

Systemic sclerosis with keloidal nodules*

Esclerose sistêmica com nódulos queloidianos

Bárbara Stadler¹
Michelle Tokarski Fontana³

Aline Paula Biazus Somacal²
Thelma Larocca Skare⁴

Emilio Weingraber¹

DOI: <http://dx.doi.org/10.1590/abd1806-4841.20132245>

Abstract: Nodular sclerosis is a rare form of presentation related to both systemic and localized forms of scleroderma. We describe the case of a patient with nodular sclerosis in order to alert the medical community to recognize this entity.

Keywords: Keloid; Scleroderma, diffuse; Scleroderma, limited; Scleroderma, localized

Resumo: Esclerose nodular é uma forma de apresentação cutânea rara relacionada tanto com a forma sistêmica como com a forma localizada da esclerodermia. Descrevemos aqui o caso de uma paciente esta forma nodular de esclerose, no sentido de alertar a comunidade médica para o reconhecimento dessa entidade.

Palavras-chave: Esclerodermia difusa; Esclerodermia limitada; Esclerodermia localizada; Quelóide

INTRODUCTION

Systemic sclerosis or scleroderma (SSc) is an autoimmune inflammatory disease characterized by localized or diffuse cutaneous thickening, pulmonary fibrosis, pulmonary hypertension and swallowing disorders among others.¹ Raynaud's phenomenon is a common finding, which may precede the disease in years.¹ In its localized form, this is a disease limited to the skin and it can take the form of a plaque, linear lesion or hemiatrophy, etc.¹

Nodular sclerosis is a rare form of SSc, secondary to an excessive fibrosing reaction and leading to the appearance of multiple cutaneous nodules, similar to keloids.²⁻⁹ We describe here a case of nodular scleroderma or keloidal scleroderma in a woman of 44 years.

CASE REPORT

A 44 years old female patient of afro-descendant origin seeks medical help with a 12 years history of Raynaud's phenomenon associated with painful

digital ulcers. Six years ago she developed arthralgia in both hands, alopecia and dyspnea on exertion. One year ago she noted skin lesions "similar to keloid", of approximately 2 to 3 cm in trunk, back and neck that gradually increased in number. Prior treatment with local corticosteroid injections was done without any improvement.

On physical examination she had microstomia, narrowing of hand fingertips with small scars and an active ulcer in 2nd right finger of 5 mm. Skin thickness was seen in skin of the hands forearms and face. In the regions of the neck, trunk and back she had numerous nodular lesions, 2 to 3 cm in diameter, not painful (Figure 1). Heart, lung and abdomen examinations were normal. A periungueal capillaroscopy was performed and showed a SD pattern (SD=systemic sclerosis pattern). Radiographs of hands, echocardiography, barium swallow and CT of the chest were normal. A respiratory function test showed restrictive ventilatory defect. Laboratory showed a positive ANA (1/640;

Received on 02.11.2012.

Approved by the Advisory Board and accepted for publication on 05.12.2012.

* Work performed at the Ambulatorio de Reumato - Dermatologia Hospital Universitário Evangélico de Curitiba - Faculdade Evangélica do Paraná (HUEC-FEPAR) - Curitiba (PR), Brazil.

Financial Support: none

Conflict of Interests: none

¹ MD, Resident in Rheumatology. Rheumatology Unit, Hospital Universitário Evangélico de Curitiba - Faculdade Evangélica do Paraná (HUEC-FEPAR) - Curitiba (PR), Brasil.

² MD, Resident in Dermatology. Dermatotomy Unit, Hospital Universitário Evangélico de Curitiba - Faculdade Evangélica do Paraná (HUEC-FEPAR) - Curitiba (PR), Brasil.

³ MD, Professor in Dermatology. Residence tutor in Dermatology - Hospital Universitário Evangélico de Curitiba - Faculdade Evangélica do Paraná (HUEC-FEPAR) - Curitiba (PR), Brasil.

⁴ MD, PhD. Rheumatology professor at the Faculdade Evangélica do Paraná (FEPAR) - Curitiba (PR), Brasil.

with fine speckled pattern) and negatives tests for anti-Scl-70 and anti-centromere. Sedimentation rate, C reactive protein, complete blood count, liver and kidney function tests were normal.

