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BRIEF REPORT

A Case of Hyperandrogenism, Insulin Resistance, and Acanthosis Nigricans Syndrome; Increase in Proliferating Cell Nuclear Antigen and Decrease in Loricrin in Acanthosis Nigricans

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Dear Editor:

HAIR-AN syndrome is an unusual multisystem disorder that consists of hyperandrogenism (HA), insulin resistance (IR), and acanthosis nigricans (AN)[1]. HAIR-AN syndrome is known to develop by various causes including underlying malignancy, systemic disease, obesity, and drug[2]. For the diagnosis of HAIR-AN syndrome, a variety of comprehensive targeted laboratory evaluations are necessary[1] as described here.

A 31-year-old woman who had been obese since a schoolgirl presented us with a variety of hyperandrogenic features such as hypertrichosis (Fig. 1A, B) and amenorrhea. In addition, she presented hyperpigmented, velvety patches on her axilla (Fig. 1C), the nape of her neck (Fig. 1D) and the dorsal aspect of her phalangeal joints (Fig. 1E). She was also a nullipara. Her height and body weight was 155 cm and 100 kg, respectively. Though serum levels of follicle-stimulating hormone, luteinizing hormone, prolactin, adrenocorticotropic hormone (ACTH), cortisol and thyroid-stimulating hormone were normal, those of testosterone (82.6 ng/dl; normal range, 10～60 ng/dl), dehydroepiandrosterone sulfate (404 μg/dl; normal range, 23～266 μg/dl) and 17α-hydroxyprogesterone (7.8 ng/ml; normal range, 0.2～4.5 ng/ml) were elevated. Serum electrolyte panel was normal. Computed tomography and magnetic resonance image pointed out neither tumors of ovarian and adrenal gland nor adrenal hyperplasia. Results of ACTH stimulation test and dexamethasone suppression test were normal. Taken together, we could exclude Cushing's syndrome, congenital adrenal hyperplasia, polycystic ovary syndrome and virilizing tumor. HbA1c was 6.3% (normal range, <5.8%). Serum Insulin level was elevated (27.1 pmol/l; normal range, 5～10 μU/ml) and 75 g oral glucose tolerance test showed excessive secretion of insulin, indicating IR. Antinuclear antibodies, anti-insulin antibody, and anti-insulin receptor antibody were negative. Histological examination on her axilla revealed epidermal papillomatosis and acanthosis with orthohyperkeratosis, and no significant inflammatory infiltrate (Fig. 1F). Finally, we diagnosed her with HAIR-AN syndrome. She has no familial histories of HAIR-AN syndrome.

An immunohistochemistry on her axilla revealed the conspicuous increase in proliferating cell nuclear antigen-positive cells, especially in basal layer (Fig. 2B) and the reduced and abnormally expanding expression of loricrin in granular and spinous layer (Fig. 2D). An immunohistochenistry on the axilla of an age-matched female healthy volunteer (Fig. 2A, C) was performed under approval of the Ethics Committee of Oita University.

The patients with HAIR-AN syndrome would have an increased risk of hyperlipidemia and secondary coronary ar-

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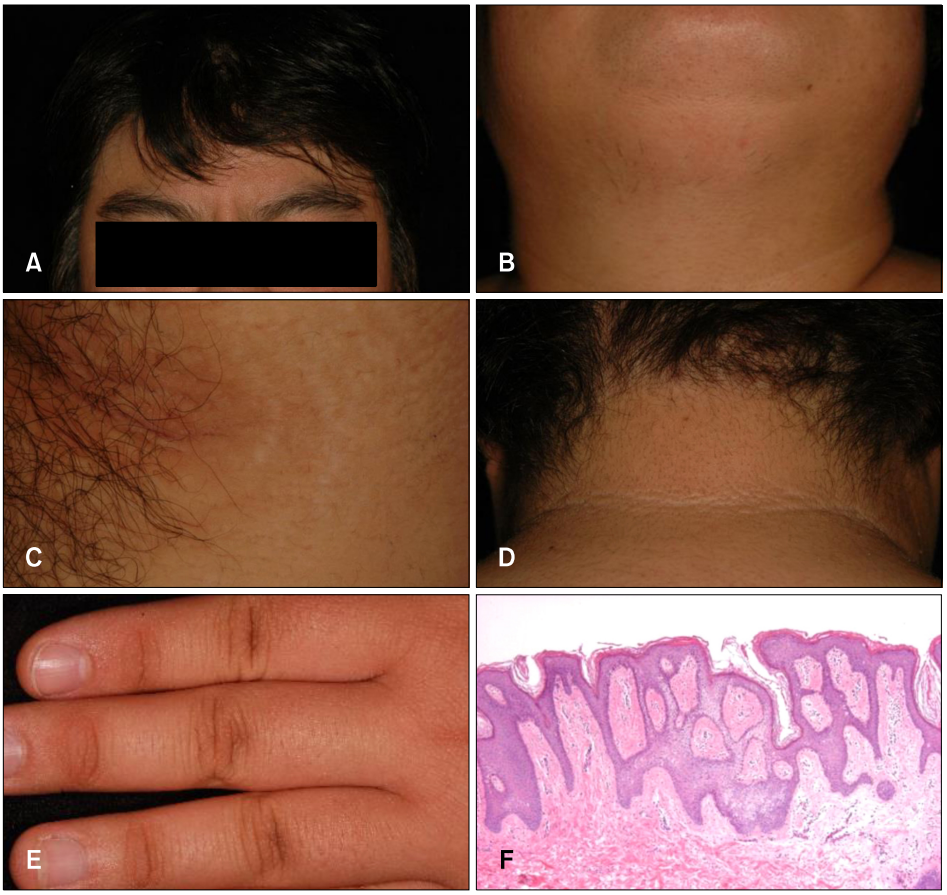

