Clinical and ultrasonographic correlation in localized cutaneous scleroderma*

Correlação clínica e ultra-sonográfica na esclerodermia localizada cutânea

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Abstract **OBJECTIVE: To describe ultrasonographic findings of localized cutaneous scleroderma and correlating them with clinical findings. MATERIALS AND METHODS: Twenty-three lesions of localized cutaneous scleroderma in 21 patients were evaluated with a Logiq 700 equipment coupled with a 6–14 MHz linear transducer. The disease stage (athrophic or inflammatory) was evaluated by a dermatologist, and the ultrasonographic findings (skin thickness and echogenicity) for both the affected and adjacent healthy regions were evaluated by a radiologist. Seven of the cases underwent post-treatment follow-up. RESULTS: All the affected regions presented loss of the normal ultrasonographic pattern of the dermis. Cases with clinically atrophic lesions (52.2%; 12/23) corresponded to reduction in the thickness and increase in the echogenicity of the dermis, and clinically inflammatory lesions (47.8%; 11/23) corresponded to decrease in echogenicity and increase in the thickness of the dermis. Post-treatment follow-up demonstrated alterations in the dermis thickness. CONCLUSION: The ultrasonographic findings allow the correlation between increase in the thickness/decrease in echogenicity of the dermis with the inflammatory phase of the disease, and decrease of the thickness/increase in echogenicity of the dermis with the atrophic phase. Also, it could be observed that it is possible to quantify the thickness of the dermis, utilizing this information associated with the clinical evaluation in the post-treatment follow-up.**

Keywords: Localized scleroderma; Ultrasonography; Dermis.

Resumo **OBJETIVO: Apresentar os aspectos ultra-sonográficos da esclerodermia localizada e relacioná-los com os aspectos clínicos. MATERIAIS E MÉTODOS: Foram analisadas 23 lesões de esclerodermia localizada em 21 pacientes. Foi utilizado equipamento Logiq 700 com transdutor linear de 6–14 MHz. Foram avaliados, pelo dermatologista, o estágio da doença (inflamatório ou atrófico), e pelo radiologista, a espessura e a ecogenicidade da derme nas regiões afetadas e sãs adjacentes. Foi feito acompanhamento de sete casos após tratamento. RESULTADOS: Todas as lesões apresentaram perda do padrão ultra-sonográfico normal da derme. Os casos de lesão clinicamente atrófica (52,2%; 12/23) corresponderam a redução da espessura e aumento da ecogenicidade da derme e os casos de lesão clinicamente inflamatória (47,8%; 11/23) corresponderam a aumento da espessura e redução da ecogenicidade da derme. Controles pós-tratamento mostraram alterações na espessura da derme. CONCLUSÃO: Os achados ultra-sonográficos nos permitem associar o aumento da espessura e a redução da ecogenicidade da derme com a fase inflamatória da doença, e a redução da espessura e o aumento da ecogenicidade da derme com a fase atrófica da doença. Notamos também que é possível quantificar a espessura da derme e usar essa informação no controle pós-tratamento associada à avaliação clínica.**

Unitermos: Esclerodermia localizada; Ultra-sonografia; Derme.

Bouer M, Chammas MC, Messina MCL, Oliveira IRS, Cerri GG. Clinical and ultrasonographic correlation in localized cutaneous scleroderma. Radiol Bras. 2008;41(2):87–91.

INTRODUCTION

Scleroderma is a disease of unknown etiology affecting the conjunctive tissue and characterized by sclerotic alteration of the skin and some other organ systems. Histological findings on the skin are: massive deposition of synthesized collagen, perivascular mononuclear cell infiltrate and vascular damages[(1)].

Scleroderma was first studied by means of ultrasonography in 1984, with a 15 MHz transducer (A-mode). In cases of focal lesions, the skin thickness was increased, and in pigmented lesions, decreased[(2)]. In 1986, and later in 1993, B-mode 10 MHz, 20 MHz and 25 MHz transducers started

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Received May 22, 2007. Accepted after revision July 24, 2007.

being utilized, and could demonstrate increase in the skin thickness in the involved regions, as well as post-treatment alterations[3–5]. In 1995, a study with a 30 MHz transducer demonstrated an increase in the skin thickness of involved regions and even a mild increase in clinically non-affected regions[6]. In 1998, post-treatment imaging of the skin with a 20 MHz transducer (B-mode) demonstrated that there may be different findings depending on the disease stage[7].