The patient underwent biopsy of two nodular lesions in the chest, which findings are shown at figures 2 and 3. In figure 2A and 2B, it can be seen that the epidermis presents with acanthosis and hyperpigmentation at basal layer. Superficial dermis is preserved and reticular dermis has increased thickness and sclerosis of collagen bundles. Collagen fibers exhibit parallel distribution. There is, also, a discrete perivascular inflammatory process. The interstices between collagen fibers is decreased and there is entrapment of eccrine glands and nerves. (Figures 2 A and B). In the figure 3 elastic fibers (darker) can be seen. They do not exist in keloids.

Based on clinical and pathological report was diagnosed with scleroderma, in its variant nodular/keloid.

Treatment was started with nifedipine 20 mg/day and aspirin 100 mg/day for Raynaud's phenomenon. To treat scleroderma nodular lesions we added systemic corticosteroids, oral methotrexate and phototherapy (PUVA).



FIGURE 1: A. Region upper chest showing firm and elastic nodules; B. Close view of nodules

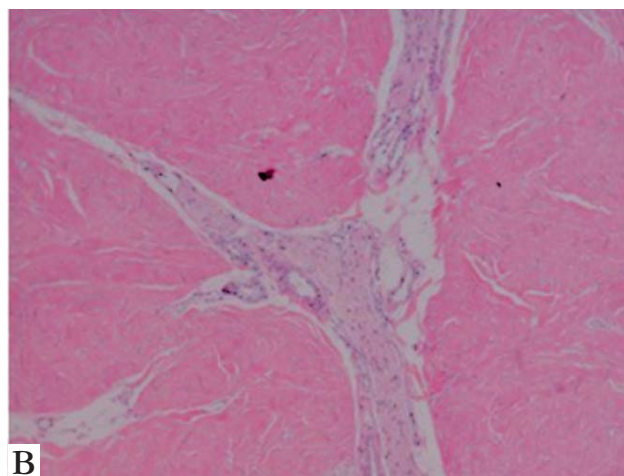
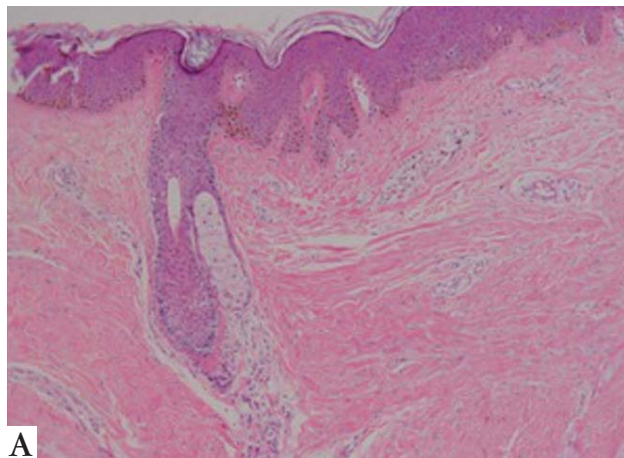


FIGURE 2: A. Histological aspect of the anterior chest nodule showing epidermis with mild acanthosis and basal layer hyperpigmentation; preserved superficial dermis, reticular dermis with sclerosis of collagen bundles and increased thickness and discrete perivascular inflammatory infiltrate. (Hematoxylin-eosin staining); B. Decreased interstitial tissue between collagen fibers and incarceration of eccrine glands and nerves. (Hematoxylin eosin staining)

