Case Report

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Scleredema Diabeticorum in a Patient with Type 2 Diabetes Mellitus

Tip 2 Diabetes Mellitus Hastasında Diyabetik Sklerödem

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Abstract

Scleredema is a rare skin disease and clinically presents as diffuse, painless induration and thickening of the skin. Scleredema diabeticorum is usually slowly progressive and characterized by insidious onset and tends to be persistent. This type of scleredema primarily affects middle-aged and obese adults. Typically, affected area is the upper part of the body including the posterior neck, interscapular region and the chest. It usually develops in subjects with diabetes mellitus of long duration and poor metabolic control. We discussed a case of scleredema in a 54-year-old woman with a history of diabetes mellitus.
Keywords: Scleredema diabeticorum, diabetes mellitus, skin complications

Öz

Sklerödem nadir bir deri hastalığıdır ve klinik olarak derinin diffüz, ağrısız endürasyonu ve kalınlaşması şeklinde görülür. Diyabetik sklerödem, sinsi başlangıç ile karakterize, genellikle yavaş ilerleyici ve kalıcı olma eğilimindedir. Bu tür sklerödem öncelikle orta yaşlı ve obez erişkinleri etkiler. Genellikle etkilenen bölgeler; interskapular bölge, göğüs ve boynun arka tarafı gibi vücudun üst kısımlarıdır. Genellikle uzun süreli ve kötü metabolik kontrollü diyabet hastalığı olan kişilerde gelişir. Burada sklerödemi olan 54 yaşında tip 2 diabetes mellitusu olan bir kadın hasta tartışılmıştır.
Anahtar kelimeler: Diyabetik sklerödem, diabetes mellitus, deri komplikasyonları

Introduction

Scleredema is a rare skin disease and clinically presents as diffuse, painless induration and thickening of the skin. It primarily affects the upper part of the body including the neck, shoulders and the upper back. Sometimes erythema and "peau d'orange" appearance might be seen. Morbidity is usually due to impaired mobility secondary to thickening of the skin (1). Scleredema usually occurs in association with diabetes mellitus, infections (especially of streptococcal origin) or monoclonal gammopathy (2). However, hyperparathyroidism (3), malignant insulinoma (4), carcinoid tumor (5) and drug reactions (6) should be considered in differential diagnosis. Tumor necrosis factor alpha (TNF-alpha) blocking agent-, infliximab, induced scleredema has been reported. Infection-related scleredema is characterized by a sudden onset and often shows complete clinical recovery after several months (1,7,8). Monoclonal gammopathy-associated scleredema is characterized by slow onset and slow progression; usually spontaneous recovery does not occur (2,9). The most common form of scleredema is associated with diabetes mellitus and also called as scleredema diabeticorum.

Scleredema diabeticorum is usually slowly progressive and characterized by insidious onset and tends to be persistent. This type of scleredema primarily affects middle-aged and obese adults. Typically, affected areas include the posterior neck, interscapular region and the chest (10). It usually develops in subjects with diabetes mellitus of long duration and poor metabolic control, however, there is no clear relationship between prognosis and control of the blood glucose levels (11). The pathogenesis of scleredema diabeticorum is not clear. The proposed mechanism is that; irreversible glycosylation of collagen and alterations in collagenase activity may lead to altered degradation and excessive accumulation of collagen (12). Furthermore; it is believed that, microvascular damage and hypoxia may contribute to the etiopathogenesis (13).

We discussed a case of scleredema in a 54-year-old woman with a history of diabetes mellitus.

Case Report

A 54-year-old woman with a history of long-standing, poorly-controlled diabetes mellitus, hypertension and coronary artery