The present study was aimed at demonstrating ultrasonographic findings as compared with clinical findings in cases of focal (or localized) scleroderma.

MATERIALS AND METHODS

Twenty-three lesions of focal scleroderma were evaluated in 21 patients (18 women and 3 men) with ages ranging between 8 and 58 years (mean age, 24.1 years), in the period between May 2001 and May 2003, with a Logiq 700 (GE Medical Systems; Milwaukee, Wis., USA) equipment coupled with a multifrequency linear transducer (6–14 MHz). Lesions were found on the trunk (15) and limbs (8) of these patients.

The study was submitted to the approval by the Committee for Ethics in Research of Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, and all of the participating patients signed a term of free and informed consent.

The studies were performed by an experienced radiologist specialized in small parts ultrasound imaging, with a thick gel layer between the transducer and the skin, and minimum pressure on the region to be scanned for not deforming the surface of the skin to be evaluated.

Parameters to be evaluated at B-mode ultrasound included: a) dermis thickness – measured from the anterior hyperechogenic line between the gel layer and the dermis surface, and the posterior hyperechogenic line between the deep dermis and the subcutaneous tissue (Figure 1); b) the dermis echogenicity – normally characterized by a hypoechogenic superficial layer and a hyperechogenic deep layer (Figure 2).

Both the region of the lesion and an adjacent healthy region of the skin were evaluated in all of the patients participating in the present study. Seven patients had a post-treatment follow-up including the evaluation of these same parameters.

The clinical diagnosis was made by an experienced dermatologist, and all of the cases had their diagnosis confirmed by means of anatomopathological studies.

RESULTS

In the thickness analysis, clinically atrophic lesions (Figure 2), corresponding to 52.2% (12/23) of cases, presented a decrease in the dermis thickness (Figure 4) as compared with the clinically normal regions (Figure 3). The mean thickness in the affected regions was 1.29 mm, whereas in the normal regions was 2.23 mm. On the other hand, clinically inflammatory lesions, corresponding to 47.8% (11/23) of cases (Figure 5), presented an increase in the dermis thickness (Figure 7) as compared with the clinically normal regions (Figure 6). The mean thickness in the affected regions was 2.90 mm, whereas in the normal regions, it was 1.90 mm (Table 1).

As regards echogenicity, in cases of atrophic lesion, the dermis presented with an increase in echogenicity (Figure 4), whereas on inflammatory lesions the dermis presented with a decrease in echogenicity (Figure 7). Loss of the typical ultrasonographic pattern of the dermis, corresponding to superficial hypoechogenicity and deep hyperechogenicity for all of the affected regions, was observed in all of the affected regions (Figures 3 and 6).

The seven patients who underwent post-treatment follow-up, presented with alteration of the dermis thickness. Three of these cases presented inflammatory lesion with decreased dermis thickness (from 2.90 mm to 2.30 mm, on average) (Figure 8), and four presented atrophic lesions, with increased dermis thickness (from 1.10 mm to 1.40 mm, on average) (Table 2).

All anatomopathological studies confirmed the clinical diagnosis of scleroderma, both in the inflammatory phase, with predominance of cell infiltrate, and in the atrophic phase, with massive deposition of synthesized connective tissue and fibrosis.

