Case and Review

Scleroderma with Nodular Scleroderma

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Abstract

Background: Nodular scleroderma is a rare variant of scleroderma which can occur in connection with systemic sclerosis or morphea. A biopsy from the lesion can demonstrate the scleroderma pattern, i.e., keloid pattern or mixed type. Treatment is challenging, and several treatments modalities have been reported with unsatisfactory results. Main Observations: We present a case of systemic sclerosis in a 50-year-old female who developed nodular scleroderma in the absence of deterioration of the scleroderma condition. Although no additional treatment was given, the lesions remained stable without progression. Conclusions: Although this condition is rare, it has been reported sporadically, and clinicians should be able to recognize this variant in cases of scleroderma presenting with firm nodules or plaques.
Case Report

A 50-year-old female presented with a 1-year history of systemic sclerosis and interstitial lung disease. Her current medications were prednisolone 5 mg, cyclophosphamide 75 mg, amlodipine 20 mg, sildenafil 50 mg, and aspirin 80 mg daily. Ten months later, she developed multiple asymptomatic papules on the neck, abdominal wall, and back (Fig. 1, Fig. 2). The lesions increased in size and number, and some lesions coalesced with plaques. She denied a previous history of surgery or trauma at the affected sites. Neither a personal history nor a family history of keloid was confirmed.

The physical examinations demonstrated sclerotic skin changes on the face, trunk, and extremities with sclerodactyly, digital pitting scars, and Raynaud’s phenomenon. There were multiple, nontender, firm skin-colored papules and plaques scattered on the neck, abdominal wall, and back. The laboratory tests revealed positive antinuclear antibody in a homogeneous pattern (titer 1:320) and positive anti-Scl70. The complete blood count, renal function, and liver function tests were unremarkable.

A 4-mm punch biopsy from the lesion on the neck was performed. The biopsy revealed thick sclerotic collagen fibers in the mid-dermis (Fig. 3). Mucicarmine staining to indicate the presence of mucin was negative. Thus, the findings were compatible with scleroderma.

Discussion

Our patient was diagnosed with scleroderma in the presence of nodular scleroderma. Nodular or keloidal scleroderma is a rare variant of scleroderma [1–5]. These terms can be used interchangeably. Nevertheless, in the literature, they are sometimes used as distinctive entities. The term "nodular scleroderma" is used when the pathological change resembles scleroderma, and the term "keloidal scleroderma" is used when the pathological change shows hyalinization of thick sclerotic collagens similar to keloid [1, 6, 7].

Nodular or keloidal scleroderma have been reported in either systemic sclerosis or localized scleroderma, usually 6 months after the presentation of systemic sclerosis [1–3, 8–17]. However, also the presence of nodular scleroderma before the onset of systemic sclerosis has been reported [12]. This condition can be found in systemic sclerosis patients either with or without active systemic involvements [1, 2, 8, 11–19].

The characteristic clinical presentations were firm nodules or plaques resembling keloid, distributed predominantly on the proximal extremities, i.e., on the chest, back, and neck. Nodular or keloidal scleroderma usually occur in middle-aged females (Table 1) [1, 4, 8, 11–14, 16–18]. Variable histopathologic changes have been reported to include characteristics of keloid or hypertrophic scars, of morphea, or of both morphea and keloid [1, 19].

The pathogenesis of this condition is still unclear. Complex interactions between cytokines, matricellular proteins, and local factors (minor trauma and vascular insufficiency) should be determined [2, 19, 20]. A role of pathogens, including acid-fast bacteria or chronic HCV infection, has been reported [11, 14, 21]. Currently, the increased activity of fibroblasts is believed to play a role. Yamamoto et al. [19] mentioned the role of increasing connective tissue growth factor (CTGF) in tissue fibrosis. Nonetheless, an increase in CTGF was identified both in the nodular lesions and in skin with scleroderma. Consequently, the increase in...
CTGF alone may not be the sole contributor to the pathogenesis of fibrosis in the lesions. Moinzadeh et al. [22] demonstrated increasing cartilage oligomeric matrix protein (COMP), collagen XII, and fibrillin-1 in nodular scleroderma lesions compared to perilesional skin and healthy skin. COMP is induced by TGF-β, which is an important cytokine in stimulating fibrosis in scleroderma and is involved in modulating the dermal collagen network as well as in sustaining fibroblast activation [22]. Additionally, highly expressed COMP has been demonstrated in keloid [23].

Since our case presented with multiple skin-colored papules and plaques, a differential diagnosis that should be considered was localized cutaneous mucinosis, which can be found as a coexisting condition with systemic sclerosis or morphea [24–28]. However, the diagnosis of localized cutaneous mucinosis should be confirmed by mucin deposition in a skin biopsy.

