Reumatologia 2017; 55, 2: 104–107
DOI: https://doi.org/10.5114/reum.2017.67607

Coexistence of diabetes mellitus type 1 with diffuse systemic sclerosis – case report and literature review

Ewa Wielosz[1], Maria Kurowska[2], Dorota Suszek[1], Maria Majdan[1]

[1]Department of Rheumatology and Connective Tissue Diseases, Medical University, Lublin, Poland
[2]Department of Endocrynology, Medical University, Lublin, Poland

Abstract

Diabetic sclerodactyly is a frequently recognized skin finding that may occur in patients with diabetes mellitus but coexistence of diabetes and systemic sclerosis is rare. We describe a case of coexistence of type 1 diabetes mellitus and systemic sclerosis in 42-year-old man with the history of Raynaud's phenomenon, progressive diffuse hardening of the skin and sclerodactyly, slowly worsening with time. The medical history included type 1 diabetes since childhood with microvascular complications. The patient presented a typical capillaroscopic scleroderma-like pattern, antinuclear antibodies and sclerotic lesions in gastrointestinal system. Summing up, our case represents the rare coexistence of autoimmune diseases like diabetes mellitus type 1 and systemic sclerosis.

Key words: capillaroscopy, diabetes mellitus type 1, diffuse systemic sclerosis, scleroderma-like lesions.

Introduction

In many patients skin changes are the markers of pathological processes taking place inside the body. They often accompany metabolic and/or endocrine conditions including diabetes, thyroid diseases, systemic connective tissue diseases like systemic lupus erythematosus and systemic sclerosis (SSc), and many others [1–5].

One of the diabetic skin conditions is the scleroderma-like syndrome. Its prevalence, according to various authors, ranges from 8% to 50% [1–3]. These changes consist in thickening and hardening of skin of the dorsal part of hands, in particular fingers, with limited joint mobility and contractures, and are defined as diabetic sclerodactyly [3].

Another skin complication of diabetes is diabetic scleroderma. The skin hardening involves the skin of face, nape, shoulders, upper parts of the trunk, upper arms. It occurs in approximately 2.5–3% of patients with diabetes [1, 4]. Scleroderma-like syndromes in the course of long-term diabetes with coexisting complications are observed quite frequently while the coexistence of diabetes with SSc is rare.

This paper describes a case of 42-year-old man with diabetes mellitus type 1 lasting for 27 years who was diagnosed with systemic sclerosis; it also presents the conducted differential diagnostics and introduced treatment.

Case report

A 42-year-old patient with suspected systemic sclerosis was first admitted to the Department of Rheumatology and Connective Tissue Diseases in Lublin in June 2010. Since the age of 13 he had been treated for diabetes mellitus type 1, at present with complications in the form of retinopathy, nephropathy, neuropathy and macroangiopathy (a history of the diabetic foot). Since 2006 he was treated for hypothyreosis in the course of Hashimoto's thyroiditis. In June 2008 the patient underwent the implantation of a hip endoprothesis due to aseptic necrosis of the femoral head, and lumbar sympathectomy. Since 2007 the patient observed Raynaud's phenomenon, progressive hardening of the skin of face, neck, décolletage, hands; he had difficulties with straightening his hands, dysphagia, pain in small joints

Address for correspondence:
Ewa Wielosz, Department of Rheumatology and Connective Tissue Diseases, Medical University of Lublin, Jaczewskiego 8, 20-090 Lublin, Poland, e-mail: ewa.wielosz@wp.pl

Submitted: 14.03.2017, **Accepted:** 7.04.2017

of fingers and toes, worsening effort tolerance. Serological tests performed in 2007 proved the presence of antinuclear antibodies with 1 : 10240 titre with antinuclear fluorescence pattern.

The physical examination confirmed sclerodactyly, hardening and smoothing of the skin of face, neck, front part of the chest, contractures in the metacarpophalangeal and proximal interphalangeal joints. No abnormalities within the respiratory or circulatory system were found.

The laboratory test results included normal values of ESR, CRP, and blood picture within the normal range. Decreased GFR (creatinine 1.3 mg/dl; eGFR – 64 ml/min), without changes in urinalysis results was observed. The arterial blood gasometry parameters (pO_2 – 94 mm Hg; pCO_2 – 40.7 mm Hg, saturation – 98%) were also within the normal range. In serological tests by indirect immunofluorescence, the presence of antinuclear antibodies with 1 : 5120 titre with nucleolar fluorescence pattern was observed; no ENA or anti-dsDNA antibodies, antiphospholipid antibodies or ANCAs were found.

In the esophagoscopy, the smoothing out of the folds of mucous membrane, spastic cardia, hypotonic esophagus were described; in gastroscopy – erosive esophagitis (GERD LA grade C). High-resolution tomography showed a single parenchymal induration with a diameter of 3 mm located subpleurally in the sixth segment of the left lung. In the echocardiogram, the generalised hypokinesia was found. The mean pulmonary arterial pressure was 25 mm. No abnormalities were found in ECG.

