sclerosis.[7,8] Since the lesions can occur at high-risk sites (such as the trunk) for the development of keloid and hypertrophic scar formation in susceptible patients, a possible role of genetic predisposition can exist.[8-12]

Some remarkable findings in this case are as follows: Firstly, our patient with generalized morphea was refractory to different treatments for progressive morphea, but her lesions had a favorable response to cyclosporine. In line with our findings, a retrospective study indicated that cyclosporine is efficient against severe morphea. The authors stated that the side effects of cyclosporine were reversible.[9]

Secondly, despite the skin induration had a favorable response to cyclosporine in our patient, she later developed keloid-like nodules. This finding may be due to changes in the microenvironment of skin with cyclosporine therapy that led to a fibrosing skin reaction. Remarkably, the appearance of nodular lesions was seen in a patient with progressive systemic sclerosis after several months of treatment with D-penicillamine, but neither discontinuation of D-penicillamine nor corticosteroid treatment resolved the lesions.[8] Thirdly, the histological findings of nodular lesions with perivascular inflammatory infiltrate and thickened collagen bundles and "trapped" eccrine glands confirmed the correct diagnosis of nodular morphea. Aside from this, the biopsy of the nodule did not show typical findings of a keloid including a characteristic histological appearance with broad, homogenous, brightly eosinophilic collagen bundles in a haphazard pattern, and a distinct elevation above the surrounding skin surface. In this context, some authors suggest that the lesions of keloidal morphea are different from that of nodular morphea.

A variety of treatment options have been attempted for the treatment of nodular morphea according to the low likelihood of spontaneous resolution of the lesions.[6] These therapeutic options include extracorporeal photochemotherapy, high-dose penicillin, stazonol, penicillamine, prednisone, cefuroxime, and imatinib.[1-6] Further studies with long-term follow-up are recommended to shed light on the clinical and histopathological aspects of this rare entity as well as available treatment options.

CONFLICT OF INTEREST

The authors have no conflict of interest to declare.

AUTHOR CONTRIBUTIONS

Hamideh Moravvej managed the patient. Zahra Asadi Kani was the pathologist who diagnosed the lesions. Sahar Dadkhahfar wrote the manuscript. Farnaz Araghi helped in image and manuscript preparation. All authors reviewed and approved the final version of the manuscript.

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