DYSMORPHOLOGY REPORT

Unknown syndrome in sibs: pili torti, growth delay, developmental delay, and mild neurological abnormalities

S K Shapira, A S Neish, B R Pober

Abstract

We present male and female sibs of consanguineous parents with features including pili torti with unusual hair shaft electron microscopic (EM) findings, growth delay, developmental delay, and mild to moderate neurological abnormalities. The features of the cases presented here have not been noted in the previously reported clinical syndromes in which pili torti may be found.

Division of Genetics, Children's Hospital, and Department of Pediatrics, Harvard Medical School, Boston, MA 02115, USA.
S K Shapira
A S Neish
B R Pober

Correspondence to
Dr Shapira,
Institute for Molecular Genetics,
Baylor College of Medicine,
One Baylor Plaza,
Houston, TX 77030, USA.

Received 4 September 1991.
Accepted 14 October 1991.

Case reports

FAMILY

The parents were healthy, of Puerto Rican descent, and consanguineous (first cousins). Two older sibs were in good health and do not share features with the probands. The family history was non-contributory.

PRENATAL/NEONATAL/CHILDHOOD

The probands were the third and fourth uncomplicated pregnancies; the mother was 22 and 24 years old, respectively, at their delivery. Birth weights were 2665 g and 2608 g, respectively. During the first two months, the infants gradually lost their newborn hair which was replaced with kinky, brittle hair of lighter colour that fell out easily. Developmental milestones were delayed compared to their older sibs, but each proband had continuous developmental progress without loss of milestones. Each had growth delay compared to their older sibs, but normal growth velocites.

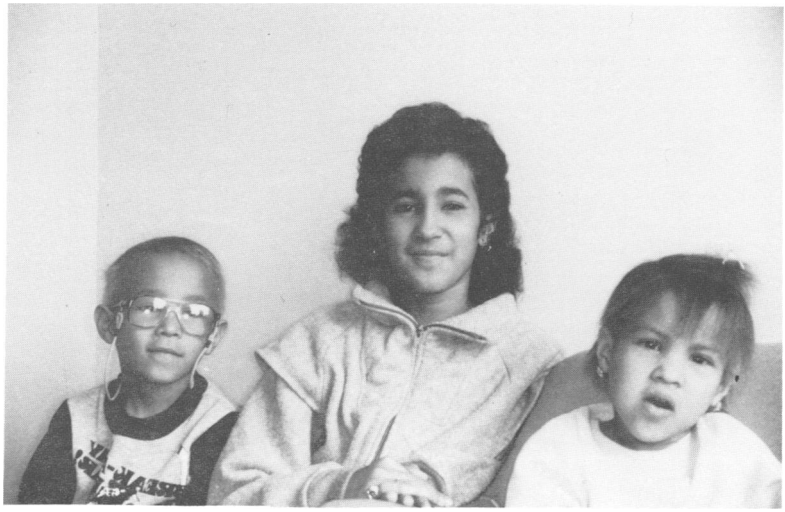

Figure. Male and female probands (left and right, respectively) with unaffected 13 year old sib (centre).

CLINICAL EXAMINATION

Male proband at 7 years (figure): weight 20·1 kg (10th centile), height 116 cm (10th centile), and head circumference 53 cm (65th centile). Female proband at 5·5 years (figure): weight 16·9 kg (25th centile), height 103 cm (5th centile), and head circumference 49·5 cm (35th centile). Both had sparse scalp hair, which was yellow-orange in colour, thin, and kinky. The hair colour fades and the skin becomes somewhat erythematous with sun exposure. The eyebrows and eyelashes were darker in colour than the scalp hair, but sparse. The skin, nails, and teeth were normal. Both had mild ligamentous laxity and both were myopic on ophthalmological evaluation. Audiology evaluations were normal. The female proband had Tanner stage III pubic hair without axillary hair or thelarche. The male proband exhibited mild generalised hypotonia with mild truncal ataxia, while the female had moderate truncal ataxia with a broad based, unsteady gait. Reflexes were normal.

INVESTIGATIONS

Prophase chromosome analyses were normal. Bone ages corresponded to chronological ages. Plasma and urine amino acids were normal and no argininosuccinate was detected. Hair amino acid analyses had normal levels of sulphur containing amino acids. Urine organic acids, biotinidase, and thyroid function tests were also normal. The male had intermittent mild raised serum lactate, pyruvate, and copper. The female had persistent mildly raised serum lactate and copper. There was normal serum ceruloplasmin and 24 hour urinary copper excretion, mildly raised serum esterified carnitine, and normal urinary acyl-carnitine profiles in both. Light microscopy of the hair

Comparison of syndromes with pili torti.

	Pili torti	Mental retardation	Growth delay	Seizures	Raised urine argininosuccinate	Low serum copper	SNHL*	Low hair sulphur
Argininosuccinic aciduria	+	+	−	+	+	−	−	−
Menkes disease	+	+	+	+	−	+	−	−
Bjornstad syndrome	+	−	−	−	−	−	+	−
Trichothiodystrophies	+	+	+	+	−	−	−	+
Probands	+	−/+†	+	−	−	−	−	−

* Sensorineural hearing loss.
† Delay in motor and language milestones.

showed thin shafts, abnormal twisting, irregular shapes, and no banding on polarised light examination. EM hair studies showed cuticle erosions and transverse fissures with no evidence of heavy metals. CT scan of the head in the male was normal.

The female had additional findings: CT and MRI scans of the head showed bilateral low density areas in the caudate nuclei and putamen, normal nerve conduction studies, and normal serum CK and aldolase. Quadriceps muscle biopsy showed fibre atrophy and a tendency to fibre type grouping suggestive of chronic mild neurogenic atrophy. There was raised DHEA, Δ4, and 17-hydroxypregnenolone, but normal FSH and LH.

Discussion

Pili torti is a rare hair abnormality characterised by small tight curls and fragility, hence resulting in short, broken hair shafts. Several distinct syndromes have been described with pili torti as an associated component, including argininosuccinic aciduria, Menkes disease, Bjornstad syndrome (pili torti and sensorineural deafness), and the trichothiodystrophies.[1-4] The common features of these syndromes are contrasted to the two probands we describe here in the table. An undescribed defect in intracellular copper metabolism is suggested by the combination of hair abnormalities, ataxia, lactic acidosis, and ligamentous laxity. We feel that these sibs represent a distinct, previously unreported, probably autosomal recessive syndrome.

1 Allan JD, Cusworth DC, Dent CE, Wilson VK. A disease, probably hereditary, characterized by severe mental deficiency and constant gross abnormality of amino acid metabolism. *Lancet* 1958;**i**:182–7.
2 Menkes JH, Alter M, Steigleder GK, Weakley DR, Sung HG. A sex-linked recessive disorder with retardation of growth, peculiar hair and focal cerebral and cerebellar degeneration. *Pediatrics* 1962;**29**:764–79.
3 Robinson GC, Johnston MM. Pili torti and sensory neural hearing loss. *J Pediatr* 1967;**70**:621–3.
4 Price VH, Odom RB, Ward WH, Jones FT. Trichothiodystrophy: sulfur-deficient brittle hair as a marker for a neuroectodermal symptom complex. *Arch Dermatol* 1980;**116**:1375–84.