Acanthosis Nigricans Associated with Vitiligo

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Acanthsis nigricans (AN) is a cutaneous marker for most commonly insulin resistance and less frequently malignant diseases. Obesity is the most common cause of AN and AN is closely related to various autoimmune and endocrine diseases. Vitiligo carries a risk for several autoimmune endocrinopathies and has been supposed to be an antibody-associated autoimmune disease. However, the simultaneous appearance of AN and vitiligo in the same person is very rare.

We report on a 12-year-old obese girl with AN and concomitant vitiligo. Cutaneous hyperpigmented velvety thickening on the neck and axillae had developed together with obesity since she was 8 years old. About 1 year ago, two coin-sized depigmented areas developed in the hyperpigmented posterior neck. Histopathological examination showed hyperkeratosis, papillomatosis and mild to moderate irregular acanthosis. In the depigmented patch, it revealed decreased melanin pigment in the epidermis. (Ann Dermatol 17(1) 9~12, 2005)

Key Words: Acanthosis nigricans, Vitiligo

INTRODUCTION

Acanthosis nigricans (AN) is characterized clinically by hyperpigmented, hyperkeratotic, verrucous plaques that bestow a velvety texture on involved skin and have a predilection for the axillae, the neck and other flexural areas[1]. It has been recognized as a cutaneous disorder with diverse associations that run the gamut from benign conditions such as obesity[2,3] to malignant states such as gastrointestinal adenocarcinama[4]. Recently, tissue resistance to insulin has been thought to play an important role in the pathogenesis of AN[5] and AN has been reported in associations with various autoimmune and endocrine diseases[3,6-8].

Vitiligo is an acquired depigmentation disorder that also carries a risk for several endocrinopathies of autoimmune nature, particularly thyroid disease but also diabetes mellitus, adrenal insufficiency and pernicious anemia[9]. The association of vitiligo with autoimmune disease[9] and the detection of autoantibodies[10] have suggested that vitilgo is an autoimmune disease. Both diseases share a similar portion in pathogenesis, but the simultaneous appearance of AN and vitiligo in the same person is very rare and only a few cases have been reported up to recently[2,11].

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CASE REPORT

A 12-year-old girl presented with pigmentary changes of the neck and axillae. This sign had developed together with obesity since she was 8 years old. About 1 year ago, two coin-sized depigmented areas developed in the hyperpigmented posterior neck. There were no subjective symptoms. She was otherwise in good health and did not take any medication. Her family history did not reveal any similar disease. Her height and weight were 148 cm and 65 kg respectively and the body mass index was 29, therefore she was considered obese. On physical examination, the patient had symmetrically distributed hyperpigmentation and velvety cutaneous

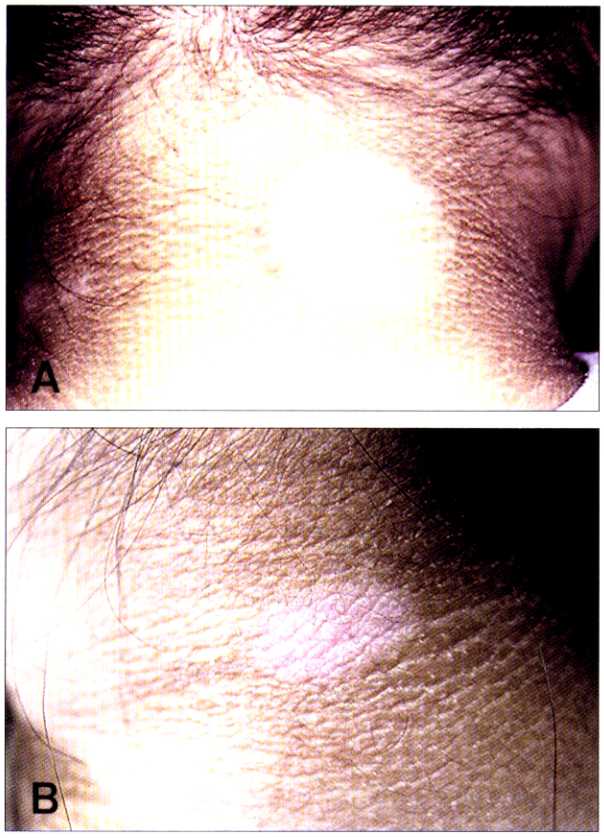

Fig. 1. The hyperpigmented velvety thickening with two sharply demarcated hypopigmented macules on the posterior neck (A, B).

