Agenesis of the lung associated with a chromosome abnormality (46,XX,2p+)

SUMMARY We describe a patient with agenesis of the left lung who also had a chromosome abnormality, probably representing a duplication of the distal part of the upper arm of chromosome 2. In addition to this finding, the existence of familial cases of lung agenesis indicate that further studies are required for better understanding of the genetic aspects of this condition.

The aetiology of agenesis of the lung is unknown. Genetic factors have been implicated since pulmonary agenesis in a father and daughter,¹ as well as in two sets of identical twins,^{2,3} were recorded. We report a 35-day-old girl with agenesis of the left lung whose karyotype showed an enlargement of the upper arm of one of the chromosomes 2. We could find no report of a patient with lung agenesis who also had a chromosome abnormality.

Case report

The patient was the product of a 38 week gestation, complicated by mild pre-eclampsia and polyhydramnios. The mother was 19 years of age and the father was 23. There was no family history of birth defects. Her birthweight was 2800 g and Apgar scores were 7 at 1 minute and 6 at 5 minutes. Respiratory distress developed soon after birth. A chest x-ray at the local hospital showed complete opacification of the left hemithorax. No fluid was obtained by thoracentesis. Respiratory distress worsened in the first day of life and the infant was transferred to the Eastern Oklahoma Perinatal Center at 20 hours of age. She was cyanotic in room air. Significant physical findings were unusual facial features with blepharophimosis, posteriorly rotated low set ears and a beaked nose, hyperextensible and elongated fingers, and ectopic anus. No breath sounds were detected on the left side. No left main stem bronchus was found at bronchoscopy.

A repeat x-ray examination confirmed the chest findings. The heart did not appear to be shifted. The right lung and bony structures were normal. An esophagram showed no abnormalities.

The infant was administered 90 to 100% oxygen in a hood. However, because of progressive CO₂ retention, she was placed on a respirator. Cardiac catheterisation with angiogram indicated the absence of the left pulmonary artery, severe pulmonary hypertension, persistent ductus arteriosus (PDA) with a right to left shunt, and a significant atrial shunt. At 15 days of age, the infant developed seizures which were controlled by phenobarbital. A CT brain scan was negative. She was able to come off the respirator at the age of 17 days, but developed stridor requiring intubation and eventually total ventilatory support. She died at 35 days of life.

At necropsy, the left lung, left stem bronchus, and bronchial and pulmonary arterial trees were absent. The heart showed a complete common atrioventricular canal. No other congenital defects were seen. Neuroblastoma in situ was found in random sections of one of the adrenal glands.

Chromosome analysis of the peripheral lymphocytes indicated an enlarged chromosome 2. G banding by the trypsin-Giemsa method showed the presence of additional positive and negative staining regions near the distal end of the p arm (figs 1, 2). This pattern is consistent with a duplication⁴ for region 2p21→25 resulting in a partial trisomy, 46,XX,dup(2)(pter→p21::p24→p21::p21→qter). R banding by incorporation of bromodeoxyuridine followed by acridine orange staining did not provide additional information. The karyotypes of the parents were normal.

FIG 1 The proband's chromosome pair No 2 from two different metaphases (G banding). The duplicated chromosome is on the left.

FIG 2 Standard ideogram of chromosome 2, indicating the extent of the duplicated region.

Discussion

Although about 200 cases with lung agenesis have been reported, there is no agreement on the aetiology of this malformation. Intrauterine infections, both bacterial and viral, and intrauterine injury have been proposed as possible causes of lung agenesis. It is of interest that agenesis of the lung has been induced in experimental animals by a diet deficient in vitamin A.⁵

Genetic factors are also thought to be responsible for some cases of pulmonary agenesis but, as mentioned above, familial cases are rare. However, many patients with this condition do not reach reproductive age, and therefore genetic aetiology may have been underestimated.

The existence of a chromosome abnormality in our patient, probably representing a duplication of a segment of chromosome 2, is of further genetic interest. It may be that this is a coincidental finding. We could find only one report in which chromosome studies had been carried out with normal results,⁶ but no mention was made of whether or not banding was done. It is obvious that similar studies should be done in future cases.

Our patient had several of the clinical findings reported in patients with the duplication (2p) syndrome. These included facial features as well as long hyperextensible fingers and toes. The patient was the product of a term pregnancy and had a normal birthweight and length for gestation. An

excellent review of the patients with duplication (2p) syndrome has indicated the presence of skeletal abnormalities of the thorax such as extra or missing ribs and sternal malformations in a number of cases.⁴ The relationship between these findings and possible defects in the underlying soft tissues is speculative at present.

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A probable case of the homozygous condition of the aniridia gene

SUMMARY A non-consanguineous union between two people with congenital aniridia is described which resulted in the stillbirth of a female fetus with complete absence of eyes, nose, and adrenal glands.

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