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Ultrasonographic aspect of subcutaneous tissue dystrophies as a result of insulin injections

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Abstract

Aims: The aim of the study was to evaluate by ultrasonography the local dystrophies caused by insulin subcutaneous injections. The insulin treated diabetic patients must inject their long life insulin into normal tissue. The objective was to add ultrasonographic arguments to the clinic examination in order to periodically reconsider the available area to be used. **Patients and methods:** Forty insulin treated patients (14 male, 26 female) were clinically diagnosed with hypertrophic, atrophic, nodular, or inflammatory-like tissue dystrophies as a consequence of injections. These local dystrophies are not always conspicuous, barely suggesting a subdermal pathology. US evaluation, mainly subcutis, was used for assessing them. **Results:** Besides the clinical signs, ultrasonography offers some distinct appearances: a simple subcutis hypertrophy, a variety of nodular-shaped or diffuse hyperechogenity, subcutis atrophy, complex multilayer changes or possible inflammatory reactions. These abnormal entities have led to erratic insulin absorption and glucose control deterioration, if the patients have continued to inject into the same areas. **Conclusions:** Ultrasound interrogation should be used as a non-invasive measure for diagnosing insulin injections local dystrophies. Once diagnosed, their future evolution should be observed. By making a real ultrasonographic map of the injected areas a functional insulin treatment could be obtained and preserved.

Key words: diabetes, subcutaneous insulin injection, ultrasonography, local dystrophies, ultrasonographic map

Rezumat

Scop: De a evalua modificările ultrasonografice care se produc în locurile de administrare subcutanatale insulinei. Administrarea preparatelor de insulină trebuie făcută în zone anatomice indemne. Din variate motive, la locul de administrare pot apărea distrofii tisulare. Intenția noastră este de a adăuga observațiilor clinice pe cele ultrasonografice, pentru reconsiderarea periodică și argumentată a ariilor de administrare. **Pacienți și metode:** Au fost luați în studiu 40 de pacienți insulinotratați (14 bărbați și 26 femei) care prezentau la palpare în zonele de administrare, arii hipertrofice, atrofice, nodulare sau sugerând inflamația. Aceste arii au fost examinate ecografic. **Rezultate:** Pe lângă semnele clinice puțin variate, examinarea ultrasonografică a oferit aspecte distincte: hipertrofia sau atrofia subcutanată, modificări de ecogenitate și textură, afectare pluritisulară și uneori inflamatorie. Injectarea în continuare a acestor arii distrofice conduce la o absorbție variabilă și imprevizibilă a insulinei conducând la deteriorarea metabolică. **Concluzii:** Ultrasonografia trebuie folosită pentru diagnosticul leziunilor distrofice induse de procesul administrării insulinei. Odată diagnosticate, acestea vor putea fi urmărite în dinamică. Alcătuirea unei hărți„de administrare" cu evaluare periodică va oferi locuri indemne și va putea menține funcționalitatea insulinoterapiei.

Cuvinte cheie: diabet zaharat, tratament subcutanat cu insulină, ultrasonografie, distrofii subcutanate, hartă ultrasonografică.

Introduction

Insulin treated diabetic patients are using insulin subcutaneous injections, performed by needles as boluses or by a continuous insulin infusion system (insulin pump). In order to preserve their pharmacokinetics, insulin should be injected into specific undamaged subcutis areas. This daily insulin treatment used for years or decades (1 to 5 administrations as boluses), represents a complex medical ritual. Often neglected, minimized, or under diagnosed by clinicians, local tissue dystrophies are the consequence of repeated trauma in the same areas [1,2,3]. These well-known side effects are clinically represented by different appearances: lipohypertrophy, lipoatrophy, nodules with or without inflammatory reactions and dermal dystrophy. These dystrophies have been known to evidence within 2-3 months after the initiation of insulin therapy especially in children. The cause can-

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not be attributed only to the lack of a specific education. Insulin absorption from these areas becomes erratic and unpredictable, leading to a glycaemic unbalance [1,3,4]. Ultrasonographic (US) interrogation of insulin injected areas is not currently available anywhere. There is a paucity of written evidence regarding this subject. The objective of this study was to evidence these abnormal areas by observing their characteristics using US. The next step could be to observe their dynamics, after avoiding injections for a while. Until now, there has been no published data about the recovered areas using US. The mapping, for a given surface, of the damaged and healthy areas is a MUST for a long life injected therapy.

