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Dilemmas in counselling: the EEC syndrome

Kong Tse, I K Temple, M Baraitser

Abstract

A family with the EEC syndrome is reported. Two sibs have the classical form of the condition with ectrodactyly, ectodermal dysplasia, and clefting. Their mother, however, has only minimal evidence, with preaxial polydactyly of the right hand and duplication of the terminal phalanx of the second toe of the left foot with 3/4 syndactyly. The dilemmas faced by the genetic counsellor are discussed in this variable autosomal dominant condition.

Variability of expression in dominantly inherited ectrodactyly is well known. Of equal importance is phenotypic variation in the EEC syndrome (ectrodactyly, ectodermal dysplasia, cleft lip/palate) to the extent that limb involvement might be the only manifestation and might not even be diagnosed clinically. We report an unusual family with the EEC syndrome that highlights the difficulties faced by genetic counsellors in predicting the variable manifestations of this autosomal dominant condition.

Case reports (fig 1)

II·4 was the fourth child of unrelated Indian parents. She was born at term after an uncomplicated pregnancy, weighing 2100 g. At birth she was noted to have bilateral cleft lip, cleft palate, and ectrodactyly of the limbs. She had a lobster claw deformity of the right hand with absence of the middle ray, and bilateral ectrodactyly of the feet with 4/5 syndactyly. The left hand was normal. The skin was noted to be dry and she had areas of alopecia. She had dental hypoplasia with recurrent caries.

Clinical Genetic Counselling Service, Queen Elizabeth Hospital, Kowloon, Hong Kong.
K Tse

Department of Clinical Genetics, The Hospitals for Sick Children, Great Ormond Street, London WC1N 3JH.
I K Temple, M Baraitser

Correspondence to Dr Temple.

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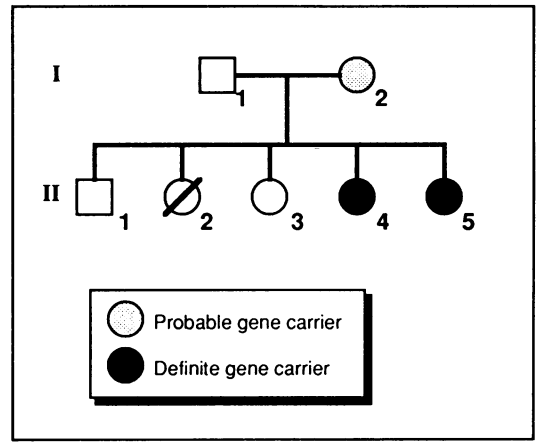

Figure 1 Pedigree.

There were early feeding problems which persisted. Motor development was normal but speech was markedly delayed. She was found to have a conductive hearing loss of 60 db and, despite insertion of grommets bilaterally, she required hearing aids for her persistent conductive deafness. She underwent multiple operative procedures to repair her cleft lip and palate, and to improve her cosmetic appearance and hand function. In addition, she needed lacrimal duct surgery for recurrent blockage.

At the age of 15 years (fig 2), she was developmentally assessed and found to have a normal non-verbal IQ, but a delayed verbal IQ equivalent to that of a 12 year old. Her hearing was assessed to be within normal limits with her hearing aids.

II·5 was born at term weighing 2300 g after an uncomplicated pregnancy. At birth she had many similar features to her sister. She was noted to have bilateral cleft lip, cleft palate, dry skin, and ectrodactyly of both hands and the right foot. Her left foot was normal. Her hair remained thin and sparse, and she too had small, hypoplastic teeth.

She had fewer early feeding problems and all motor milestones were achieved at appropriate times. However, she required bilateral grommets for a 50 dB conductive hearing loss and her speech was delayed. Her verbal IQ was 62 when she was assessed at the age of 9 years, but her performance IQ was within normal limits (fig 3).

