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Breast hypoplasia and disproportionate short stature in the ear, patella, short stature syndrome: expansion of the phenotype?

EDITOR—The ear, patella, short stature syndrome (EPS or Meier-Gorlin syndrome) is a rare disorder characterised by microtia, absent or hypoplastic patellae, and proportionate pre- and postnatal growth retardation. In 1994, published reports of the disorder were reviewed by Boles *et al*.[1] To date, over 17 patients have been described.[1–5] Inheritance is autosomal recessive as evidenced by an almost equal number of male and female patients, as well as affected sibs, occurrence of consanguineous matings, and the absence of clinical abnormalities in the parents. Here, we describe two unrelated patients with the EPS syndrome and breast hypoplasia. This is a hitherto unreported finding that may be a part of the syndrome in adult females. Furthermore, the disproportionate short stature which was present in our patients may be a skeletal manifestation of the EPS syndrome.

Patient 1 was the first child of non-consanguineous parents. Clitoral hypertrophy and hypoplastic labia minora were noted after birth. She was referred at the age of 14 years because of dysmorphic features and delayed breast development. Her menarche started at the age of 12 years and she had regular periods. Psychomotor development had been satisfactory. Hearing was normal. Physical examination showed disproportionate short stature (height 1.47 m (<3rd centile), arm span 1.33 m, arm span for height <<3rd centile). Head circumference was 53.3 cm (25th centile). There was microtia (ear length <3rd centile) and micrognathia (fig 1). She had a narrow thorax. Puberty was Tanner stage P5M1 (fig 2). A skeletal survey showed bilateral absent patellae. Endocrine studies were normal. She had been treated with ethinyloestradiol which resulted in minimal breast development.

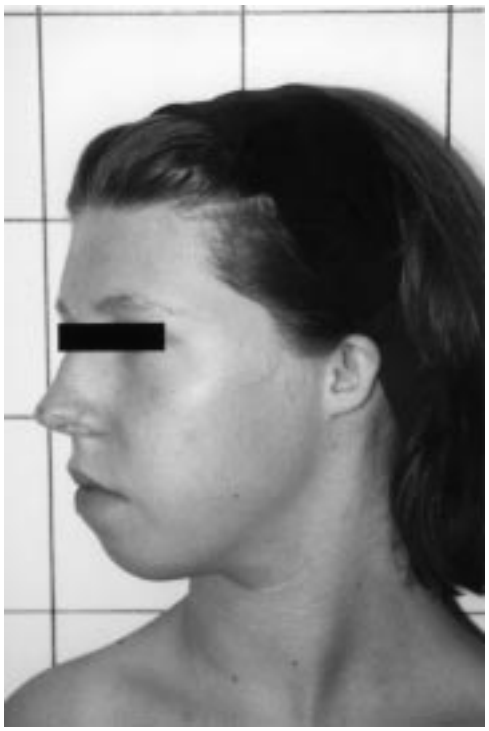

Figure 1 Case 1 aged 14 years. Note microtia and micrognathia.

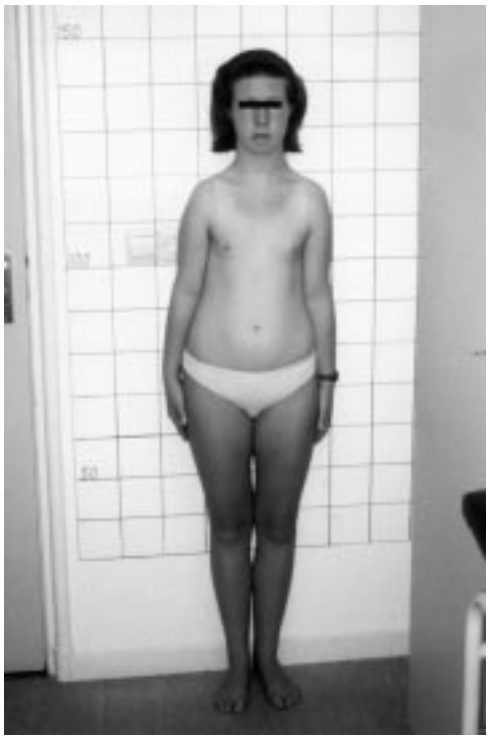

Figure 2 Case 1 aged 14 years. Note disproportionate short stature and breast hypoplasia.

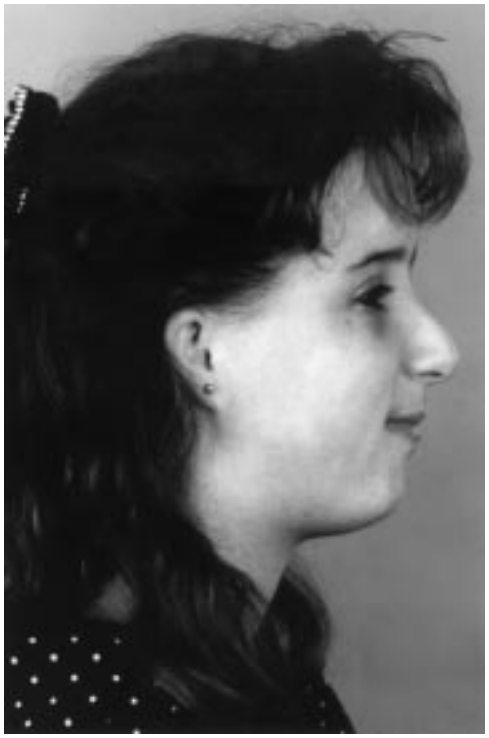

Figure 3 Case 2 aged 15 years. Note microtia and beaked nose.