Fig. 1. Hypertrichosis on her face (A: eyebrows, B: chin) and hyperpigmented, velvety patches on her axilla (C), the nape of her neck (D) and the dorsal aspect of her phalangeal joints (E). Histological examination revealed epidermal papillomatosis and acanthosis with orthohyperkeratosis, and no significant inflammatory infiltrate (F). (F) H&E, ×40.

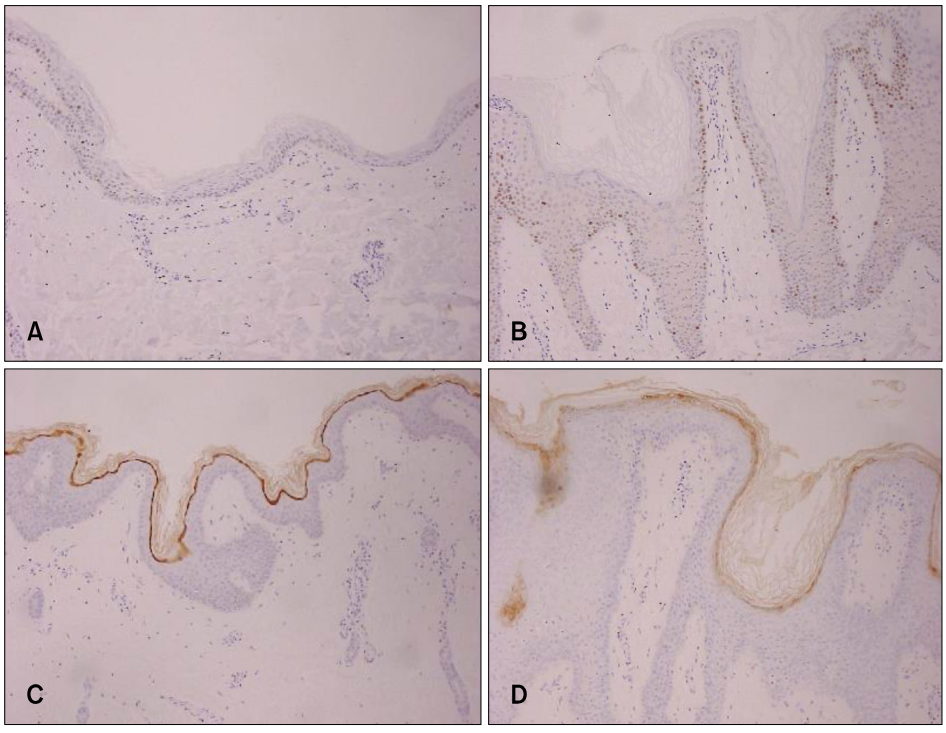

Fig. 2. Immunohistochemical staining on axilla of the patient revealed the conspicuous increase in proliferating cell nuclear antigen (PCNA)-positive cells, especially in basal layer and the reduced and abnormally expanding expression of loricrin in granular and upper spinous layers. (A) PCNA in a healthy volunteer, (B) PCNA in the patient. (C) loricrin in a healthy volunteer, (D) loricrin in the patient. A~D: ×100.

tery disease. Considering that patients with HAIR-AN syndrome often present with cosmetic concerns such as virilization and AN, dermatologists must maintain a high index of suspicion for HAIR-AN syndrome.

It has been hypothesized that AN is caused by long-term exposure of the keratinocytes to excessive insulin via binding of insulin-like growth factor receptors (IGF-R) with resultant hyperplasia of the skin[3]. In fact, insulin-like growth factor accelerates keratinocyte proliferation[4]. Expression of loricrin was enhanced in IGF-1R-deficient murine keratinocyte[5]. However, *in vivo* expression of proliferation and/or differentiation-related molecules on AN has not been reported. The present results of the immunohistochmistry support those *in vitro* studies and clearly demonstrate that hyperproliferation and abnormal differentiation of epidermis took place under insulin resistant condition *in vivo*, presumably via IGF-R signaling.

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Hydrofluoric Acid Burn on a Fingertip Treated Successfully with Single Session of Subcutaneous Injection of 6.7% Calcium Gluconate

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Dear Editor:

Hydrofluoric acid (HF) is one of the most corrosive acids and can produce progressive and serious tissue necrosis with severe pain[1]. Prompt first aid is mandatory to reduce damage after HF cutaneous exposure[2]. Herein we report a case of HF burn on a fingertip treated successfully with a single session of subcutaneous injection of small volume and low concentration of calcium gluconate. A 28-year-old man touched 50% HF last evening while he put experimental apparatuses in order in a laboratory. He wash-

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