Patients and methods

The consent of our patients as well as the ethical approval from the local committee was obtained. A descriptive study on 40 diabetic subjects, under insulin treatment using subcutaneous insulin injections has been conducted. There were 14 males and 26 females with an age range between 15 and 65 years. The time frame for insulin injections was between 3 and 35 years. The number of insulin boluses made by penfill devices varied from 1 to 5/day. Many of the patients, due to different reasons re-used the needles and did not tailor the injection technique and needles length for a given injected area. All 40 patients showed local complications in or around the injected sites. The upper and the lower abdomen, the anterior and the lateral aspects of thighs and arms as well as the buttocks are usually the recommended areas to be injected [1]. By clinical exam, the nodular or diffuse subcutaneous hypertrophy, the subcutaneous atrophy and the inflammatory-like areas were carefully inspected, palpated and recorded as photos for educational reasons. Clinically abnormal appearances were US interrogated. Normal areas near the affected ones were considered as reference. The normal dermis is homogenously hyperechoic (by comparison with subdermal fatty tissue) and ranges between 1 to 4 mm in thickness. The boundary between dermis and the subcutis layer is normally regular and well defined. The subcutis tissue offers US a hypoechoic background, meaning fat lobules and a hyperechoic connective web with very thin septa between lobules. Deeper, the hyperechoic muscularis fasciae can be seen [5]. The affected areas by their thickness, echogenity, echotexture, delineation between dermis, subcutis and muscularis layers as well as the subcutis vasculature were examined. The split screen images compared the affected areas on the left with normal ones on the right. Any abnormal subcutis thickness was defined as hypertrophy or hypotrophy. US appearance of any entirely or partially disturbed hypoechoic subcutis background was considered abnormal. Any irregular or invisible delineation between offended layers was recorded. Different planes were made to minimize the under diagnosis and to look for a low velocity Doppler signal (color and PW). Gentle compression was made throughout examination with no intention to deform and in order to appreciate echotexture, thickness, and shape of tissue abnormalities. We used a diagnostic ultrasound imaging equipment FF sonicUF-750 XT (Fukuda Denshi) and a 7.5-9 MHz linear transducer. Vascularity was defined using color and low-velocity PW interrogation.

Results

Inspection revealed the diagnosis of hypertrophic lipodistrophy for 35 (88%) patients and lipoatrophic areas for 2 (8%) patients. Nodular lesions were diagnosed by palpation in 22 (55%) diabetics patients. Inspection in conjunction with palpation diagnosed 8 (20%) cases of mixed pathology. Clinical exam also put into evidence the discoloring of dermis, not necessarily in conjunction with dermal dystrophy, in 10 (25%) patients. Skin ultrasonography and histology of the offended tissues were out of our research.

B mode US interrogation was performed in split-screen imaged: on the left the offended tissues, on the right the normal ones. Some conspicuous cases are presented.

The following subtypes of subcutaneous lesions were found: – the simplest subcutaneous hypertrophy (12 cases, respectively 30%) (fig 1).

- a hypertrophic nearly-normal echogenic subcutis layer, by comparison with normal tissue: 1.2 cm vs. 0.50 cm
- a paucity of hyperechoic connective septa dispersed by some hypertrophic fatty lobules

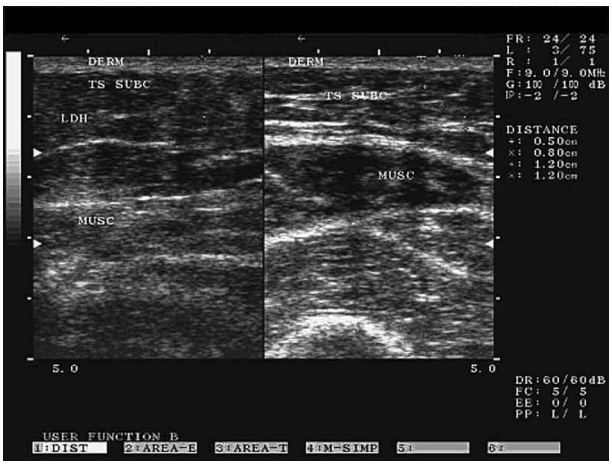


Fig 1. The simplest subcutaneous hypertrophy: 1.2 cm vs 0.5 cm the normal subcutaneous tissue.