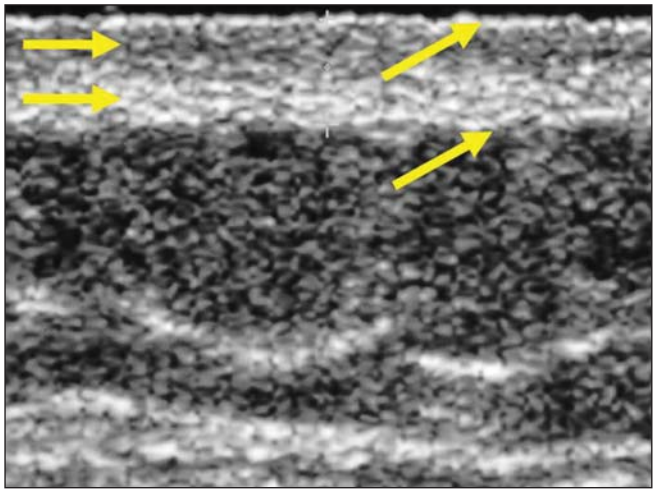

Figure 1. Ultrasonography of a normal skin. Sloping arrows show the limits of the dermis, and the horizontal arrows, the two layers of the dermis (superficial – hypoechogenic, and deep – hyperechogenic).

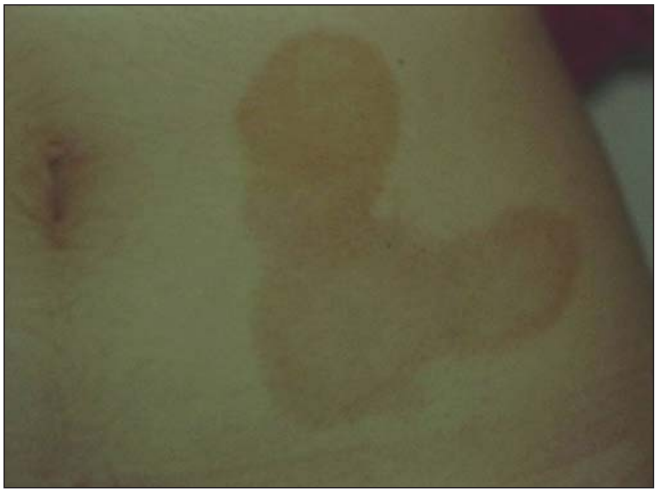

Figure 2. Picture of the skin of a patient affected by localized scleroderma. Typical pigmented skin in the atrophic phase of the disease.

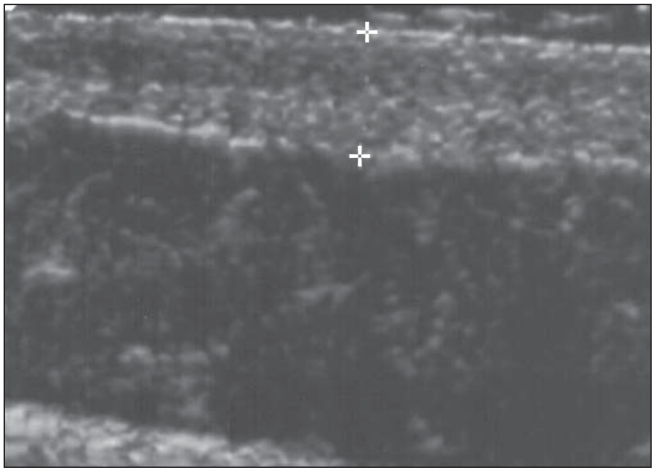

Figure 3. Ultrasonography of the region adjacent to an area of atrophic lesion. The typical feature of preserved skin can be observed (between crosses).

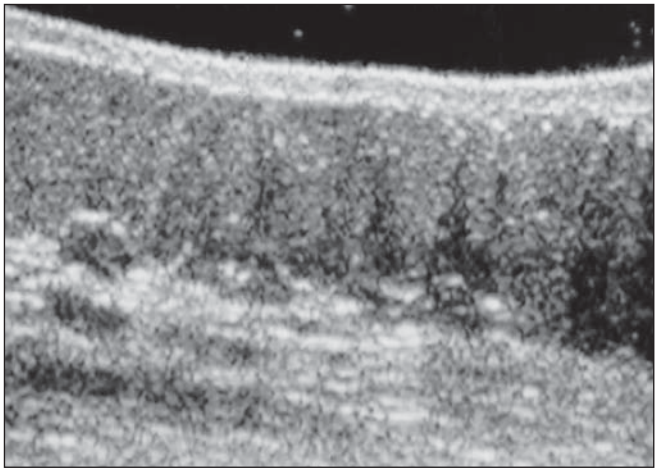

Figure 4. Ultrasonography of the region of atrophic lesion. Decreased dermis thickness, hypoechogenicity and loss of definition between superficial and deep layers can be observed.