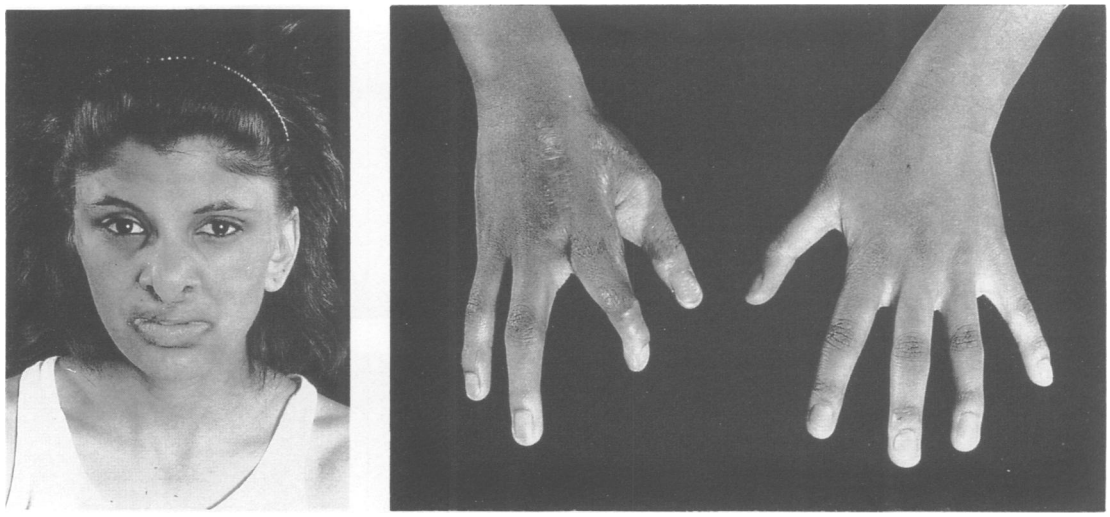

Figure 2 II·4 aged 15 years. Note the bilateral cleft lip. There is ectrodactyly of the right hand with absence of the middle ray.

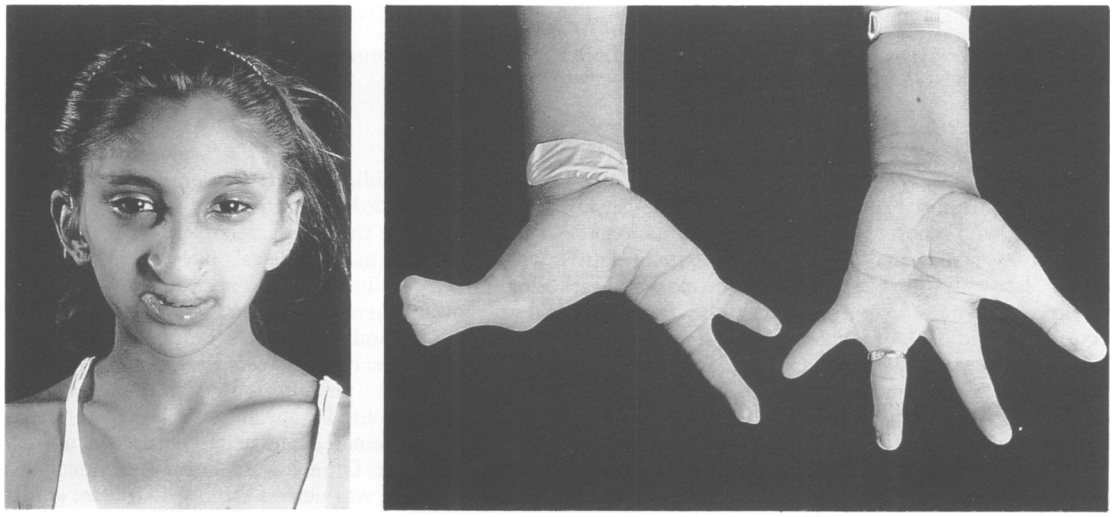

Figure 3 II·5 aged 9 years. Note the bilateral cleft lip and facial similarities to her sister. There is ectrodactyly of both hands.

The family were concerned about offspring risks of the two girls and were referred for genetic counselling. No other family members were thought to be affected.

However, the mother (I·2), who had enjoyed good health throughout her life, was noted on examination to have preaxial polydactyly of the right hand and duplication of the terminal phalanx of the second toe of the left foot with 3/4 syndactyly, as shown in fig 4. She had no cleft lip or palate and her skin, hair, teeth, and nails were normal. She was the fifth child of non-consanguineous Indian parents. Her sibs and parents lived in India, but from the history no other members of the family had similar limb abnormalities or facial clefting.

I·1 was examined and is clinically normal. The other two living sibs (II·1, II·3) are reported to be normal, but have not been formally examined. II·2 was stillborn without any obvious external abnormalities.

