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Diabetic Scleredema

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TOYOTA, T., UMEZU, M., OIKAWA, N., SANOYAMA, R., SUZUKI, S., SUZUKI, H., NAKAJIMA, Y. and GOTO, Y. *Diabetic Scleredema*. Tohoku J. exp. Med., 1983, **141** (4) 457-461 —— Many skin lesions are specific for diabetes mellitus. Necrobiosis lipoidica, lipoatrophy and idiopathic bullae (bullosis diabeticorum) are usually associated with diabetes. However, diabetic scleredema has not been noticed by internists, although dermatologists have paid attention to such a cutaneous manifestation. We reported a clinical case of a female diabetic patient aged 15 who had been afflicted with diabetic scleredema. She had been treated with insulin since 5 years of age. She noticed stiffness of the skin in April 1980. Skin biopsy showed thickness of the dermis and accumulation of acid mucopolysaccharide. After control of blood glucose with continuous subcutaneous insulin infusion (CSII) and administration of tocopherol acetate and hyaluronidase, the skin lesion improved. Etiology of diabetic scleredema is unknown. Such skin lesion which is observed frequently in insulin dependent obese patients is different from a category of scleredema of Buschke. ———— diabetic scleredema ; insulin ; hyaluronic acid

Krakowski et al. (1973) described clinical features of diabetic scleredema which has been considered as a dermatome in diabetic patients. The skin lesion should be discriminated from the classical form of scleredema of Buschke (1900), which is preceded by some acute infectious illness and occurs with about equal frequency in children and adults.

Diabetic scleredema comes out in some diabetic patients who are usually severe and resistant to insulin. All patients reported by Krakowski et al. (1973) were obese. As sufficient details have been not always available in the literature, we can hardly understand completely the entity of the skin lesion. Recently in a female patient with juvenile insulin-dependent diabetes, scleredema occurred. We describe the patient with diabetic scleredema and summarize clinical features of a hundred patients with such a skin lesion reported in the literature.

CASE REPORT

Female, aged 15 with a 10-year history of diabetes. She had been treated

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with lente insulin since the onset of diabetes at 5 years of age. In August 1979, the lente insulin was substituted for NPH insulin, 60 units (Retard Leo insulin, Nordisk), but it was very difficult to control blood glucose. In April 1980, she felt stiff lower extremities and gained body weight. The skin lesion was extended to whole body except the legs.

The skin biopsy revealed swelling and splitting of the collagenous bundles. The findings were consistent with those of diabetic scleredema. On January 22, 1981 she entered Tohoku University Hospital.

Physical examination showed obesity. She was 147 cm in height and 62 kg in body weight (Fig. 1). There was systolic murmur, most intense over the pulmonic valve area. Palpation of the liver was unable because of stiffness of the abdomen. The tendon reflexes in the lower extremities were decreased. The skin in the region of the face, neck, shoulder, upper back and sides of the abdomen was thickened and hard. Tenderness and restriction of motion were noted.

Laboratory findings. The erythrocyte sedimentation rate was increased, 84 mm in an hour and 112 mm in 2 hr. Blood cell count was normal. The fasting blood glucose reached over 500 mg per 100 ml. Creatinine clearance was 15 ml per min. The urine analysis showed a + positive protein, a ## positive glucose and a # ketone body.

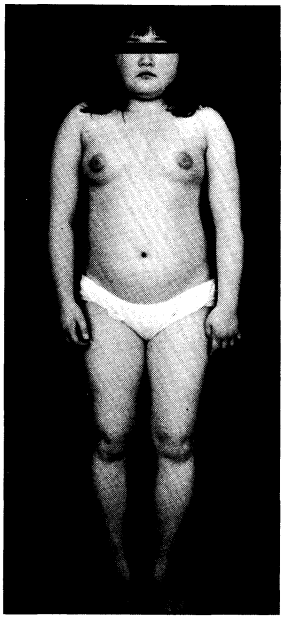

Fig. 1. The present patient. She has been treated with insulin since the onset of diabetes at 5 years of age. The skin is elastic and sclerotic. Neither pigmentation or striae cutis is observed.

On the electrocardiogram sharply increased R-wave at lead II. X-ray of the chest revealed remarkable protrusion of the left second arc of the cardiac silhouette. On the ultrasonogram the liver and spleen were enlarged. BMR was − 3%, T_3 1.3 ng per ml, T_4 5.8 μg per 100 ml, TSH 3.0 μU per ml, being all within normal range. High value of ACTH was suppressed by a small dose of dexamethasone (0.5 mg).

Fundoscopy showed early change of pre-proliferative retinopathy ($Scott_{IIIa}$). Motor and sensory nerve conduction velocities were delayed. The skin biopsy performed on February 19, 1981 showed thickening of the dermis with increased collagenous fibers which were enlarged, scattered and split (Figs. 2 and 3). Deposited substance between collagenous fibers was identified histologically as acid mucopolysaccharide because alcian blue and colloidal iron stains revealed metachromasia which became orthochromatic after the treatment with hyaluronidase.