The treatment of nodular scleroderma is challenging. Several treatment modalities are mentioned in the literature, including topical or intralesional steroids, systemic steroids, topical calcipotriene, psoralen photochemotherapy, cyclosporine, D-penicillamine, methotrexate, extracorporeal photochemotherapy, and excision [1, 2, 4, 11–18, 29, 30]. However, these treatment modalities have shown unsatisfying results. A review of the reports on nodular or keloidal scleroderma in the past 10 years (Table 1) revealed that 1 case demonstrated stable nodular scleroderma without any specific treatment [16]. Interestingly, immunosuppressive agents that have previously been received cannot prevent the development of nodular or keloidal scleroderma [11–13, 16].

The condition of systemic sclerosis in our case has been stable, and the patient was not concerned about its appearance. Therefore, we decided to closely observe and monitor her for any progression of the lesions. After 4 months, the lesions have remained stable.

In conclusion, we presented a case of systemic sclerosis with multiple lesions of nodular scleroderma. Although this condition is rare, it has been reported sporadically, and it should be considered in scleroderma patients clinically presenting with firm nodules or plaques.

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Statement of Ethics

The patient gave her written informed consent.

Disclosure Statement

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Fig. 1. Multiple skin-colored papules and plaques on the neck.
**Fig. 2.** Multiple skin-colored papules and plaques on the abdominal wall.
Fig. 3. There are thick, sclerotic collagen fibers in the mid-dermis, extending to the deep dermis and superficial part of the subcutaneous layer. HE, ×40.
Table 1. Demographic characteristics and treatments of the reported cases of nodular or keloidal scleroderma in the past 10 years

| First author, year [ref.] | Sex   | Age, years | Distribution of lesions | Diagnosis                          | Duration of lesions | Treatments                                                                 | Results                                      |
|---------------------------|-------|------------|-------------------------|------------------------------------|-------------------|---------------------------------------------------------------------------|---------------------------------------------|
| Kassira, 2015 [13]        | female | 40         | chest, neck, abdomen    | localized scleroderma              | 4 weeks           | MTX 17.5 mg/week for 6 weeks                                               | reduced firmness, no new lesions             |
| Kokpol, 2015 [14]         | female | 63         | neck, trunk             | systemic sclerosis, chronic HCV infection | 1 year            | intralesional TA 5–10 mg/mL and ultrapotent topical steroid cream         | modest clinical improvement                 |
| Spierings, 2015 [15]      | male   | 76         | back, abdomen           | systemic sclerosis, monoclonal gammopathy | 1 year            | n.a.                                                                      | n.a.                                        |
| Stadler, 2013 [18]        | female | 44         | trunk, back, neck       | systemic sclerosis                 | 6 years           | systemic steroids, MTX, PUVA                                               | n.a.                                        |
| Sen, 2013 [17]            | female | 26         | chest, upper extremities, trunk | systemic sclerosis                | 6 years           | n.a.                                                                      | n.a.                                        |
| Heath, 2012 [12]          | female | 13         | face, neck, trunk, extremities | systemic sclerosis                | 2 years           | calcipotriene/betamethasone dipropionate ointment                         | soften the lesions                           |
| Le, 2012 [16]             | female | 70         | abdomen, neck, upper back, chest | systemic sclerosis                | 1 year            | surgical removal of large nodules                                          | no report of recurrent disease              |
| Le, 2012 [16]             | female | 45         | abdomen, neck, upper back, chest | localized scleroderma              | 3 years           | no treatment                                                              | stable lesion                               |
| Wriston, 2008 [1]         | male   | 51         | mid-chest, back         | systemic sclerosis                 | 8 years           | intralesional TA 10 mg/mL                                                  | no change                                   |
| Wriston, 2008 [1]         | female | 30         | chest, arms, thighs     | systemic sclerosis                 | 2 years           | intralesional TA 10 mg/mL                                                  | modest improvement                          |
| Melani, 2005 [11]         | female | 22         | trunk, neck, abdomen, thighs | systemic sclerosis                | 2 years           | D-penicillamine, systemic steroid                                           | no change                                   |
| Yamamoto, 2005 [19]       | male   | 29         | arms, chest             | systemic sclerosis                 | months            | n.a.                                                                      | n.a.                                        |
| Yamamoto, 2005 [19]       | male   | 34         | chest                   | systemic sclerosis                 | several months    | n.a.                                                                      | n.a.                                        |
| Yamamoto, 2005 [19]       | female | 60         | neck, back              | systemic sclerosis                 | months            | n.a.                                                                      | n.a.                                        |

n.a., not available; MTX, methotrexate; TA, triamcinolone; PUVA, psoralen photochemotherapy.