Concise Report

Ultrasonography is a sensitive tool for monitoring localized scleroderma

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Objective. To examine the usefulness of ultrasonography (USG) for monitoring paediatric localized scleroderma (LS).

Methods. A retrospective chart review of six paediatric patients who had USG of their LS.

Results. USG detected several abnormalities in active lesions including increased blood flow, increased echogenicity and loss of subcutaneous fat. USG findings corresponded with clinical assessment, and documented regeneration of subcutaneous fat and reduction in lesion size during treatment. In one patient, USG was more sensitive than magnetic resonance evaluation.

Conclusion. USG was found to be a sensitive tool for assessing the activity and extent of LS lesions in paediatric patients. Further studies are needed to assess its general applicability for monitoring these patients.

KEY WORDS: Localized scleroderma, Ultrasonography, Paediatric, Treatment, Monitoring.

Introduction

Localized scleroderma (LS) can present in several different forms including isolated circumscribed (plaque) morphoea, generalized morphoea and linear scleroderma [1]. LS can cause significant morbidity, including disfigurement, growth disturbances, limitation of joint mobility and neurological problems [2]. No randomized controlled study has been done to determine effective therapies in children; success has been reported with various regimens of methotrexate and corticosteroids in retrospective case studies [3–5]. Studies are limited by lack of validated outcome measures. Although lesions initially often have a distinct border and are erythematous or violaceous, these changes fade during treatment, making it difficult to accurately assess lesion extent and activity. Skin texture assessment by the modified Rodnan skin score may not be valid in children as their skin texture changes during development, such that healthy children were found to have scores in the same range as adult systemic sclerosis patients [6]. In severe LS, imaging studies, generally magnetic resonance (MR) or computed tomography (CT), can detect various defects including loss of subcutaneous tissue, changes in the underlying bone, intracranial calcifications and white matter abnormalities [7]. Thermography can document asymmetrical temperature distributions in paediatric patients with LS, and normalization of temperature with treatment [5, 8].

Some adult studies have found ultrasonography (USG) to be a useful tool in patients with scleroderma, both systemic and localized. These studies have generally shown a thickening of the skin (corium) that thins towards normal with effective treatment [9, 10]. One case report used USG to monitor corium thickness in a child with linear scleroderma during penicillin G treatment [11]. We have found that USG can be a sensitive tool for assessing LS in paediatric patients, and find differences in the subcutaneous tissues than what has previously been reported.

Materials and methods

The sequential sonograms of six children with LS were retrospectively reviewed, along with clinical information, including patient’s age and gender, duration of disease, location, size and appearance of lesion(s), treatment course and response and other imaging studies. The HUMC hospital’s IRB approved this study.

The sonograms were performed on an Acuson Sequoia 512 machine using a high frequency (10–14 MHz) transducer with preset software parameters for small parts. In order to increase visibility of the near field and avoid compression of tissues by the transducer, a thick layer of ultrasound gel was used. The presence of a visible, anechoic, superficial layer of ultrasound gel on the image demonstrated the lack of tissue compression. Affected sites were viewed with comparable unaffected sites on dual screen mode. Both grey scale and colour Doppler were performed. Large lesions were measured by marking skin at sites of transition and measuring distance between markings. Lesions within the size of the probe (5 cm) were measured directly on screen.

Results

Six paediatric patients with LS underwent sequential USG. The patients with active disease included a 14-yr-old boy with left facial circumscribed deep morphoea extending from the lower border of his eyelid to the upper border of his lip (Patient 1), a 4-yr-old girl with linear scleroderma lesions on both sides of her right ankle (Patient 2), and a 10-yr-old girl with unilateral pansclerotic/generalized morphoea that included her entire left arm, parts of her back and sacroiliac region (Patient 3). All were treated with methotrexate and corticosteroids. The other three patients had clinically inactive or stable disease at the time of study.

Patient 1 had a 1-yr history of progressive left facial circumscribed deep morphoea, with loss of lower lid eyelashes, thinning of subcutaneous tissue over the malar region and thinning of the left upper lip prior to beginning intravenous pulse corticosteroids (solumedrol 1 g/dose, 3 days/month) and oral methotrexate. His initial USG was performed after 5 months of treatment; this showed thinning, increased echogenicity and hyperaemia of the subcutaneous fat in the left infra-orbital and malar regions (Fig. 1A). Clinical improvement was seen after 6 months of treatment, with decreased hyperpigmentation and less induration over the malar region and lip. Solumedrol was then discontinued, but increased pigmentation and lip thinning recurred after 3 months. USG at this time showed the same
pattern of thinning, hyperaemia and increased echogenicity. Oral pulse prednisone (500 mg po q day × 3 days/month) was started; methotrexate was continued. After 3 months of re-treatment, hyperaemia was no longer seen on USG; the increased echogenicity was unchanged (Fig. 1B). His clinical appearance had not changed. After 6 months of re-treatment, hyperaemia returned without a change in the increased echogenicity (Fig. 1C). The patient showed increased pigmentation over the infra-orbital to malar region, and thinning of the lip. After 8 months of re-treatment, additional increases in hyperaemia and echogenicity were seen (Fig. 1D; data not shown). Further darkening of the entire lesion had occurred. His laboratory studies were normal at screening, and remained normal throughout his treatment course.

