LETTERS TO THE EDITOR

Cornelia de Lange syndrome with ring chromosome 3

The report of Lakshminarayana and Nallasivam[1] concerning a patient with ring chromosome 3 and Cornelia de Lange syndrome recalls an earlier controversy. We had followed the cue of Falek *et al*[2] in suggesting a relationship between chromosome 3 and the syndrome of Brachmann and de Lange.[3] Francke and Opitz[4] emphasised the superficiality of this resemblance, and personal experience with five cases of dup(3q) syndrome[3 5] has documented several differences between the two malformation patterns. As with dup(3q) patients, the photograph published by Lakshminarayana and Nallasivam[1] resembles the gestalt of Cornelia de Lange syndrome but has atypical manifestations. Absent are the grim facies and micromelia, while the presence of a dilated cisterna magna, as pointed out by the authors, is unusual. Their case is also very different from our ring 3 patient[6] and it is unfortunate that the location and variability of the breakpoints were not specified.[1] Begging for examination now is the parental origin of 3q regions in 3q partial trisomy/monosomy and Cornelia de Lange syndrome. Could the quantity and imprinting[7] of unbalanced material explain their similarities and differences?

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Linear skin defects and congenital microphthalmia: a new syndrome at Xp22.2

We read with interest the two recent articles describing a new syndrome consisting of irregular linear areas of erythematous skin hypoplasia involving the head and neck, with eye findings that included microphthalmia, corneal opacities, and orbital cysts.[1 2] Cytogenetic analysis in two cases showed a translocation between chromosomes X and Y, with breakpoints at Xp22.3 and Yq11.2.[1] A third case had a terminal deletion of the X chromosome from Xp22.2–pter.[2] Parental studies were normal.

Four years ago we examined a newborn female with identical skin findings of the head and neck, bilateral microphthalmia, and corneal opacities, whom we believe, in retrospect, had the same syndrome. She also had a terminal deletion of the X chromosome, with the breakpoint at Xp22.2. We report this case to present additional findings.

Case 1. This female was born at 36 weeks' gestation after an uncomplicated pregnancy. Delivery was by caesarian section because of fetal distress. Copious amounts of amniotic fluid were noted. Birth weight was 2200 g (10th to 25th centile). At birth, the skin and eye abnormalities noted above were seen. There was a high forehead, frontal upsweep of the hair with bilateral parietal hair whorls, hypertelorism, prominence of the nasal root, low set ears with a prominent antihelix and underdeveloped superior portion of the helix, flat philtrum, and micrognathia (fig 1). A left diaphragmatic hernia caused severe respiratory distress which ultimately led to death, after unsuccessful surgical repair. Necropsy showed absence of the septum pellucidum with an ectopic area of grey and white matter, 1·5 cm diameter, in the right cerebral hemisphere, which bulged superiorly and medially and displaced downwards to the corpus callosum.

Case 2. The mother of this female is a healthy 23 year old gravida 2, para 1, SA 1 woman of normal intelligence.

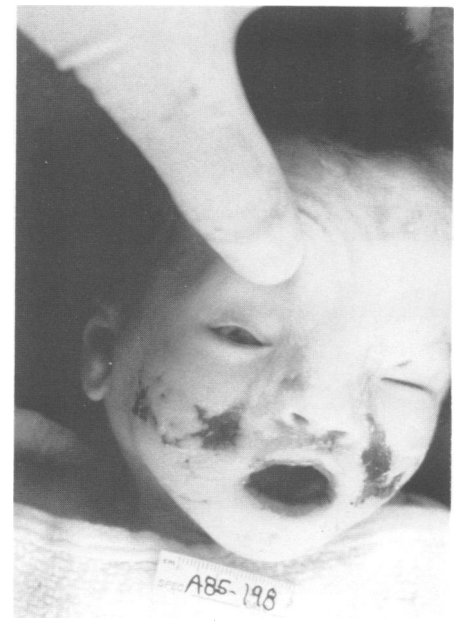

Figure 1 Case 1. Note the irregular linear areas of erythematous skin hypoplasia involving the head and neck.

Her height is less than the 3rd centile. She has a 3 to 4 cm area of patchy depigmented skin over her right shoulder, visible with the naked eye (fig 2), and larger depigmented patches on the lateral aspect of the left leg, seen with an ultraviolet light. Three out of four wisdom teeth are unerupted.

Both mother and daughter have an identical terminal deletion of X, with the breakpoint at Xp22.2.

It seems likely that the mother and daughter described here represent two further cases of the putative X linked dominant syndrome reported previously.[1 2] This is the first familial example, and documents extreme intrafamilial variation. The abnormalities in the child are more severe than those described previously, causing death, whereas the mother has minimal manifestations. She has short stature, which is often associated with terminal deletions of the X chromosome.[3] The patchy depigmentation she exhibits is unusual in two ways. Firstly, the distribution is odd, since it does not affect the face and neck, the site of neonatal skin involvement; secondly, there is reduced pigmentation, whereas the previous cases of this syndrome showed hyperpigmentation with time.

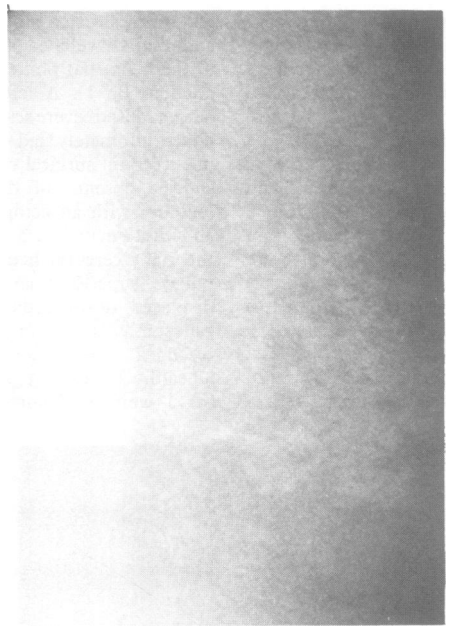

Figure 2 Case 2. Patchy depigmented skin over the right shoulder.

The mechanism underlying intrafamilial variation is unclear. It could be because of different patterns of X inactivation; however, those studies were not performed. Alternatively, it may represent an imprinting effect.

The presence of a diaphragmatic hernia in this child and dental anomalies in the mother increases the overlap with Goltz syndrome, while the central nervous system disruption enhances the similarity to incontinentia pigmenti. The latter has recently been mapped to Xq28,[4] although several earlier reports had suggested localisation of the gene to Xp11.[5] Ultimately, differentiation between these conditions should be assisted by molecular analysis.

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