Patient 2 was also the first child of non-consanguineous parents. At the age of 5 years, she had surgery on her coronary sutures because of craniosynostosis. The girl was lost to follow up until the age of 15 when she was referred for evaluation of short stature and absence of breast development. Menarche had occurred at 13 years and she had regular periods. Psychomotor development was satisfactory. Hearing was normal. Physical examination showed an adolescent female with disproportionate short stature (height 1.43 m (<3rd centile), arm span 1.32 m, arm span for height <<3rd centile). Head circumference was 51.5 cm (<3rd centile). She had small, round ears, a beaked nose, and a small mouth (fig 3). Narrow shoulders with hypoplastic breasts were noted (fig 4). Puberty was Tanner stage P5M1. A skeletal survey showed bilateral hypoplastic patellae. Chromosome analysis showed no abnormalities and endocrine studies were normal. She underwent plastic surgery for enlargement of her breasts.

Both our patients showed microtia, short stature, and absent or hypoplastic patellae, which are all characteristic of the EPS syndrome (table 1), but we found our patients' breast hypoplasia and disproportionate build remarkable. It is possible that these two features may have been overlooked in previously reported patients. Alternatively, it cannot be excluded that they represent uncommon features present in only a subset of patients with EPS syndrome. To date, nine males and eight females with EPS syndrome have been reported (table 1). Six of the female patients were younger than 10 years. One female at the age of 17 had small breasts[3] and the other female aged 55 had normal secondary sexual characteristics.[2]

In both our patients, arm span for height was far below the 3rd centile, which is indicative of disproportionate short stature. Most other patients were reported to have proportionate short stature.[1 4] However, details about arm span, sitting height, or subischial leg length are not available except for two patients described by Cohen *et al*.[6]

In 1994, Lacombe *et al*[3] postulated that the EPS syndrome could be the human equivalent of the *short-ear*

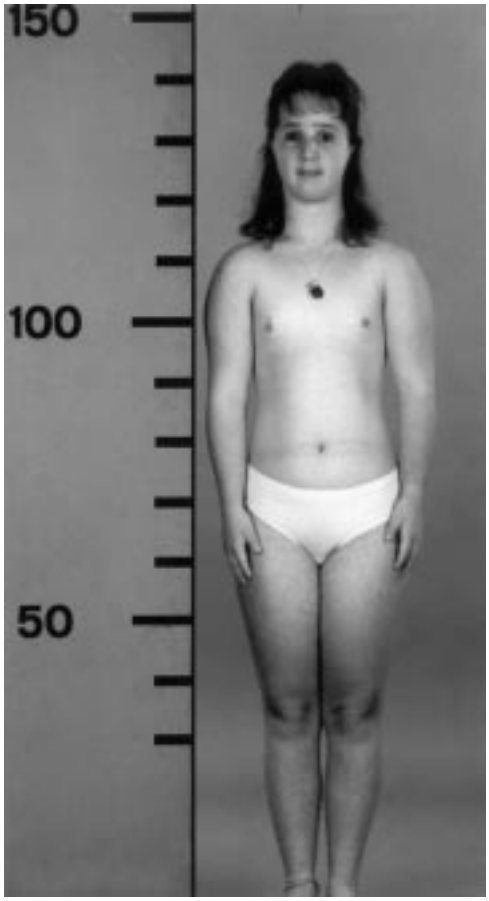

Figure 4 Case 2 aged 15 years. Note disproportionate short stature, narrow shoulders, and absence of breast development.

murine disorder resulting from mutations in the bone morphogenetic protein 5 gene (*BMP-5*). This hypothesis has not yet been tested by molecular studies. Experiments showed that *BMP-5* deficient mice have a lower cross sectional geometry and a significant reduction in length of the femora.[7] In theory, this growth reduction, if present in the humeri, could lead to disproportionate short stature with reduced arm span. We hypothesise that disproportionate short stature in humans with EPS syndrome may result from a molecular defect in the *BMP-5* gene. However, underdevelopment of breast tissue is, to our knowledge, not a feature of *BMP-5* deficient mice. Additional studies may yield further information about the role of the *BMP-5* gene in the EPS syndrome.

