GENETIC COUNSELING, Vol. 18, No 3, 2007, pp 325-330

A NEW CASE OF HAIRY ELBOWS SYNDROME (HYPERTRICHOSIS CUBITI)

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Summary: *A new case of hairy elbows syndrome (hypertrichosiscubii):* Hairy Elbows Syndrome (Hypertrichosis Cubiti; OMIM# 139600) is a rare syndrome, and characterized by the presence of long vellus hair localized on the extensor surfaces of the distal third of the arms and proximal third of the forearm bilaterally. Occasionally hypertrichosis of other body regions may accompany hairy elbows. About half of the reported patients have short stature. Aside from short stature other relatively rare abnormalities related with this syndrome were also described. Most of the reported cases were sporadic, but autosomal dominant as well as autosomal recessive inheritance patterns have also been postulated. In this report, we present a girl with Hairy Elbows syndrome who has both characteristic and uncommon findings of the syndrome. She has excessive hair on her elbows, along with short stature, microcephaly, joint hyperlaxity, thin-long-webbed neck, dysmorphic facial features and mental retardation.

Key-words: Hairy Elbows syndrome – Hypertrichosis cubiti— Short stature

INTRODUCTION

Familial hypertrichosis cubiti (HC) syndrome was initially described in 1970. From the time of first description of the syndrome in two siblings, 29 additional cases have been reported (2, 8). It is a rare form of localized hypertrichosis that is charcterized by long, coarse hair on the distal third of the arm and the proximal third of the forearm bilaterally. Lanugo type of hair usually appears in the time of infancy, becomes coarser during early childhood and regresses at adolescence (12). Reported dysmorphic features were not enough to make a phenotypic correlation among HC patients but propotionate short stature, developmental delay, facial dysmorphysm and minor skeletal anomalies are seem to be related with HC syndrome (1-3, 5, 8-12). In this report a girl with hairy elbows, mental ratardation, short stature, and facial dysmorphic features has been described. Also she had additional findings which were not described before.

CASE REPORT

The patient was an 8 year-old Turkish girl. She was born to healthy first cousin parents. Her mother was 39-year-old and 165 cm tall, her father

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was 44-year-old and 160 cm tall. Her brother was 22-year-old, and 180 cm tall, and he had mental retardation, speech disorder (but we had no chance to examine her brother). Her birth weight was 3100 g (50th centile); her birth length and head circumference were not recorded. The family did not define localized hypertrichosis in her brother but we also know that hairy elbows maybe masked by male type of hair distribution.

The patient was referred to us for having short stature and developmental delay. On her physical examination, she was 117 cm tall (3rd centile), 14.5 kg weight (< 3rd centile), and her head circumference was 48 cm (< 3rd centile). She had a thin stature, triangular and asymmetric face, high forehead with thick eyebrows, mild hypertelorism, downslanting palpebral fissures, bilateral ptosis, long eyelashes, high and wide nasal bridge, hypoplasia of alae nasi, thin upper lip, prominent upper incisors, big and anteverted ears, thin-long-webbed neck, and hyperextensible elbows with hypertrichosis (Fig. 1a-b). The hair on the elbows was unusually longer, darker, and coarser (Fig. 1c). Other ectodermal structures including skin, teeth, nails showed no abnormalities and there was no other extra hair growth on her body, apart from hypertrichosis on her elbow regions (Fig. 1b-c). She was suffering from frequent upper respiratory tract infections.

Routine biochemistry tests for renal, liver and thyroid functions were found as normal. Her IGF-I 137,7 ng/dl (N:106-250 ng/dl) and IGFBP-3 3022,5 ng/dl (N:2000-7740 ng/dl) levels were found to be normal; Celiac antibody screening test was normal. Other common causes of