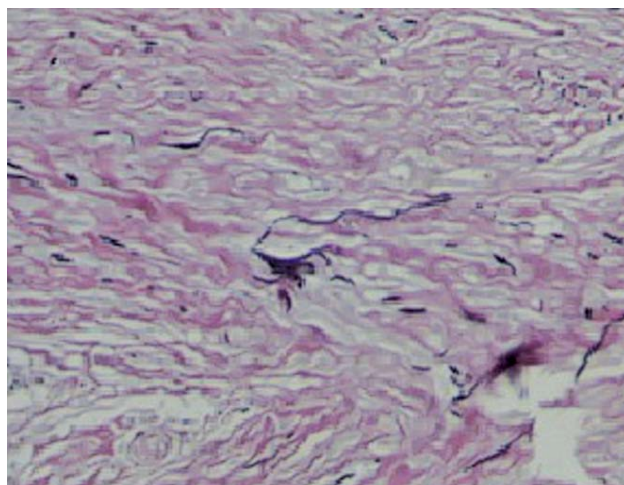


FIGURE 3: Presence of elastic fibers (in dark). (Weigert staining)

DISCUSSION

The first report of nodular lesions in patients with scleroderma was done in 1854 by Thomas Addison; in 1894, Unna called this condition "keloid-like scleroderma".^{4,10} Subsequently, in 1904, a number of cases with plaques resembling keloids have been reported in the German and French literature using the term "tuberous morphea" and in 1913, as "nodular scleroderma".⁴ In 1954, Korting concluded that the reported cases of scleroderma with nodules or plaques were different manifestations of the same disease process and this concept was supported in 1960 by Cabré and Landes, who described both types of lesions in a same patient.⁴ Since then, "nodular sclerosis" and "scleroderma keloid" has been used in the literature interchangeably.^{4,9,10} In 2003, Lombadeira *et al*⁴ had identified 33 cases descriptions of such cases in the literature.

It is known that this form of presentation may overlap both a common form of systemic and localized SSc; it was also described in previously healthy individuals and in those with progeria.^{2,4-6} At present case we considered a superposition of nodular and limited form of systemic sclerosis.

Typical lesions can be considered as true exophytic nodules with collagen material that microscopically show thickened and sclerotic collagen fibers without fibroblasts.⁹

Nodular sclerosis affects mainly young and middle-aged women.⁵ The nodules can appear both in regions of normal skin or in areas already affected by SSc, with preference for the upper limbs, chest, neck, trunk, abdomen and thighs.^{3,4,5,7} Sometimes they assume a linear distribution.⁸ The lesions are painless, although some patients may complain of local itch-

ing.⁴ In general, these lesions appear soon after diagnosis of SSc when the patient is in the acute phase of cutaneous lesions.⁸ It is believed that they represent an aberrant form of the inflammatory response in patients who have a tendency to form keloids or in skin sites with high preference for keloids formation.^{6,9} The described patient had an afro-descendent genetic background, which suggests a greater predisposition to keloidal formation. However the observation that the nodules usually appear early in the disease has not been verified in our patient, since she had 12 years of evolution when the nodules appeared.

Another given explanation for the appearance of nodular form of SSc is that there is increased activity of TGF- β . This is a cytokine which plays a crucial role in collagen synthesis.^{3,5} It is linked to the stimulation of proliferation fibroblast, extracellular matrix production, reduction of activities of matrix metalloproteinases and increase of proteinase inhibitors.⁵ Recently Yamamoto *et al* have also described increased local expression of CTGF (Connective tissue growth factor) in nodular scleroderma patients.⁵ The formation of CTGF is TGF- β induced and its expression has been increased in fibroblasts from patients with classic forms of SSc.⁵

Response to treatment is poor.² Several treatment modalities have been tried, among them phototherapy, prednisone, cefuroxime doxycycline, NSAIDs, cyclosporine.^{4,6} Recently, an *in vitro* study with imatinib (Gleevec®) has been shown to reduced proliferation of dermal fibroblasts in patients with systemic scleroderma.⁶ PUVA and topical calcipotriol seems to give a satisfactory response in some lesions.^{4,8,9} □

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MAILING ADDRESS:

Thelma Larocca Skare
Rua: Sete de Setembro, 4713
80240 000 - Curitiba - PR
Brazil
E-mail: tskare@onda.com.br

How to cite this article: Stadler B, Somacal APB, Weingraber E, Tokarski Fontana M, Skare TL. Systemic sclerosis with keloidal nodules. *An Bras Dermatol*. 2013;88(6 Suppl 1):S75-7.