– the diffuse hyperechoic subcutaneous dystrophy (22 cases, respectively 55%) (fig 2):

- diffusely inhomogeneous hyperechoic thickened subcutis with no well defined boundary between dermis/subcutis

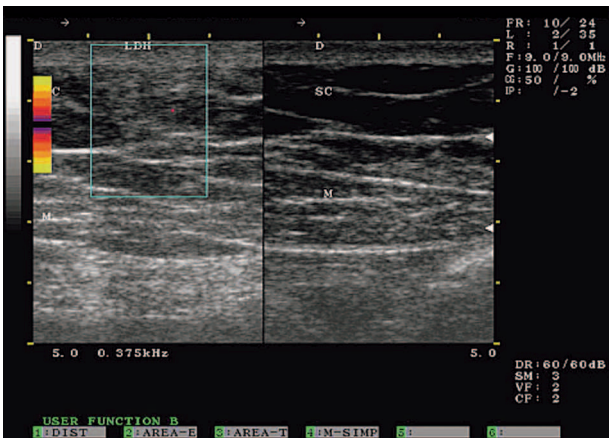


Fig 2. A thickened diffusely hyperechoic subcutis layer making almost invisible the boundary between dermis/subdermis.

– the nodular hyperechoic subcutaneous dystrophy (13 cases, respectively 32.5%) (fig 3):

- an inhomogeneous hyperechoic nodule with a hypoechoic halo within a thickened subcutis layer
- different incidences for color and PW Doppler signal, suggested a possible inflammatory reaction corresponding with the clinical appearance

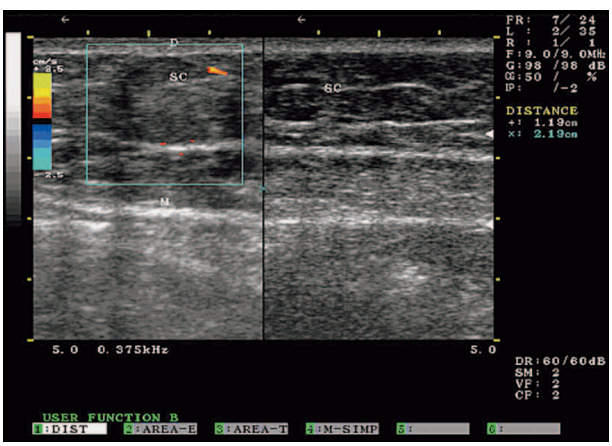


Fig 3. Thickned subcutis presenting a focal hyperechogenic nodular shaped with a hypoechoic halo.

– focal and diffuse hyperechoic subcutis dystrophy (8 cases, respectively 20%) (fig 4):

- apparently normal thickened inhomogeneous hyperechoic subcutis background with nodular shaped echostructure
- fibrotic areas within nodules lead to the acoustic shadowing

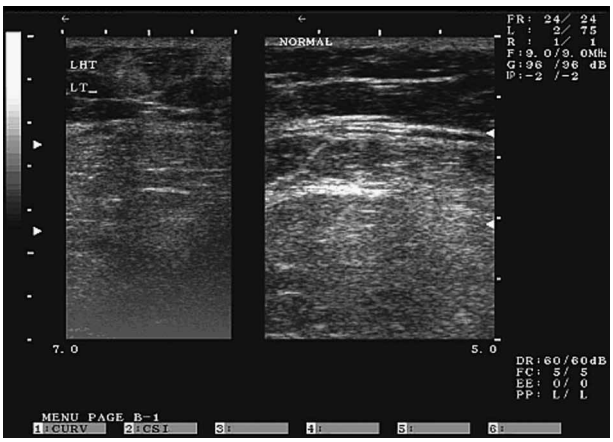


Fig 4. Inhomogeneous hyperechoic subcutis background with normal thickness; nodular shaped echotexture probably containing fibrotic tissue with posterior acoustic shadowing.

– nodular hypoechoic subcutaneous dystrophy (3 cases, respectively 7.5%) (fig 5):

- a thickened subcutis layer heterogeneously hyperechoic making indistinct the delineation between dermis and subcutis
- hypoechoic irregular shaped lesions as part of a macronodular echotexture; they seem to be necrotic or liquefaction areas (a previously haematoma cannot be excluded)

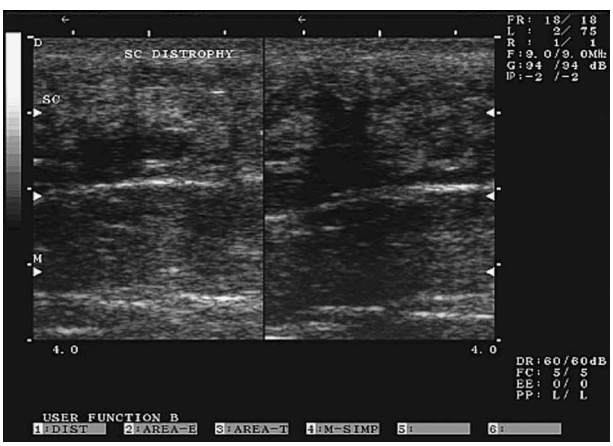


Fig 5. Split screen images of a pathological area showing irregular hypoechoic areas which suggest a necrotic or liquefaction component of a macronodular hyperechoic tissue. A previously large haematoma could also be discussed.