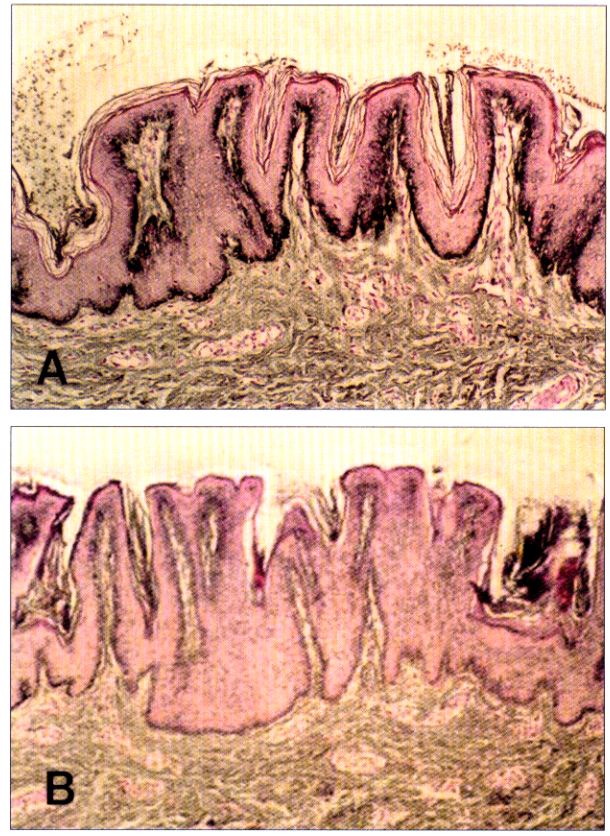

Fig. 2. Histopathologic findings showed hyperkeratosis, papillomatosis and mild to moderate irregular acanthosis (A, B). The depigmented region presented decreased melanin pigment (B) (Fontana-Masson stain, ×100).

thickening of the neck and axillae, and two well demarcated depigmented macules in the hyperpigmented posterior neck, 2.5×2.5 cm and 2.5×2.0 cm in diameter respectively (Fig. 1).

Laboratory findings were normal, including complete blood cell counts, urinalysis, liver and kidney function tests and electrolytes. Plasma levels of growth hormone, follicle-stimulating hormone, luteinizing hormone, glucagon, 17 α-hydroxyprogesterone, dehydroepiandrosterone, testosterone, and estradiol, and the result of the thyroid function test were normal. Tumor markers (CEA, CA15-3, CA 19-9, CA125, α-FP) were within the normal range. Ultrasonography of the abdomen was normal. Basal insulin (7.2 μIUml) and C-peptide (1.4 ng/ml) levels were normal. The fasting serum glucose and 75-gram oral glucose tolerance tests showed within the normal ranges. However, the patient showed exaggerated responses of 120 min serum insulin (83.2 μIUml) and C-peptide (6.66 ng/ml) after the glucose load. Histological examination of a skin biopsy from the neck showed hyperkeratosis, papillomatosis and mild to moderate irregular acanthosis (Fig. 2A). In the depigmented patch on the neck, it revealed decreased melanin pigment in the epidermis on Fontana-Masson stain (Fig. 2B) and remarkably diminished numbers of melanocytes in the basal layer with S-100 protein.

As she was diagnosed to have obesity with hyperinsulinemia, we recommended diet therapy and weight reduction.

DISCUSSION

Acanthosis nigricans has been recognized as a cutaneous disorder with distinctive clinical and histologic features, and with diverse associated

diseases. Clinically, it presents hyperpigmanted velvety thickening of the skin, predominantly in the intertriginous areas such as the axillae, the neck, and the genital and submammary regions[1]. Histologic examination reveals hyperkeratosis and papillomatosis but only slight irregular acanthosis and usually no hyperpigmentation[12]. It has been reported in associations with not only various autoimmune and endocrine diseases[3,6-8] but also less frequently malignant disease[4]. It was divided into four types by Curth[13]: malignant, benign, syndromic and pseudo-acanthosis nigricans. Although the precise etiology of AN remains unclear, it is probably caused by an elevated level of a factor stimulating keratinocytes and dermal fibroblasts at the cell receptor level[5]. In AN associated with malignancy, it is suggested that transforming growth factor-α released from the tumor cells may stimulate keratinocyte proliferation via epidermal growth factor receptors[14].

Obesity is the most common cause of AN and insulin resistance[1]. Insulin resistance can be associated with hyperisulinaemia, usually in patients with a normal blood glucose level. It has been suggested that insulin at high level may activate insulin-like growth factor receptors and mediate epidermal proliferation[5]. We experienced a case of AN with severe obesity and concomitant vitiligo. Although her fasting serum glucose and oral glucose tolerance test were within the normal limits, she had exaggerated insulin and C-peptide responses to glucose load. These data indicated an subclinical insulin-resistant state. AN may have either clinical or subclinical insulin resistance, so some experts recommend investigation of this possibility in these patients[5].

Antibodies against the insulin receptor have been identified in some patients with AN[7]. This explains the association of AN with other autoimmune processes. AN may also be associated with a variety of full-blown classic autuoimmune disease in the absence of diabetes[6]. Vitiligo also has been reported in association with several endocrinopathies of autoimmune nature including thyroid diseases, addison's disease, diabetes mellitus and other autoimmune disease[9], and the presence of circulating antimelanocyte antibodies have been reported[10]. It is supposed that vitiligo is an antibody-associate autoimmune disease. When these hypotheses are taken into consideration, it can be suggested that the onset of AN may predate a variety of classic autoimmune diseases or can be associated with a disordered immunoreactivity. This may possibly help to explain the association of AN with other autoimmune processes such as vitiligo in our patient.

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