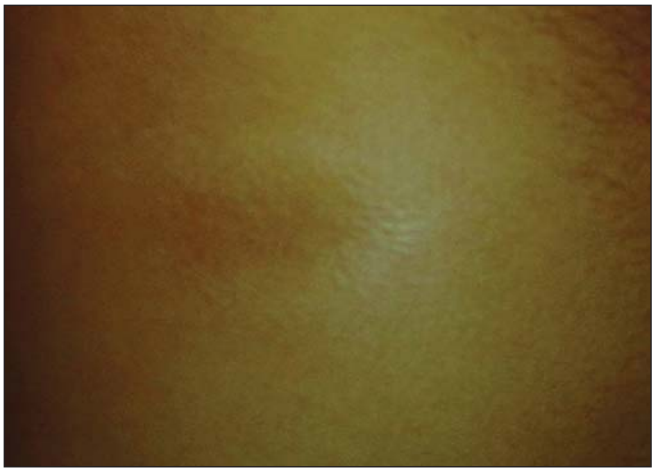

Figure 5. Picture of the skin of a patient affected by localized scleroderma. Typically elevated, slightly hypopigmented lesion in the inflammatory phase of the disease.

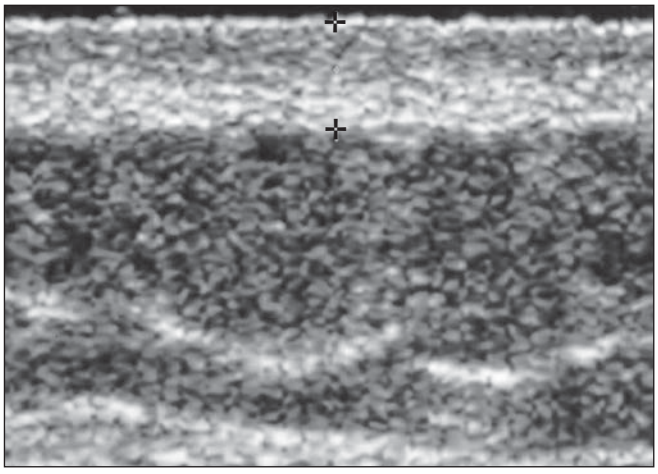

Figure 6. Ultrasonography of the region adjacent to the area of inflammatory lesion. A typical feature of preserved skin is observed (between crosses).

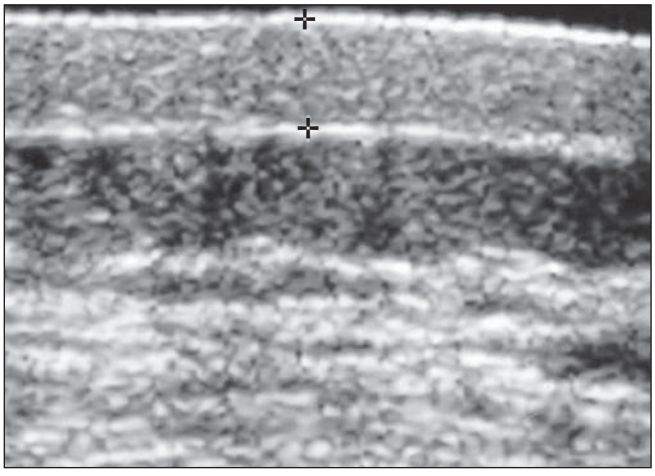

Figure 7. Ultrasonography of the region of inflammatory lesion. Note the increased thickness of the dermis (hypoechogenic) and loss of definition of the limit between superficial and deep layers (between crosses).