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disease was referred to our department of endocrinology. She had a history of diabetes mellitus for 17 years and has been on insulin therapy for 6 years. Recently, she was diagnosed with diabetic neuropathy and non-proliferative retinopathy. Diabetic nephropathy was not detected. In anamnesis, she complained of gradually-developing and hardening erythematous plaques on the neck and upper back. She denied having any illnesses including infections and she did not remember any fevers, chills, nausea, vomiting, diarrhea, or weight loss when the lesion appeared. She had been using metformin (2000 mg/day), premixed insulin (50 U/day), carvedilol (6,25 mg/day), ramipril (2.5 mg/day), rosuvastatin (10 mg/day), and acetylsalicylic acid (100 mg/day). Physical examination revealed 84 kgs of weight and 155 cms of height. Body mass index was calculated as 35 kg/m^2. Her blood pressure was 130/80 mm/Hg. Edematous, erythematous plaques on the posterior neck and upper back were seen on examination (Figure 1). Other systemic evaluations were normal. A complete blood count and comprehensive biochemical panel were normal with the exception of a fasting blood glucose level of 277 mg/dL. Urinalysis showed glycosuria and no protein. Hemoglobin A1C (HbA_{1c}) was 11.8%. The patient was examined by a dermatologist and skin biopsy was performed. On histopathologic examination, epidermis was normal but there was prominent separation of collagen fibers throughout the dermis in addition to the thickening of the dermis and the coarsening of collagen (Figure 2A and 2B). Focal alcian blue-positive mucine was also detected (Figure 2B inset). Histopathological findings were consistent with scleredema. She showed no signs of infection. Urine test was negative for urine infection and group A streptococcal infection was excluded by the throat culture. The erythrocyte sedimentation rate and C-reactive protein levels were within the normal range. Anti-Scl-70 antibodies and anti-nuclear antibody levels were also within the normal range. Serum protein electrophoresis and immunofixation was performed and a monoclonal gammopathy was excluded. There was no history of TNF-alpha inhibitor drug use and scleredema related to the drug reactions was also excluded. Scleredema was thought to be secondary to diabetes. She was started on intensive insulin regimen and glucose levels decreased to the normal range. For diabetic neuropathy, she was started on gabapentin therapy. For scleredema, she was started on local psoralen ultra-violet A (PUVA) therapy. After 2 months of the therapy, the redness and the edema of the skin partially disappeared, the mobility of the back improved, and the skin of the upper back was softer.

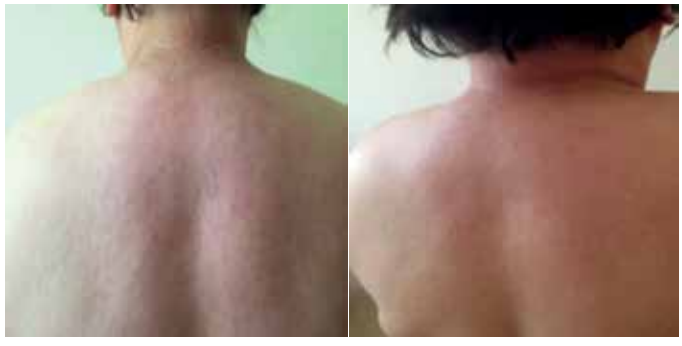

Figure 1. Scleredema in the upper back and interscapular region of the patient

Discussion

In the literature search, scleredema diabeticorum usually developed in obese subjects with long-standing and poorly controlled diabetes mellitus, usually complicated with diabetic microangiopathy (1,14,15,16). In a review of 7 cases of scleredema diabeticorum, the mean age at onset was 54 years, the mean duration of diabetes was 13 years and the patients reported to have a high frequency of diabetic complications (17). Our patient was obese, had poorly controlled diabetes mellitus and had microvascular complications consistent with the cases in

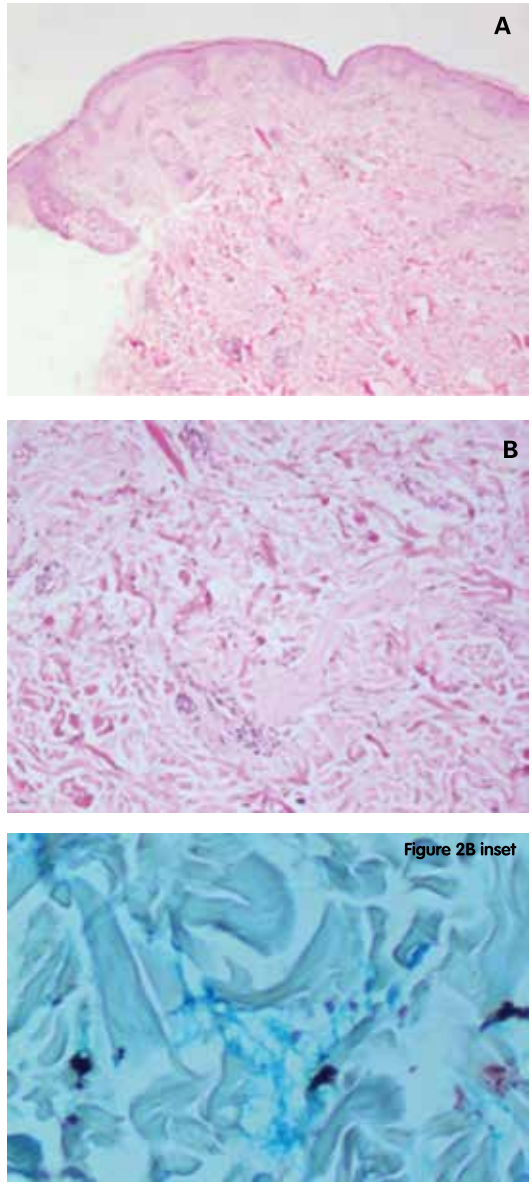

Figure 2. A, B) Low power view of the skin biopsy. Separation of the collagens may be seen in this power (A) but more easily detectable at higher magnification (B). Alcian blue positive focal musin was detected at the deep dermis (B inset) (Ax40, Bx100, Cx200)

the literature. The pathogenesis of scleredema diabeticorum is largely unknown. The proposed hypothesis suggests that hyperglycemic metabolic state leads to fibroblast activation and increased collagen and causes scleredema. However, it was reported in the literature that scleredema might develop in a poorly controlled diabetes mellitus and it might appear before the diabetic complications occurred (11). In this report, it was noted that this mechanism was thought to be not enough to explain the pathology as the signs of microvascular complications appeared later than the development of the skin disorder.