Patient 2 presented with a 3-week history of an expanding shiny, warm, erythematous-violaceous irregular lesion on her right lateral lower leg; this linear lesion extended over most of her lower leg. She was found to have a second lesion that extended on the dorsum of her right foot from between the first two toes towards her ankle, and developed a third lesion on the medial side of her right foot after beginning treatment; all lesions showed thinning of the skin, and loss of subcutaneous tissue. She was started on intravenous pulse corticosteroids (solumedrol 30 mg/kg/dose, 3 days/month) and subcutaneous methotrexate within 2 months of onset of her linear scleroderma. She had an elevated erythrocyte sedimentation rate (ESR) (61, normal to 30), no autoantibodies and other laboratory studies were normal; a skin biopsy confirmed the diagnosis of LS. After 1 month of treatment, her ESR had normalized and an MRI showed loss of subcutaneous fat with enhancement in the skin along the lateral aspect of her right leg; no muscle abnormality was noted (Fig. 2A). An USG performed after 2 months of treatment showed thinning to complete loss of subcutaneous fat, and increased echogenicity of underlying fat and muscle (Fig. 2B). She had hyperaemia in the muscle on the affected side (Fig. 2C). On physical exam, her skin had a thicker texture, with loss of subcutaneous tissue. After 4 months of treatment, hyperaemia and increased echogenicity were no longer present, and she was taken off corticosteroids by the next month. Clinically, her skin showed some softening with persistent subcutaneous tissue loss. Two months later, a repeat USG showed continued absence of hyperaemia and echogenicity, with some regeneration of

![Fig. 1. USG of Patient 1's face in the infra-orbital and malar region. (A) Initial USG shows loss of subcutaneous fat on the affected left side compared with the unaffected right side. Brackets delineate thickness of subcutaneous fat (F). There is also increased echogenicity in the fat on the left. (B) USG with Doppler flow performed after 3 months of re-treatment with oral pulse corticosteroids and methotrexate shows no difference in blood flow between the affected and unaffected sides. The dotted white circles indicate some of the larger areas of blood flow. There is persistent loss of the subcutaneous fat. Ticks on the bar above figure = 0.5 cm. (C) USG with Doppler flow performed after 6 months of re-treatment shows hyperaemia on the left side of the face. Ticks on the bar above figure = 0.5 cm. (D) USG with Doppler flow performed after 8 months of re-treatment shows an increase in hyperaemia on the left side of the face. Ticks on the bar above figure = 0.5 cm.](https://academic.oup.com/rheumatology/article-abstract/46/8/1316/1787022)

![Fig. 2. MRI and USG of lower leg of Patient 2. (A) MRI with gadolinium performed after 1 month of treatment shows loss of subcutaneous fat in the right lateral leg. There is enhancement of the overlying skin, indicated by arrow. No abnormal signal is seen in the underlying muscle. (B) USG performed after 2 months of treatment shows thinning to complete loss of subcutaneous fat on the right side. There is increased echogenicity of subcutaneous fat and underlying muscle in the affected right leg. Ticks on the bar above figure = 0.5 cm. (C) USG with Doppler performed after the second month of treatment shows increased blood flow in the right leg. The dotted white circle indicates some of the larger areas of blood flow. The areas of Doppler signal on the left side are artefact and do not represent true blood flow. Ticks on the bar above figure = 0.5 cm. (D) USG with Doppler performed after 6 months of treatment shows no difference in blood flow between the affected and unaffected leg. There has been some regeneration of the subcutaneous fat in right leg compared with earlier studies. Fib, fibula. Ticks on the bar above figure = 0.5 cm.](https://academic.oup.com/rheumatology/article-abstract/46/8/1316/1787022)
Measurement of the lesion size. Ticks on the bar above figure of the fat loss can be readily detected, as indicated by arrows. This allows direct assessment. Pulse intravenous corticosteroids (solumedrol 1 g/dose of prednisone and subcutaneous methotrexate with some improvement. Contractures of her fingers and elbow, and was begun on oral treatment, but flared after being tapered off medicines after 3½ yrs, responded to initial methotrexate and prednisone improvement was also seen.

Subcutaneous fat on methotrexate alone (Fig. 2D); clinical improvement was also seen.