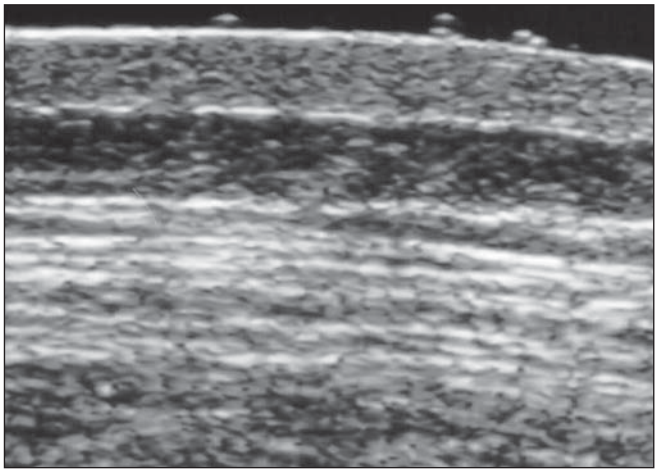

Figure 8. Ultrasonography of the region of inflammatory lesion after 30 days of treatment. Despite the decrease as compared to the previous study (Figure 7) still increased thickness of the dermis is observed.

Table 1 Dermis thickness and echogenicity, and corresponding clinical findings for each patient.

Patient	Normal area adjacent to the lesion	Area with lesion		
	Dermis thickness (mm)	Dermis thickness (mm)	Dermis echogenicity on the area with lesion	Clinical feature of the area with lesion
1	2.30	2.90	Decreased	Inflammatory
2	2.55	1.70	Increased	Atrophic
3	2.30	1.10	Increased	Atrophic
4	3.10	1.20	Increased	Atrophic
5	3.10	1.30	Increased	Atrophic
6	1.65	1.15	Increased	Atrophic
7	2.45	3.30	Decreased	Inflammatory
8	2.45	3.55	Decreased	Inflammatory
9	1.70	2.35	Decreased	Inflammatory
10	2.00	1.00	Increased	Atrophic
11	1.60	0.80	Increased	Atrophic
12	1.10	1.20	Decreased	Inflammatory
13	2.40	1.50	Increased	Atrophic
14	1.90	1.30	Increased	Atrophic
15	1.80	1.50	Increased	Atrophic
16	2.20	4.50	Decreased	Inflammatory
17	1.50	2.50	Decreased	Inflammatory
18	1.60	3.40	Decreased	Inflammatory
19	2.70	1.90	Increased	Atrophic
20	1.40	1.90	Decreased	Inflammatory
21	1.80	2.60	Decreased	Inflammatory
22	1.70	1.10	Increased	Atrophic
23	1.60	2.00	Decreased	Inflammatory

Table 2 Pre- and post-treatment measurements of dermis thickness, and corresponding clinical findings.

Patient	Clinical feature of the area with lesion	Pre-treatment dermis thickness (mm)	Post-treatment dermis thickness (mm)
1	Inflammatory	2.90	2.50
2	Inflammatory	3.50	2.60
3	Inflammatory	2.20	1.90
4	Atrophic	1.20	1.50
5	Atrophic	1.20	1.40
6	Atrophic	1.00	1.40
7	Atrophic	1.10	1.30

DISCUSSION

The utilization of ultrasonography with high frequency transducers in the evaluation of dermatologic diseases has increased with recent technological developments and the demand for a reliable and non-invasive method to aid the dermatologist in the visualization of abnormalities such as tumors or other less aggressive diseases occurring under the affected skin. In 1979, Alexander & Miller were the first to apply ultrasonography in dermatology to measure the skin thickness[8]. From that time on, many other studies about the most different dermatological diseases have been developed, utilizing already available equipment/transducers as well as other devices especially designed for this purpose.

The normal skin is made up of three different layers: a) epidermis, a 0.06–0.6 mm-thick layer with two types of cells – keratinocytes and melanocytes; b) dermis, a 1–4 mm-thick layer constituted of an extensive network of blood and lymphatic vessels, connective tissue, nerves, glands, fibroblasts, histiocytes and mastocytes, divided into papillary dermis – more superficial and thinner, with loose connective tissue, and reticular dermis, deeper and with a dense connective tissue; c) subcutaneous tissue, with a variable thickness, consisting predominantly of fat cells.

