Aplasia cutis congenita with chromosome 12q abnormality

J Y Khan, C Moss, H P Roper

Abstract

A 32 week, small for dates baby with aplasia cutis congenita had an unbalanced translocation, being monosomic for distal 12q and trisomic for distal 1q. As far as is known, the association between extensive skin defects and a chromosomal abnormality has not been reported before.

Keratin genes have been located in a different area of 12q, but this case may indicate other candidate areas to explore. Karyotyping should be undertaken in all babies with aplasia cutis.

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Case report

A boy was born to a 24 year old healthy, primigravida Asian mother at 32 weeks' gestation. There was no parental consanguinity, nor was there any history of illness or medication during pregnancy. Screening for α-fetoprotein was declined by the parents. Intrauterine growth retardation had first been noted on ultrasound scan at 31 weeks' gestation. Dexamethasone was given three days before delivery and the infant was delivered by elective Caesarean section at 32 weeks.

At birth the baby did not need active resuscitation. The Apgar scores were 9 at one minute, and 10 at five minutes. His birthweight was 0.985 kg (below third centile) and head circumference 28.5 cm (10th centile). The placenta weighed 240 g and looked normal. There was no evidence of fetal papyraceous. The baby had normal skin on the chest overlying the ribs, the back, the hands up to the wrists, the feet up to the ankles, the elbows and on small areas of the scalp and face with sparing of the vertex. The estimated area of affected skin was 25%.

In these sites the skin was thin, shiny and translucent, with easily visible dermal vessels. The intervening skin was normal with no blistering (figure). Ophthalmological examination and cranial ultrasound scan produced normal results. There were no dysmorphic features. The baby remained stable initially. The skin lesions were dressed with paraffin gauze.

By day 6 he had developed clinical signs of a patent ductus arteriosus (PDA). The diagnosis was confirmed by echocardiography and the PDA closed with indomethacin with no ill effects. Oral feeding was established with a preterm baby formula milk, but despite adequate intake (>100 Kcal/kg) he failed to gain weight. He then developed a *Staphylococcus aureus* bacteraemia and superficial infection. He was treated with intravenous vancomycin to which the organism was sensitive. Flexion deformities of his fingers and toes developed around day 12, followed a few days later by black discoloration of his fingertips and the tips of his right and left great toes. The baby deteriorated and died at 16 days of age.

Results

Chromosomal analysis showed an unbalanced translocation between chromosomes 1 and 12 [46,XY,−12,+der(12)(1;12)(q42.13;q24.33)]. There was extra material derived from chromosome 1 on the long arm of one copy of chromosome 12. The baby was therefore trisomic for the distal portion of 1q and monosomic for the end of 12q. The father's karyotype was 46XY. The mother had a balanced translocation between chromosomes 1 and 12 [46,XX,t(1;12)(q42.13;q24.33)], but she appeared normal on examination.

Discussion

This baby had the rare abnormality of extensive aplasia cutis congenita. Frieden\(^1\) classified this into nine categories based on clinical appearance, associated abnormalities, chromosomal abnormalities and the presence or absence of teratogens and intrauterine infections. There are two major forms of the condition:

1. (1) skin defects involving the scalp alone – usually the vertex. This is the more common manifestation and is thought to be transmitted as an autosomal dominant trait;
2. (2) more extensive disease of the trunk and limbs, with or without scalp involvement, where an autosomal recessive mode of inheritance predominates.

Similarly distributed areas of limb cutis aplasia, as seen in our patient, have been

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Baby with extensive aplasia cutis congenita.
reported by Carmi et al.\textsuperscript{2} in an infant with severe, recessive epidermolysis bullosa and pyloric stenosis, but we found no evidence of gastrointestinal manifestations. Aplasia cutis congenita may occur in either sex and there is no racial predilection. Although genetic forms (autosomal dominant and autosomal recessive) have been reported,\textsuperscript{3} the aetiology remains unknown. Extensive aplasia cutis congenita can be detected antenatally by raised alpha fetoprotein.\textsuperscript{4}

Mannino et al.\textsuperscript{5} found a strong association with fetus papyraceus where transfer of thromboplastin from the dead fetus to the surviving twin resulted in vascular thromboses in utero. This caused focal areas of ischaemia with tissue necrosis. The lesions in the case reported here were distributed similarly to those seen when there is a dead monozygotic twin, although there was no evidence of fetus papyraceus.

Aplasia cutis congenita has been reported in certain chromosomal abnormalities, including trisomy 13 and 4p-. Zakowski et al.\textsuperscript{6} reported a case of focal aplasia cutis in tetrasomy 12p in which mosaicism for isochromosome 12p was associated with the clinical features of Pallister-Killian syndrome. Our patient had none of the features described in that report and, although we did find that there was an abnormality of chromosome 12, it involved 12q rather than 12p (and monosomy rather than tetrasomy).

It has been suggested that a basic generalised epithelial defect affecting the ectoderm and, to a lesser extent, the endoderm, may cause skin defects to areas exposed to frequent pressure or friction, such as rubbing of the limbs against each other and against the trunk or face. This theory may also account for other congenital abnormalities – for example, cleft lip or palate, tracheoesophageal fistula, colobomas, microphthalmia, hydrocephalus and mental retardation – sometimes seen in aplasia cutis congenita, by causing disruption of embryonic and fetal development of other organs. Secondly, aplasia cutis congenita may be a manifestation of epidermolysis bullosa. It has been suggested that there may be genetic linkages between the loci for aplasia and that for epidermolysis bullosa and pyloric stenosis.\textsuperscript{2}

Some of the simplex forms of epidermolysis bullosa are caused by keratin gene mutations, two clusters having so far been identified in the pericentromeric region of chromosome 12 (12q11-q13) and on the long arm of chromosome 17 (17q21-q23).\textsuperscript{7} In our case the break point on chromosome 12 (12q34.33) did not involve these sites. Karyotyping is mandatory in the baby or fetus with aplasia cutis congenita.

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