– subcutaneous atrophy (2 cases, respectively 8%) (fig 6).

One of these subjects was a child with an insulin treatment for 3 years. Atrophy seems to be an immunological consequence:

- 0.35 cm thickness of the atrophic area vs. 0.90 cm thickness of the nearby normal one
- a normal boundary between dermis/subcutis

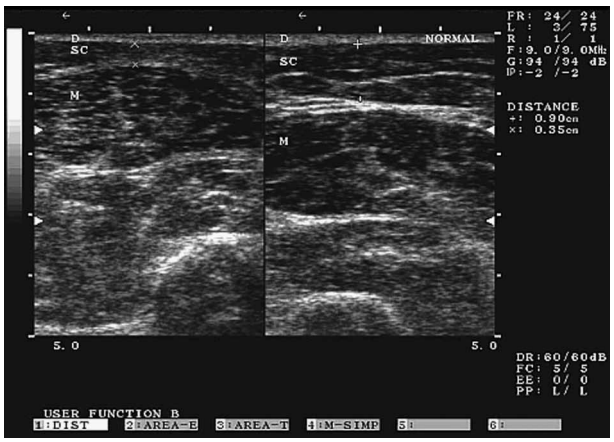


Fig 6. The damaged atrophic subcutis layer of 0.35 cm vs 0.90 cm the normal nearby one.

– a complex multilayer dystrophy (9 cases, respectively 22.5%) (Fig7).

In this category of patients was an insulin treated diabetic patient with central obesity and very thin thighs. The use of an inappropriate insulin injection technique with a needle length of 12.7 mm (longer than that given area requires) had led to a muscle trauma:

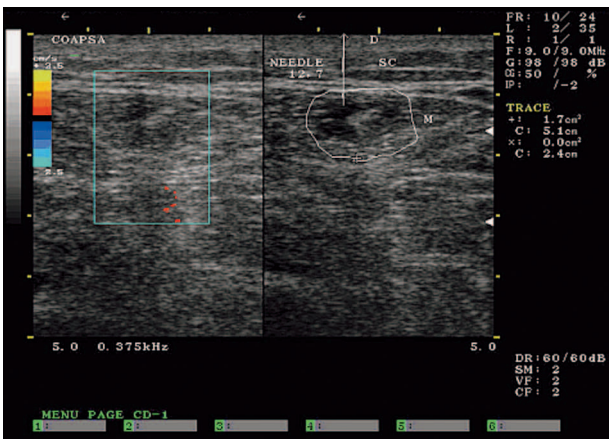


Fig 7. A split screen image of a complex multilayer dystrophy: irregular focal thickend borderless dermis; inhomogenous hyperechoic subcutis; hypo/hyperechoic nodular shaped muscularis echotexture possible due to repeatedly local haemorrhages. A misused injection technique and insulin needle longer (in this case 12,7 mm) than this given area needs for, are two of the offenders.

- irregular boundary between dermis/subcutis layers and a thickened focal dermis mainly visible on the left
- a heterogeneous hyperechogenic subcutis
- inhomogeneous hypo/hyperechoic nodular echotexture within muscle, suggesting haematoma of different ages.

Discussion

Subcutis tissue pathology induced by the injected drugs, including insulin has not yet a large US evidence [6,7,8]. Insulin treatment should be made into undamaged skin and into subcutaneous fat layers in order to maintain its normal absorption. Systematic rotation of injection sites within the same anatomic area (1 cm distance from the previous one), some specific and individualized injection devices and a specific educational program help to avoid dystrophic lesions [1]. The thickness of the subcutis layer depends on the body mass index, fat distribution and anatomical area [1,2,5]. Needle lengths depend on the subcutis thickness of a given area. Inappropriate needle length, repeatedly used, or a vicious injection technique are well-known tissue offenders [2,3,4].