The image of a normal skin, from the surface to the inner layers, will show:

- The anechogenic gel layer intermingled with hyperechogenic spots typical of its internal component.
- A fine, echogenic line corresponding to the interface between the gel and the skin (epidermis). Because of its typical, very thin thickness, the epidermis appears ill-defines at US scans, except in the foot sole and hypothenar region, where the thickness is higher. Even so, a fine hypoechogenic layer only can be visualized with higher frequency or 20 MHz transducers.
- A hyperechogenic layer corresponding to the dermis, where the superficial and deep layers can be differentiated with transducers of 13 MHz or more — the first layer, slightly hypoechogenic and heterogeneous, and the second one, more hyperechogenic and homogeneous. Hypoechogenic lines corresponding to hair follicles can be obliquely seen across this layer. The dermis echogenicity is variable with age; it appears hypoechogenic in neonates, with a mild increase in echogenicity in older infants, and pronounced increase with the adult age. In the elderly, a more echogenic layer is observed at the level of the superficial dermis, mainly because of the exposure to the sunlight. The dermis is divided into papillary dermis – more superficial and thinner, with loose connective tissue, and reticular dermis, deeper and with a dense connective tissue, the latter being most frequently affected in cases of scleroderma.
- A hypoechogenic layer (adipous tissue)

with intermingled hyperechogenic strias (fibrous septae), corresponding to subcutaneous tissue with variable thickness. Generally, the limit between this layer and the dermis is well-defined, although nonlinear.

– A hyperechogenic layer, corresponding to the muscular fascia[9].

Scleroderma physiopathology is complex and consists in three main factors: vascular damage, mononuclear cell infiltrate, and massive deposition of newly synthesized connective tissue, remarkably collagen. Apparently, these three factors occur simultaneously, initially with predominance of cellular infiltrate, with an increase in the dermis thickness corresponding to the inflammatory phase of the disease, and latter predominance of deposition of connective tissue and fibrosis, with decrease in the dermis thickness, corresponding to the atrophic phase of the disease[1].

The ultrasonographic findings are compatible with the histological findings: clinically atrophic lesions presented a decrease in the dermis thickness, and clinically inflammatory lesions showed an increase in the dermis thickness. The studies developed by Serup[2], Akesson et al.[3], Myers et al.[4] and Ihn et al.[6] have reported increase in the thickness of the dermis in the regions affected by scleroderma, probably because the inflammatory phase predominated in the cases evaluated.

Atrophic lesions presented an increase in the dermis echogenicity, whereas inflammatory lesions presented a decrease in the echogenicity. Additionally, in the affected areas, there was a loss of differentiation between the superficial and deep layers of the dermis which has not been described in other studies and that can be explained by the diffuse involvement of the reticular dermis; in the case of edematous predominance, by the presence of cellular infiltrate and inflammatory process; and in the atrophic case, by fibrosis and higher collagen concentration.

During the treatment, alterations were observed in the dermis thickness, with inflammatory lesions presenting a decrease in the thickness of the dermis, and atrophic lesions presenting an increase, however, the differentiation between the superficial and deep layers of the dermis could not be established. Other authors[3,4,7,10,11] have concluded that ultrasonography is useful for a later post-treatment follow-up.

Finally, ultrasonographic findings allow the association between the increase in the dermis thickness/ decrease in the dermis echogenicity and the inflammatory phase of the disease, where edema and inflammatory process predominate, and the association between the decrease in the dermis thickness/increase in the dermis echogenicity and the atrophic phase of the disease, where loss of the skin elasticity and dermis cells compaction may be observed. Also, one can observe that it is possible to quantify the dermis thickness, utilizing this information in the post-treatment follow-up to indicate, or not, an improvement associated with the clinical evaluation.

The development of transducers with higher frequencies as well as devices with higher resolution can improve the post-treatment evaluation of the dermis thickness, and also de detection of alterations on clinically normal regions.

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