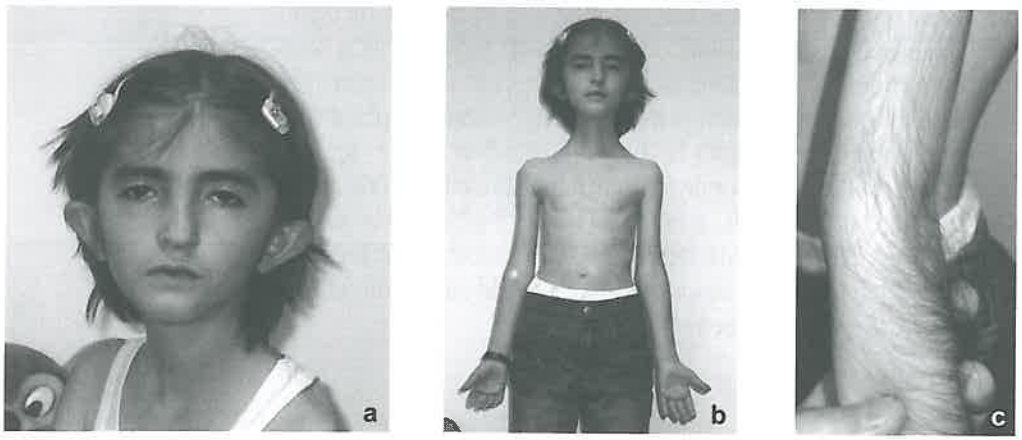

Figure 1: Anterior view of the patient; (a, b) note thin stature, triangular and asymmetric face, high forehead, thick eyebrows, downslanting palpebral fissures, mild hypertelorism, bilateral ptosis, long eyelashes, high and wide nasal bridge, hypoplasia of alae nasi, thin upper lip, anteverted big ears, thin-long-webbed neck. (c) note hyperextensible elbow with hypertrichosis.

chronic malnutrition such as, gaita analysis for parasites, lipid, reducting substance, and the pH of gaita were normal. Patient was also consulted to pediatric psychiatry to rule out anorexia nervosa because of her low weight; she had not any psychiatric disorder but her IQ score 70 (WISC-R) revealed borderline mental retardation.
Her bone age was delayed for 2 years compared to her chronological age, which is a finding cosistent with constitutional short stature. The karyotype of the patient was revealed as 46,XX. Also we have excluded 22q11 microdeletion by fluorescent in situ hybridization with commercial VCFS probes (Vysis; DiGeorge, ARSA).

DISCUSSION

Localized hypertrichosis is commonly present in association with a nevus or over a spina bifida. The presence of overgrowth of hair on the lateral aspects of the elbows was first described in 1970 in two patients with short stature by Beighton *et al.* (2). Since the first descrtiption of the Hairy Elbows (Hypertricosis Cubiti) syndrome, a total of 31 cases have been reported in the literature (1-3, 5, 6, 8-12). The lanugo type of hair usually appears in infancy, becomes coarser during childhood and regresses at adolescence. Rarely hypertrichosis may also be found on the face, trunk and tighs (1, 11, 12), and this condition is either isolated or associated with other physical abnormalities.
We present an eight year-old Turkish girl with hairy elbows, mental retardation, short stature, dysmorphic features. Most of the HC cases are sporadic, but genetic heterogeneity may exist and autosomal dominant as well as autosomal recessive inheritance patterns have been postulated (3, 5, 8). In the present case, because of the healthy consanguineous parents, autosomal recessive inheritance seems to be the transmission pattern. Although she has an older brother who suffered from mental retardation, we could not learn if he had other symptoms as they lived in another city and we had no chance to examine him. We only learn that their common finding was mental retardation. The brother may also have had Hypertrichosis Cubiti syndrome but it was difficult to be defined by family because of male type hair distribution. Unfortunately, it is not clear that he has the same disorder or not.
Generally HC has not systemic manifestations, so reassurance to the parents seems to be the only therapy (10). However Macdermot *et al.* described a mother and her daughter with disproportionate short stature, delayed bone age and a number of minor abnormalities in skeletal survey. They were unable to ascertain whether skeletal disorder is a part of HC syndrome or HC and skeletal anomalies coexist as diffe-

rent pathologies in this family (5). The first cases with HC reported by Beighton *et al.* had short stature and following reports revealed an association between Hairy Elbows syndrome and short stature; half of the cases (16/32) including the presented case had short stature (1-3, 5, 6, 8-12). In our patient short stature was proportionate, and no apparent skeletal anomaly was found. Short stature may also be accompanied with low weight (<3rd centile) in Hairy Elbow syndrome (8, 9) as seen in our case. Furthermore, mental retardation is a relatively common finding of the syndrome (8).

In addition to consistent dysmorphic findings of HC, our patient had unreported features. Comparison of reported findings and the dysmorphic features of presented case is shown in Table I.