The paucity of clinical signs was in contrast with the multiple abnormal US pathological findings in our study. The same person could present different types of subcutaneous lesions as a result of the aggressive factors previously described. One of our patients became one of these US abnormal entities with violent metabolic and clinical consequences. He was a 64 year-old with a 34 year history of insulin injections and he announced the escalation of his daily insulin dosage. Previously he had used 70-80 u/day but at admission he was using 205 u/day in order to maintain the same glycaemical values. This schedule had been self made, on the basis of his self monitoring. The inspection of the heavily injected areas for decades, below the navel, showed some reddish, warmer hypertrophic areas, spontaneously painless, except when injected. Palpation revealed some deeper nodular entities. A complex US substrate of the affected areas was revealed. A hypertrophic inhomogeneous hyperechoic subcutis with hypoechoic halo encircled nodules; not clearly delineated dermis/subcutis boundary; some linear hyperechoic entities suggested a fibrotic reaction to the long-lasting trauma (fig 8). Color and a low velocity PW Doppler signals were also recorded. US examination suggested an ongoing macro nodular echotexture supported probably by cellulites. Many hypoechoic strands, tend to separate fat lobules which remain relatively hyperechoic by comparison, suggesting an inflammatory edema (not necessarily an infectious one). Deeper, some irregular hypoechoic echotexture probably related to a posthaemorrhagic fat

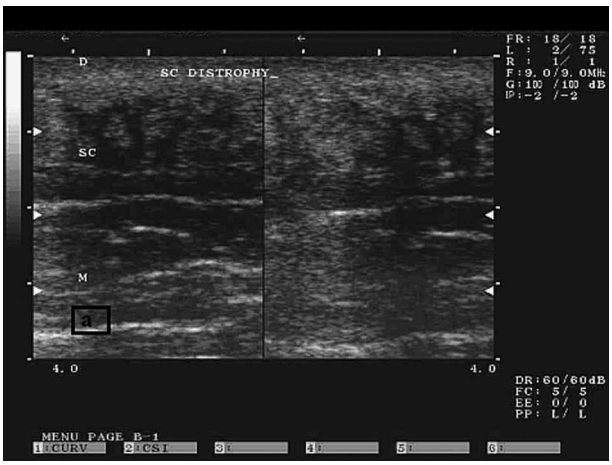


Fig 8. A split screen image of a damaged hyperechogenic subcutis layer with fat lobules encircled by larger hypoechoic strands suggest an advanced nodular shaped edema. The inner and the deeper irregular hypoechogenicity do not exclude fat necrosis as a consequence of haemorrhages.

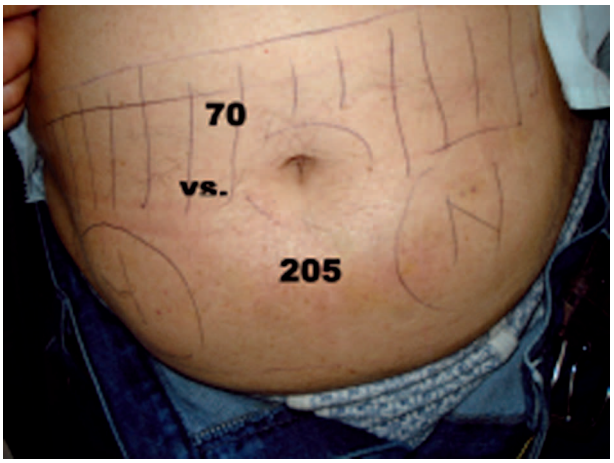


Fig 9. Hypertrophic areas below navel, reddish and warmer by comparison with the above navel areas. No spontaneously pain only when injected. Palpation reveals some deeper and firmless nodules (marked N in this photo). Erratically insulin absorption from these areas was claiming much more insulin for an almost normal response. Looking for another undamaged area (grid above navel) is mandatory in order to restore insulin demands (205u vs 70u).

necrosis process could be seen. We decided to inject the normal areas above the navel, with a rapid and dramatic decreasing of the insulin dosage to 70u roughly/day (fig 9). These types of subcutaneous lesions are already described in literature [5,9,10].

Subcutaneous insulin absorption is a resultant of insulin qualities (short, intermediate, long acting or analog variants, physico-chemical characteristics) added to the physiological factors [11] and to the specific insulin injection devices and techniques. Besides all of these known factors, an immunological reaction cannot be excluded at least for the atrophic forms. A repeated trauma in a given place adds mechanical disruption, a sterile or infectious inflammation by itself [5]. Because of this fatty reconstruction by overusing of a given place, a slower or faster anyway unpredictable insulin absorption is reached. Patients must preserve as many areas possible where they need to make injections because of their long life treatment.

Further studies are needed for assessing the evolution of these lesions and the time required for their resolution.

Conclusions

Carefully and periodically inspection for insulin injection sites should be made, in order to diagnose insulin injected dystrophies. Ultrasonographic appearances must be added to the clinical ones. The insulin treated patients, irrespective of their age, cannot afford to damage many areas during their life-time injection treatment. Due to this fact a US map of the abnormal and available areas should be periodically made.

Competing interest
No conflict of interest.

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