Patient 3 developed pansclerotic/generalized morphea at age 5½ yrs, responded to initial methotrexate and prednisone treatment, but flared after being tapered off medicines after 3 yrs. When she presented to our clinic at age 9 yrs, she had flexion contractures of her fingers and elbow, and was begun on oral prednisone and subcutaneous methotrexate with some improvement. Pulse intravenous corticosteroids (solumedrol 1 g/dose x 3 days/month) replaced oral prednisone after 10 months, with marked improvement in skin texture and joint mobility 3 months later. Her USG, after 11 months of pulse treatment, showed thinning and hyperaemia of subcutaneous fat and muscle, without increased echogenicity (Fig. 3A). A repeat study 3 months later showed loss of hyperaemia, and persistent muscle atrophy (Fig. 3B). Patient 3 has continued to improve on this treatment with increased joint mobility, skin softening and decreased hyperpigmentation.

The three stable patients consisted of a 7-yr-old girl with a forehead circumscribed deep lesion for 5 yrs that had been treated with hydroxychloroquine and topical corticosteroids (Patient 4), a 13-yr-old girl with generalized morphea of her right arm, calf and abdomen for 3 yrs that had been intermittently treated with topical corticosteroids and calcipotriene (Patient 5), and a 17-yr-old boy with an 11-yr history of generalized morphea of his abdomen, arms and thighs, treated with penicillamine, then changed to oral methotrexate when he presented to our clinic 3 yrs ago (Patient 6). Patient 4 had been off treatment for 2 yrs and suffered a mild flare that stabilized on topical corticosteroid for over 1 yr, and off topical corticosteroid for 3 months. The USG of Patients 4 and 5 showed loss (Patient 4) or thinning (Patient 5) of the subcutaneous fat, but no hyperaemia or increased echogenicity (Fig. 3C; data not shown). With methotrexate treatment, Patient 6 had a decrease in the size of his lesion, decreased hypopigmentation and skin softening. An USG after 2½ yrs of methotrexate treatment showed no abnormalities compared with uninvolved tissue. He is being tapered off methotrexate without a change in his clinical exam or USG findings.

Discussion
We have found that USG can detect several changes associated with LS in paediatric patients. These include loss of subcutaneous fat and muscle, increased blood flow (hyperaemia) and increased echogenicity. Hyperaemia and increased echogenicity appear to be signs of active lesions; these changes were not seen in the three stable patients, and disappeared from the USG of patients that responded well to treatment (Patients 2 and 3). Although Patient 1 improved clinically during re-treatment with corticosteroids and methotrexate, his USG continued to show increased echogenicity. Clinical deterioration became apparent 3 months later. Subsequent sonograms showed a return of hyperaemia, with progression in the level of hyperaemia and echogenicity over time; these changes were associated with further clinical worsening.

In this case, the USG appeared to be more sensitive than clinical examination or laboratory studies at detecting disease activity.

As expected, loss of subcutaneous tissue was found in both active and stable patients. USG was able to document lesion size more accurately than clinical exam because lesion borders, as indicated by changes in subcutaneous fat thickness and/or appearance, were readily detected by USG. This allowed us to use USG to document changes in lesion size and subcutaneous tissue regeneration with treatment.

Compared with other currently available imaging methods, USG appears to offer several advantages in children. Unlike CT or X-rays, USG does not use ionizing radiation. Sedation of the child is not required as it often is for MRI. In our one patient that had both studies (Patient 2), USG was more sensitive than MRI as it detected muscle abnormalities not seen on MRI ± gadolinium, and enabled better visualization of the area of subcutaneous fat loss and fat thinning. Potential artifact can occur with MRI when studying skin abnormalities due to its proximity to the surface of the coil; this does not occur with USG.

Thermography has been used in clinical investigations of paediatric LS patients [8], but equipment is less readily available and studies require a temperature-controlled environment. Moreover, thermography may be less specific at detecting activity in facial and scalp LS, and in older lesions [12]. Sonography, however, has its own obstacles. Although USG can provide absolute measurements for some disease parameters such as lesion size and tissue thickness, only qualitative assessment of hyperaemia and increased echogenicity is possible. The degree of hyperaemia and increased echogenicity can only be assessed in comparison with uninvolved tissue. USG may be more useful for tracking the proportion of the LS lesion exhibiting these findings, rather than for assessing fluctuations in the intensity of these signals over time.

Our study is limited by our small sample size and its retrospective design. Further investigations are needed to determine the sensitivity and reliability of USG for assessing and monitoring paediatric patients with LS. If USG is found to be a valid tool, it will aid our ability to develop standardized measurements to be used in clinical trials and help determine optimal therapy for these patients.
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The authors have declared no conflicts of interest.

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Rheumatology key messages

- USG can detect several abnormalities in the subcutaneous tissue of paediatric patients with LS.
- USG can be used to monitor changes in patient lesions during treatment.
- Changes seen on sequential ultrasounds correlated with clinical findings.