

SHORT COMMUNICATION

Generalised Acanthosis Nigricans in Childhood with Short Stature Associated with Poor Response to Growth Hormone Provocation

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Acanthosis nigricans (AN) is a skin disorder characterised by skin hyperpigmentation and thickening, especially in the intertriginous regions. AN is usually classified as either malignant, benign, obesity-associated, syndromic, unilateral, acral, drug-induced and mixed (1). A generalised form of AN frequently occurs together with internal malignancy in adult patients, but it is rare in childhood (2–7). Here, we report a paediatric case of generalised AN associated with short stature accompanied with decreased growth hormone levels.

CASE REPORT

A 3-year-old Japanese girl was brought to our hospital with expanding skin darkening and thickening on the neck and trunk that had begun two and a half years previously. She did not have any symptoms at birth or family history of endocrine disorders. On presentation, she had generalised hyperpigmentation with a velvety texture, which was pronounced on the neck, axillae and groin area (Fig. 1). Skin biopsy from the side of the abdomen revealed hyperkeratosis and epidermal papillomatosis with basal melanosis. A diagnosis of generalised AN was made. The patient was not obese and no abnormalities were found on the following examinations: anti-insulin antibody, anti-insulin re-

ceptor antibody, fasting blood sugar level, cholesterol, triglyceride, haemoglobin A1c, adrenocorticotropic hormone, aldosterone and thyroid hormone.

On follow-up at the age of 7, short stature was perceived. Her height was 104.8 cm, which was –2.84 standard deviations from the mean and her weight was 17.7 kg. Her arm span was about 44 cm, which was not short compared to her height. Her father and mother were 165.0 cm and 160.0 cm in height, respectively. Growth hormone stimulation test due to arginine, clonidine and levodopa were 11.2 ng/ml (normal value: 0–6.0 ng/ml), 5.9 ng/ml (0–6.0 ng/ml) and 5.4 ng/ml (0–6.0 ng/ml), respectively. Insulin-like growth factor (IGF)-1 level was 162 ng/ml (95–437 ng/ml). Fasting insulin level was 2.2 µU/ml (5.0–25.0 µU/ml). Magnetic resonance imaging showed atrophy of the pituitary gland but no pituitary tumours. However, there were no abnormalities in anterior pituitary hormones other than growth hormone. Atrophy of the pituitary gland was diagnosed as empty sella. No clear improvement of skin symptoms was obtained with vitamin D3 and urea ointment. Growth hormone replacement therapy somewhat improved her height, but not her skin symptoms.

DISCUSSION

Generalised AN is common in adult AN but not in childhood AN (2–10). We did not find any other diseases except poor response to growth hormone provocation in this patient. The pathogenesis of AN remains unclear, but a relation with resistance with hyperinsulinaemia (obesity, endocrine abnormalities) has been suggested. It is speculated that tumour secretory products may have insulin-like activity in malignant AN, however, our case did not have hyperinsulinaemia. Most cases of benign AN are inherited as an autosomal dominant trait, but our patient had no family history of AN. She had no body disproportion and this case was not considered to be related to *FGFR3* mutation. She had pituitary gland atrophy and was categorised as syndromic AN, which is occasionally associated with type 2 diabetes and endocrine disorders, such as Cushing's syndrome and adrenal insufficiency. Growth hormone deficiency has not been reported in association with AN. However, growth hormone deficiency should be examined as a comorbidity in childhood AN.



Fig. 1. Generalised hyperpigmentation with a velvety texture, which was pronounced on the neck, axillae and groin area.

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