We have described two females with EPS syndrome in which both breast hypoplasia and disproportionate short

Table 1 Clinical features of the EPS syndrome

Features	*Published reports*	*Patient 1*	*Patient 2*
Sex	9 male/8 female	F	F
Height <3rd centile	12/17*	+	+
Proportionate short stature	2/15†	−	−
Disproportionate short stature		+	+
Microtia	17/17	+	+
Absent or hypoplastic patellae	11/17‡	+	+
Early closure or prominent cranial sutures	6/17§	−	+
Clitoromegaly	3/8	+	−
Breast hypoplasia¶		+	+

*Height >3rd centile was noted in three patients; in two patients height was not reported.
†Seven other reported patients had proportionate short stature. However, span measurements were not reported.
‡Three other patients had normal patellae.
§Three patients had normal sutures; no information on the other eight patients.
¶One patient had small breasts, seven of nine female patients were too young to notice breast hypoplasia.

stature were present. These features may be associated with the EPS syndrome. Identification of other patients with EPS syndrome and breast hypoplasia and disproportionate short stature may further support this suggested association.

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Pili torti et canaliculi and agenesis of the teeth: report of a new "pure" hair-tooth ectodermal dysplasia in a Norwegian family

EDITOR—The ectodermal dysplasias comprise a heterogeneous group of inherited developmental disorders affecting tissue and organs of ectodermal origin. Their classification was developed by Freire-Maia and Pinheiro,[1] with malformations of the hair, teeth, nails, and sweat glands as the major criteria. Ectodermal dysplasias are thus divided into 11 subgroups based on a minimum of two ectodermal signs with or without other developmental defects.

A Norwegian family with structural hair abnormalities associated with agenesis of the teeth is reported. The mode of inheritance is consistent with an autosomal dominant pattern.

The investigation for hair and tooth abnormalities in the family started with a then 16 year old boy (IV.3, fig 1), who was under dermatological treatment for an X linked ichthyosis. Blood lipoprotein electrophoresis showed increased migration of the low density lipoprotein (LDL) fraction compared to normal, consistent with steroid sulphatase deficiency. Interestingly, the blood LDL fraction in his mother, who suffered from dry skin, also showed increased migration, pointing towards carrier status for X linked ichthyosis.[2] His maternal grandfather was said also to have suffered from scaly skin. He had, however, died several years ago and clinical examination was therefore not possible. No other person in the family suffered from ichthyosis.

Further, it had been recognised that several persons on the paternal side of his family suffered from stiff and rough hair that seemed to break easily.

The boy had preferred to keep his hair short because it then was easier to treat the scaling of the scalp. He had therefore not been aware of increased breakage of hair. However, his hair felt rough and stiff (fig 2), and there was a discrete area of partial alopecia on the top of his head. Scanning electron microscopy of his hair showed twisted hair shafts combined with longitudinal grooves, pili torti et canaliculi (fig 3). He also had agenesis of the lower premolar teeth (35 and 45) (fig 4). There was no gingival fibrosis and no nail abnormality. The boy was of normal intelligence, had normal sweating and normal hearing, no generalised hypertrichosis, and no ophthalmological abnormalities.

The younger of his two sisters (IV.5, fig 1) had neither hair abnormalities nor agenesis of the teeth. The older of his two sisters (IV.4) also had agenesis of the teeth (12 and 22) (fig 5). She had no problems with breakage of hair and scanning electron microscopy of her hair showed no structural hair changes.

Hair samples from his mother showed no alterations. However, hair samples from both his father (III.2) (fig 6)

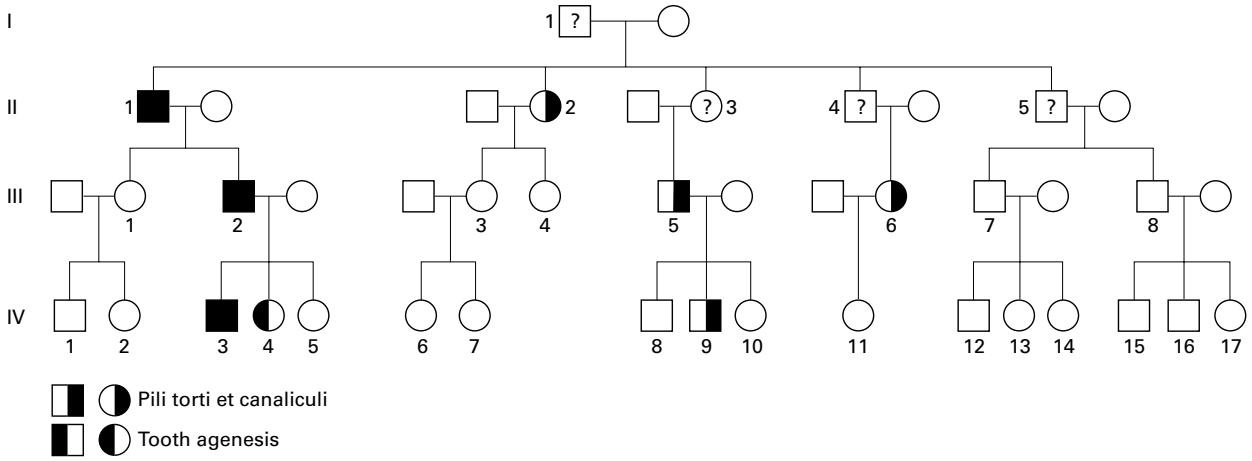

Figure 1 Family pedigree.