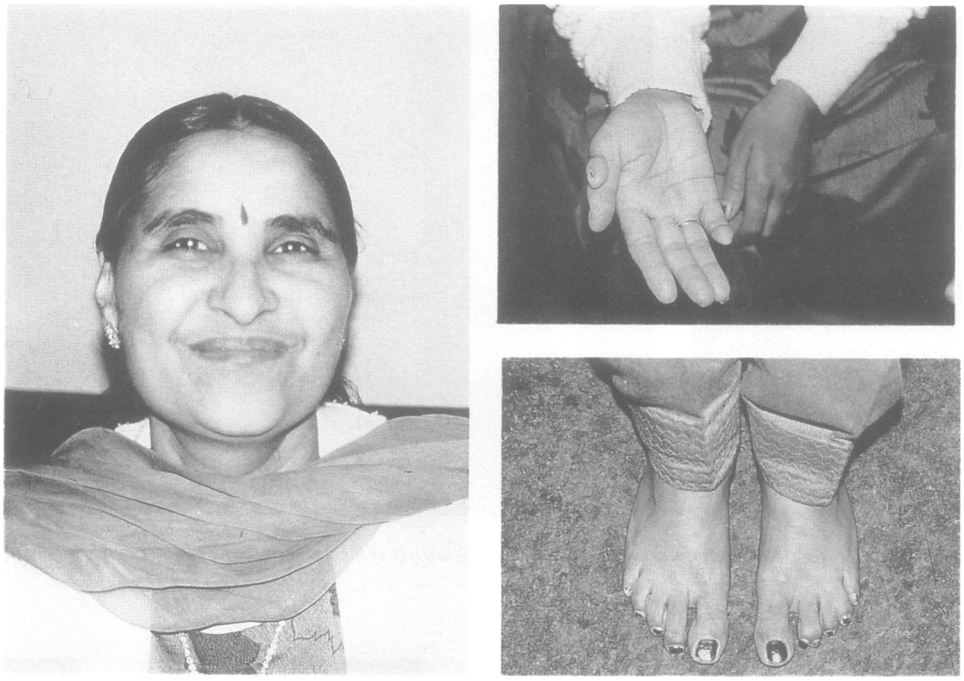

Figure 4 I·2. Note the preaxial extra digit on the right hand with no other evidence of ectrodactyly. There is duplication of the second toenail on the left foot with 3/4 skin syndactyly. Note normal lips and hair.

Discussion

The EEC syndrome was first described by Rudiger *et al*[1] in 1970, who reported a girl with a combination of ectrodactyly, ectodermal dysplasia, and cleft lip and palate. Classically, in this syndrome, the skin is thin and dry, the nails are dystrophic, the teeth are hypoplastic, and the hair is sparse with patchy areas of alopecia. A lobster claw deformity with syndactyly or absent digits is the most common limb manifestation of the condition, but occasionally there is polydactyly or a duplication of part of a digit.[2]

II·4 and II·5 described in this report have the classical features of the condition. The cosmetic consequences have been of particular concern to the two girls and each has undergone many corrective operations. Conductive deafness and speech delay have been an important problem in both girls, although non-verbal intelligence is within normal limits.

The inheritance of the syndrome is autosomal dominant. Variable expression is well documented in large multigeneration families.[3] Kuster *et al*[4] described a three generation family in which three members had ectrodactyly alone, two members had ectodermal dysplasia and facial clefting, and one member had ectrodactyly and ectodermal dysplasia.

Non-penetrance has also been reported. In 1963 Walker and Clodius[3] noted instances of non-penetrance, where obligate gene carriers had no obvious manifestations of the condition and other such reports exist, although there are relatively few examples where the 'normal subjects' have been formally examined by a clinician. This is clearly important, as in our family where the mother had been reported as normal by the family before our examination. Pries *et al*[5] in 1974 described two sisters with the EEC syndrome with phenotypically normal parents. Similarly, Lewis and Pashayan[6] described two affected half sibs (one female, one male) born to a normal mother, but the fathers were never examined and paternity testing was denied. Non-penetrance, germline mosaicism, or autosomal recessive inheritance could be put forward as possible mechanisms of inheritance in these cases.

Variable penetrance and expression makes genetic counselling in the EEC syndrome difficult. The mother (I·2) has minimal features. On clinical examination there is no real evidence of ectrodactyly. She has preaxial polydactyly in one hand and duplication of the terminal phalanx of her second toe and 3/4 syndactyly in one foot. Both these manifestations have rarely been described in patients with the EEC syndrome,[2 7] but without other features, it can only be in restrospect that this woman can be considered to be a gene carrier of the syndrome.

This report highlights the mistake that could be made in genetic counselling. Not only could one miss the very variable and minor manifestations of ectrodactyly and not counsel for the severe limb anomalies that can occur in gene carriers, but it raises the possibility that when counselling subjects with ectrodactyly alone, they should be warned that ectodermal dysplasia and facial clefting may accompany the ectrodactyly in affected offspring.

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