It is possible to diagnose scleredema clinically, however, biopsy should be performed for definitive diagnosis. Histopathologic findings include normal epidermis, thickening of the reticular dermis, absence of fibroblast proliferation and reduced elastic fibers. Slight perivascular lymphocytic infiltrates are usually seen by microscopic examination (9,18). Several treatments including antibiotics, immunosuppressants, chemotherapy, radiation therapy, tamoxifen, and phototherapy have been tried, but there is no established treatment for the disease. If infection is confirmed, antibiotics can be used. In scleredema diabeticorum, tight glicemic control is the first step of the treatment, although there is no clear relationship between glucose control and disease prognosis (11). In few reports it was noted that tight glicemic control produced an amelioration of the scleredema. In a review of four diabetic cases, scleredema improved partially after a decrease in HbA_{1c} from 9.3 to 7.9% (19). In another report, in five patients of 11 who had scleredema secondary to diabetes, lesions were partially improved after tight glicemic control (15).

Different therapeutic modalities with variable successes have been reported as case reports or small case series. There is no comparative data and no approved algorithm for scleredema treatment. The efficiency of phototherapy, including UVA-1 treatment, PUVA therapy, narrow-band ultraviolet B phototherapy and photophoresis has been reported in the literature (20,21,22,23,24,25,26,27,28). In a few case reports, good results have been obtained with electron-beam therapy (29) and tamoxifen (30) therapy in scleredema diabeticorum. Immunosuppressants, including methotrexate and corticosteroids have been examined but the benefit was not clear (31,32). Several authors have also reported some benefits with various types of radiation therapy (33,34). The real mechanism of PUVA being of benefit on scleredema may be related to an increase in collagenase synthesis by fibroblasts and by inhibiting de novo synthesis of type 1 collagen (35). Brenner et al. (36) concluded that because of the paucity of valid therapeutic alternatives, phototherapy and photochemotherapy with UVA1 or PUVA may also be useful in scleroderma.

Fibrosing disorders, such as scleroderma and scleromyxedema are associated with scleroderma like skin changes and included in the differential diagnosis of diabetic scleredema. Scleroderma can be differentiated easily from scleredema by the presence of raynaud phenomenon, antinuclear antibodies, extractable nuclear antibodies like anti-SCL-70 and anticentromere antibodies and the distribution of sclerosis. Unlike scleredema, skin involvement of scleroderma usually begins at the hands and distal extremities. Scleromyxedema is a rare condition associated with monoclonal gammopathy and characterized by massive accumulation of mucin in the skin. Clinically, scleromyxedema appears as indurated plaques and erythematous firm papules. Histopathologic findings play an essential role in the differential diagnosis. Unlike scleredema, fibroblast proliferation in the dermis is a characteristic histopathologic feature of scleromyxedema (10,37).

In conclusion; scleredema diabeticorum is a rare complication of diabetes. It can be clinically and histopatologically differentiated from other fibrosing disorders. In diabetic patients with scleredema, it is recommended to perform a serum protein electrophoresis for the definitive diagnosis as the monoclonal gammopathy is one of the causes of scleredema. There are different approaches for the treatment. Tight glycemic control is recommended but the efficiency has not been proven. Ultraviolet A-1 phototherapy and PUVA seem to be the most effective treatments for this disease.

Ethics

Informed Consent: It was taken.
Peer-review: Externally and Internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: Işılay Kalan Sarı, Mukadder Koçak, Şenay Arıkan Durmaz, Önder Bozdoğan, Concept: Işılay Kalan Sarı, Şenay Arıkan Durmaz, Design: Işılay Kalan Sarı, Data Collection or Processing: Işılay Kalan Sarı, Mukadder Koçak, Şenay Arıkan Durmaz, Önder Bozdoğan, Analysis or Interpretation: Işılay Kalan Sarı, Mukadder Koçak, Şenay Arıkan Durmaz, Önder Bozdoğan, Literature Search: Işılay Kalan Sarı, Mukadder Koçak, Writing: Işılay Kalan Sarı.
Conflict of Interest: No conflict of interest was declared by the authors.
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