The pulmonary function testing results were also within the normal range: the six-minute walk test – 540 m, diffusing capacity (DLCO) – 98% of predicted, without the features of restriction (TLC – 104% of the normal predicted value).

In the capillaroscopic examination, disorganisation of the microvascular array, numerous megacapillaries, branching capillaries, microbleeding and avascular areas were observed.

The radiological examination of hands and feet showed periarticular osteoporosis with the stricture of interphalangeal joints of hands, subluxations in interphalangeal joints of feet, massive calcification in arterial walls of both hands.

No pathological changes were observed in the ultrasound examination of the thyroid gland and abdominal cavity.

In the histopathologic examination of the skin section in the upper arm region, extensive hardening of the collagen of the dermis, thinning of the epidermis, decreased number of skin appendages were observed.

Based on the clinical picture and further tests, diffuse systemic sclerosis with gastrointestinal manifestations was diagnosed. The treatment with cyclophosphamide given in monthly intravenous infusions was initiated. Until January 2011 the patient received in total 2.8 g of the drug with good tolerance. Azathioprine was administered as a continuation therapy. Additionally he received insulin given in subcutaneous injections 6–7 times/24 hours, hypotensive drugs (amlodipine, carvedilol, furosemide, losartan), carbamazepine, acetylsalicylic acid and thyroxine. In course of observation, the condition of patient was stable. He didn't develop neoplastic disease.

Discussion

Skin lesions in diabetes mellitus develop most often as the consequence of long-term disease. They can be divided into changes pathogenetically associated with diabetes, including among others scleroderma-like syndrome and diabetic scleroderma as well as changes in the course of infections, diabetic complications and drug-induced skin changes [5]. According to literature data, the scleroderma-like syndrome and diabetic sclerodactyly in particular is – next to dry skin – the most common skin manifestation of diabetes mellitus type 1 and is strongly related to the duration of the disease [6]. The etiopathogenesis of scleroderma-like conditions in diabetes mellitus has not been definitively established although its relationship with the nonenzymatic glycation of collagen has been suggested; high blood glucose levels may also stimulate the proliferation of fibroblasts and production of other components of extracellular matrix resulting in skin hardening [5, 7].

In many cases, the differentiation of histopathological changes in diabetic scleroderma-like syndrome from changes in the course of systemic sclerosis can be difficult [7].

The prevalence of diabetic sclerodactyly increases significantly in patients with diabetes occurring before 15 years of age and the disease duration > 5 years [6]. According to some authors the prevalence of scleroderma-like conditions is related to the presence of vascular complications in diabetes and frequent blood glucose fluctuations [6], the opinions however differ because, according to Yosipovitch et al. [8], no relationship between the occurrence of scleroderma-like changes and diabetic microangiopathy and metabolic control in young patients with diabetes mellitus type 1 has been confirmed. In turn, the correlation between the presence of skin changes and contractures was established [8]. Pavlovič et al. [6] examined 212 patients with diabetes mellitus type 1, young men in majority, and found that the scleroderma-like changes were more common in the group with three times longer duration of the disease.

The patient we describe in this paper is a man with long-term diabetes which developed before the age of 15. The disease was associated with numerous late complications including retinopathy, nephropathy, neuropathy or diabetic macroangiopathy. The major diagnostic issue in this patient was the differentiation between diabetic skin hardening and skin changes in systemic sclerosis. The hardening of the skin of fingers and toes with contractures developed after many years of the disease. Numerous data suggested that the skin findings in our patient can be the late complication (symptom) of diabetes mellitus type 1. The arguments against this opinion included, apart from sclerodactyly, the presence of generalised features of sclerosis on the skin of face, neck and décolletage. They are more supportive of the SSc diagnosis. In the works of Yosipovitch et al. [8] the diffuse skin hardening covering in particular the neck, upper part of the back, arms and thighs was observed only in 6% of patients with long-term diabetes mellitus type 1. The changes of this kind defined as diabetic scleroderma are observed more often in obese elderly patients with diabetes mellitus type 2 [8]. The patient we describe here is a young slim man with diabetes mellitus type 1.

The histopathology was typical for the diagnosis of systemic sclerosis. Nevertheless, the histopathological changes not always allow differentiation and the diffuse skin hardening can also be associated with diabetes.

Sclerodactyly can occur in both cases. There are however a few features which allow differentiating these conditions. The Raynaud's phenomenon is not observed in sclerodactyly or diabetic scleroderma while it occurs in approximately 99% of patients with systemic sclerosis [7, 9]. The test which enables the differentiation of SSc from scleroderma-like syndromes in the course of diabetes is capillaroscopy, which shows the microcirculation abnormalities in nailfold capillaries. In the advanced diabetes mellitus, the capillaroscopic changes characterised with the reduced blood flow in capillaries can be observed, without, however, changes typical for scleroderma microangiopathy like megacapillaries or avascular areas [10].

Another differentiating symptom is the presence of autoantibodies typical for SSc, i.e. anti-centromere antibodies oranti-Scl-70 antibodies, calcinosis, teleangiectasias or interstitial lung disease which are not observed in diabetic patients [7, 9].