Course in hospital. The patient complained of stiffness sensation of the skin, restriction of movement and headache. Pitting edema due to latent right cardiac insufficiency was present concomitantly with scleredema. Therefore, we admin-

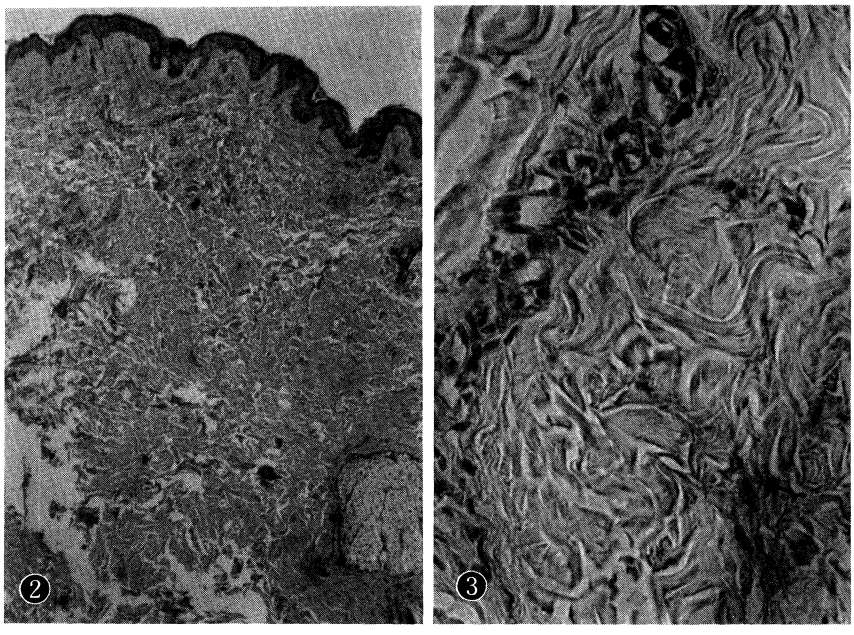

Fig. 2. Histology of the skin of nuchal region (H.E. stain, ×40). Collagenous fibers are increased, enlarged and split. The dermis is replaced by collagenous fibers. Deposited substance between collagenous fibers is identified as acid mucopolysaccharide with alcian blue stain.

Fig. 3. Higher magnification. Splitting of collagenous fibers are remarkable. H.E. stain, × 200.

adminadministered diuretic drug, a tablet of Lasix, to her. After two weeks, pretibial edema disappeared and body weight was decreased from 62 kg to 59.5 kg, albeit sclerotic change of the skin was unchanged. In spite of injections of MC-actrapid insulin 80 units per day, blood glucose was very high and unstable. From February 2, 1981 to March 31, 1981, the continuous subcutaneous insulin infusion (CSII) had been done, resulting in improving her condition slightly. Unfortunately, because retinopathy was worsend, photocoagulation treatment was performed. Conventional therapy of insulin was begun again after completion of CSII therapy. When NPH insulin was injected, she felt increased stiffness of the skin and could fail to move her fingers. Replacement of NPH insulin by lente insulin lessened the stiffness. On June 9, 1981, vitamin E (tocopherol acetate 300 mg per day) was begun. On July 19, hyaluronidase 200-500 units per day was injected subcutaneously every day, continuing until August 31 without evaluating efficacy of hyaluronidase. In September her body weight was 51 kg and the skin lesion was considered to be improved.

Discussion

Although reports of so called scleredema in diabetic patients appeared in 1949, Krakowski et al. (1973) were the first to coin the name diabetic scleredema. We summarized clinical features of a hundred patients with diabetic scleredema in the literature. As shown in Table 1, mean age is 50.8 years old. Ratio of male to female is 1.2. Half of such patients are treated with insulin and more than half

Table *Diabetic scleredema, 100 cases*

	%
Male	54
Female	45
Unknown	1
Treatment	
Insulin	30
Oral drug	13
Diet	2
Unkown	55
Fasting blood glucose (mg per 100 ml)	
Under 140	11
140-180	10
Over 180	33
Unkown	46
Complications	
Retinopathy	34
Neuropathy	14
Nephropathy	11
Macroangiopathy	26
Hypertension	22
Unknown	24

patients are in poor control, showing fasting blood glucose over 180 mg per 100 ml. Seventy-six patients are complicated with diabetic micro- and macroangiopathies. From the literature, diabetic scleredema is confined to adult diabetic patients. The skin lesion tends to occur in insulin treated obese patients.

Our case was typical example of diabetic scleredema except the onset of the skin lesion at her adolescence. Scleredematous skin was caused by an increase in acid mucopolysaccharide due to disturbed metabolism of the mucopolysaccharide in diabetic patients (Fleischmajer and Lara 1965; Fleischmajer et al. 1970). If accumulation of hyaluronic acid was causing diabetic scleredema, injection of hyaluronidase could improve the skin lesion. However, we did not obtain any conclusion with regard to efficacy of hyaluronidase in this case. Vitamin E is a candidate for medicine to improve diabetic scleredema. Prognosis of this skin lesion is poor, without tendency to spontaneous remission.

Finally it is important to descriminate between diabetic scleredema and scleredema of Buschke (1900). The latter form appears in both children and adults, and develops after acute infectious illness of the upper respiratory tract, and disappears within 1.5 years. Usually antimicrobial drugs, adrenocortical hormone, hyaluronidase and vitamin E are used for the therapy. Up to now, diabetic scleredema has not been paid enough attention it deserves. If we look for the skin lesion in diabetic patients, we will be finding more frequently such a lesion. It is necessary to inspect carefully the nuchal region of diabetic patients.

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