Also presented case has some common clinical features with Floating-Harbor syndrome. Floating-Harbor syndrome (FHS) is characterized by a clinical triad of (a) short stature with significantly delayed bone

Table I: comparison of previously reported clinical findings in HC patients and features of the present case

Reported Findings	**Frequency**	**Present Case**
Hypertrichosis on elbows	31/31	+
Sex (F/Total)	22/31	F
Short stature	15/31	+
Dysmorphic facial features	9/31	+
Limb Anomalies*	5/31	+
Retarded motor/mental development	6/31	+
Hypertrichosis on other parts of the body	4/31	-
IUGR	3/31	-
ADHD	2/31	-
DM	1/31	-
Other findings	Hypotonia, brachycephaly, dolicocephaly, small forehead, high forehead, asymmetric face, round face, elongated expressionless face, hypertelorism, ptosis, down slanted palpebral fissures, epicanthus, high arched palate, short nose, low nasal root, pointed nose, small mouth, thin lips, irregular margin of teeth, prominent jaw, large ears, umblical hernia, cliteromegaly, delayed bone age	Thin stature, microcephaly, triangular-asymmetric face, high forehead, thick eyebrows, long eyelashes, high and wide nasal bridge, hypoplasia of alae nasi, prominent upper incisors, thin-long-webbed neck, hyperlaxity, delayed bone age

*Including mild finger/toe anomalies; F: Female; IUGR; Intrauterine Growth Retardation; ADHD: Attention Deficit Hyperactivity Disorder; DM: Diabetes Mellitus (2, 3, 5, 8, 12).

age, (b) expressive language delay, usually in the presence of normal motor development, and (c) a triangular face with a prominent nose and deep set eyes (4, 6, 7). Short stature with delayed bone age and dysmorphic facial features are common clinical findings in our case, but short stature is not as severe as seen in Floating-Harbor syndrome. Speech delay is a major and distinctive feature of Floating-Harbor syn-

Table II: Comparison of Floating-Harbor syndrome, presented case and hypertrichosis cubiti syndrome

Clinical Features	Floating-Harbor Syndrome (OMIM# 136140)	Present Case	Hypertrichosis Cubiti* (OMIM# 139600)
Inheritance	OD, sporadic	AR ?	Sporadic, OD, AR
Height	Short stature	+	Short stature
Head and neck	Triangular face	Triangular, asymmetric face	Asymmetric/ elongated/round face
	Posteriorly rotated ears	Anteverted big ears	Large ears
	Deep-set eyes	-	-
	Long eyelashes	+	-
	Prominent nose	Prominent nose	Short nose
	Wide columella	+	-
	Smooth philtrum	+	-
	Thin lips	+	+
	Broad mouth	-	-
	Downturned mouth	+	-
	Short neck	-	-
	Low posterior hairline	-	-
Neurologic	Expressive language delay	Borderline MR, no speech delay	MR, Expressive language delay
Musculo-skeletal System	Delayed bone age	+	+
	Joint laxity	+	-
Other	Hirsutism	Hypertrichosis	Hypertrichosis
	Celiac disease	Normal antibody screening	-
	Normal endocrinologic studies (growth hormone, Som-C, thyroid function)	Normal	DM

*Although the phenotype of hypertrichosis cubiti syndrome is not clearly defined, hypretrichosis of the elbows is a constant feature of this disorder, and short stature, mental retardation, language delay are commonly associated findings, more reports are needed

OD: Autosomal dominant; AR: Autosomal recessive; MR: Mental retardation (4, 6-8, 12)

drome (2, 8, 12) and not present in our case. Comparison of clinical findings of FHS and HC syndrome with our case are summarized in Table II. We postulate that Hypertricosis Cubiti and Floating-Harbor syndromes maybe allelic variants because of their similar clinical features. HC syndrome and FHS share some clinical findings with 22q11 deletion syndromes and should be considered in the differential diagnosis. We exclude this syndrome by performing FISH analysis in our patient.

Our patient's mother was 39 years old, and her father was 44 years old at the time of patient's birth. Advanced parental age maybe important in Hairy Elbows syndrome, but unfortunately, parental age of HC patients rarely reported in literature, so we do not know if there is a relationship between HC and advanced parental age.

Further cases with well defined dysmorphic features are needed to establish the hypertrichosis cubiti phenotype.

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