Dysphagia may be indicative of both SSc and diabetic complications. In the described case the diagnosis of SSc was supported by the long-term Raynaud's phenomenon, typical scleroderma microangiopathy, dilatation of esophagus and the presence of antinuclear antibodies in high titres. Yet, it cannot be excluded that skin changes in the course of long-term diabetes mellitus type 1 overlap with scleroderma skin changes.

The literature presents many reports of sclerodactyly in diabetes [5–7, 11].

The cases of coexistence of diabetes mellitus with systemic sclerosis are scarce. However, both diabetes mellitus type 1 and SSc are autoimmune diseases, so their coexistence is realisable. The literature describes the case of coexistence of diabetes mellitus type 1, morphea and celiac disease in an 11-year-old girl and the case of coexistence of diabetes mellitus type 1, celiac disease, systemic lupus erythematosus and SSc in a 15-year-old girl as the results of multidirectional autoimmunisation [12, 13]. In the literature, we didn't find any other such cases. Although, Peralta-Amaro et al. [14] described prevalence of metabolic syndrome and insulin resistance in SSc and they found that 36% of patients presented metabolic disturbances in SSc.

It is commonly known that the autoimmune diseases with the presence of organ specific antibodies like diabetes mellitus type 1 or autoimmune thyroiditis can coexist with diseases characterised by non-organ specific antibodies like SSc or other systemic connective tissue diseases. It is also well-known that different autoimmune diseases may coexists together. Moreover, Koumakis et al. demonstrated, that diabetes mellitus type 1 is more likely to occur in first-degree relatives of patients with SSc. To conclude, autoimmune diseases cluster within families of patients with SSc [15].

Summing up, our case represents the rare coexistence of autoimmune diseases like diabetes mellitus type 1 and systemic sclerosis. The diagnostic problems relating to the differentiation of skin lesions in the course of diabetes mellitus from skin changes in the course of SSc requiring detailed analysis and numerous additional serological tests and imaging have to be emphasised.

Given the fast progressing and highly intensified skin changes, pathology of gastrointestinal tract, high titres of autoantibodies, the treatment with intravenous cyclophosphamide for 6 months was introduced according to the regimen applied in systemic sclerosis, followed by the immunosuppressive treatment with azathioprine.

The authors declare no conflict of interest.

References

1. Kłubo-Gwieździńska J, Juniuk R. Zmiany skórne jako markery chorób gruczołów dokrewnych. Endokrynol Pol 2003; 54: 203-210.
2. Thiboutot DM. Dermatological manifestations of endocrine disorders. J Clin Endocrinol Metabol 1995; 80: 3082-3088.

3. Levin NA, Greer KE. Cutaneous manifestations of endocrine disorders. Dermatol Nursing 2001; 13: 185-195.
4. Kenneth R, Feingold MD, Elias PM. Endocrine-skin interactions – cutaneous manifestations of pituitary disease, thyroid disease, calcium disorders and diabetes. J Am Acad Dermatol 1987; 17: 921-940.
5. Al-Mutari N. Skin diseases seen in diabetes mellitus. Bull Kuwait Inst Med Spec 2006; 5: 30-39.
6. Pavlović MD, Milenković T, Dinić M, et al. The prevalence of cutaneous manifestations in young patients with type 1 diabetes. Diabetes Care 2007; 30: 1964-1967.
7. Gruson LM, Franks A. Scleroderma and diabetic sclerodactyly. Dermatol Online J 2005; 11: 3.
8. Yosipovitch G, Hodak E, Vardi P, et al. The prevalence of cutaneous manifestations In IDDM patients and their association with diabetes risk factors and microvascular complications. Diabetes Care 1998; 21: 506-509.
9. Foti R, Leonardi R, Rondinone R, et al. Scleroderma-like disorders. Autoimmun Rev 2008; 7: 331-339.
10. Lambova SN, Muller-Ladner U. The specificity of capillaroscopic pattern in connective autoimmune diseases. A comparison with microvascular changes in diseases of social importance: arterial hypertension and diabetes mellitus. Mod Rheumatol 2009; 19: 600-605.
11. Haustein UF. Scleroderma-like lesions in insulin-dependent diabetes mellitus. J Eur Acad Dermatol Venereol 1999; 13: 50-53.
12. Firoz EF, Kamino H, Lehman TJ, et al. Morphea, diabetes mellitus type 1, and celiac disease: case report and reviev of the literature. Pediatr Dermatol 2010; 27: 48-52.
13. Zeglaoui H, Landolsi H, Mankai A, et al. Type 1 diabetes mellitus, celiac disease, systemic lupus erythematosus and systemic scleroderma in a 15-year-old girl. Rheum Int 2010; 30: 793-795.
14. Peralta-Amaro AL, Cruz-Dominguez Mdel P, Olvera-Acevedo A, et al. Prevalence of metabolic syndrome and insulin resistance in systemic sclerosis. Rev Med Inst Mex Seguro Soc 2015; 53: 476-483.
15. Koumakis E, Dieude P, Avouac J, et al. Familial autoimmunity in systemic sclerosis- results of a French-based case control family study. J Rheumatol 2012; 39: 532-538.