

De Novo Interstitial Deletion of Chromosome 1p with Absent Corpus Callosum-A Case Report

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Abstract

Deletion of short arm of chromosome 1 is a rare clinical entity and there are no clearly defined phenotype. We report a case of deletion of the short arm of chromosome 1, which is believed to be the first case among the Chinese population. This baby was also found to have some Robinow Syndrome-like features as well as absent corpus callosum which have never been reported in deletion of chromosome 1p.

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Introduction

There are not many cases of deletion of chromosome 1p reported in literature. The diagnostic clinical features are not well defined. However, common clinical features of deletion of chromosome 1p are facial dysmorphism, low set ears, high-arched palate, clinodactyly and congenital heart defect.

De novo deletion of chromosome 1 was first described by Aarskog in 1968. Structural anomalies of chromosome 1 which allow the fetus to continue to develop until term, are rare.

Case Report

A baby girl was born to a 26-year-old gravida 3 para 0 Chinese mother. She had two previous spontaneous abortions. There was no parental consanguinity. Her antenatal period was uneventful. The infant was born normally at term. Her weight was 2.8 kg (50th centile). The head was large measuring 38 cm (95th centile) with a wide anterior fontanelle. The length was 45 cm (10th centile). She had the following dysmorphic features: fetal facies with ocular hypertelorism (Fig. 1), low set ears, upturned nostrils, short philtrum, high-arched palate, webbed neck and widely spaced nipples. The arm span was 38 cm with mesomelic shortening of limbs. The hands were broad and short. The thumbs were proximally placed and the examination of the little fingers

revealed clinodactyly. There was grade 3/6 pan-systolic murmur and two-dimensional echocardiography showed patent ductus arteriosus and atrial septal defect of ostium primum type. Examination of the genitalia showed hypoplastic labia minora and absent clitoris (Fig. 2). Cranial ultrasonography revealed absence of corpus callosum (Fig. 3). Ultrasonography of the abdomen showed normal kidneys. Skeletal survey showed that the ulna and radius were shortened. The metacarpals were also short and the thumbs were proximally positioned. The spine was normal. Karyotyping showed interstitial deletion of chromosome 1p(46XX,del(1)(p22p32) (Fig. 4). Parental karyotyping were normal. The infant developed congestive cardiac failure on the second day of life. The parents, however, decided to take the baby home, against medical advice, on the fifth day of life. She died a few hours later at home. No autopsy was done.

Discussion

Short arm deletions of chromosome 1 are rare' and there are only 14 reported cases so far. Various segments have been involved.' A large de novo deletion of chromosome 1 was first described by Aarskog in 1968.² This was before the banding era and it was noted that the deleted segment was a large part of a distal early replicating region and therefore was most likely a terminal

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Fig. 1. The baby with fetal facies.

deletion of 1p. It is now established that partial deletion of an autosome is compatible with life.² Smaller deletions are more likely to survive to term than those more proximal to p36.¹

The clinical features in cases of deletions of chromosome 1p have been heterogenous and do not allow the delineation of any specific clinico-cytogenetic syndrome.² Because of the small number of published cases, there is little possibility of establishing specific chromosomal segment loss and phenotype.¹ As deletion of short arm of the chromosome 1 is rare, there are no clearly defined clinical features. However, Howard and Porteus¹ described the following features: low set ears, pre-auricular pit and skin tags, narrow palpebral fissures, high-arched palate, bulbous nose, short neck, cryptorchidism, arachnodactyly, drumstick phalanges and overlapping second toes.¹ Bene et al³ described round face, half open mouth, micrognathia, malformed ears, convex thorax, widely spaced nipples, genu valgum and open anterior fontanelle.

Peterson and Warburgh⁴ reported a case with features of microcephaly, low hair line, synophrys, freckled face

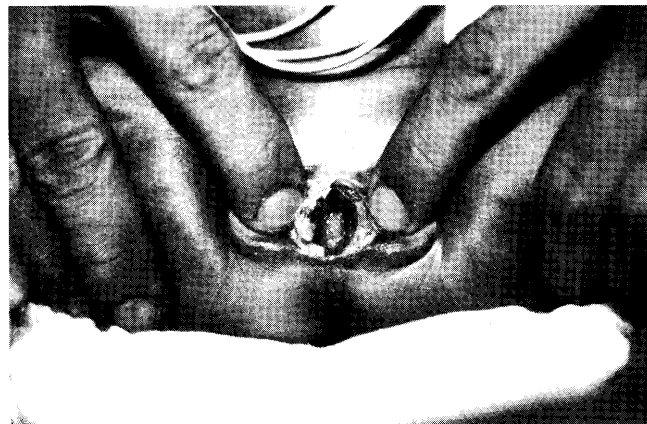


Fig. 2. Absent clitoris and hypoplastic labia minora.



Fig. 3. Cranial ultrasonography showing widely separated anterior horns of the lateral ventricles as shown by the arrows indicating absent corpus callosum.

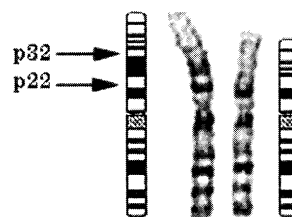


Fig. 4. Karyotyping showing interstitial deletion of chromosome 1.

and primitive ears. The child was also found to have bilateral microphthalmia with coloboma of the iris and choroid, short neck, clinodactyly and proximal implantation of the thumbs bilateral equinovarus and valgus deformities of the big toes. Our case did not have any ocular abnormality. Another case was reported with undescended testes without any dysmorphic features at birth, but subsequently developed language delay and psychiatric problems.⁵ He was also suspected to have Prader-Willi syndrome with almond-shaped eyes with epicanthic folds, clinodactyly and unusual facies.⁵ Lai et al⁶ published two cases with features of hypertelorism, microphthalmia and absent lens in the left eye, pupillary abnormality, freckled face, thick rounded ears, high-

arched palate, clinodactyly, proximally-implanted thumbs, mild talipes halux valgus and developmental delay.

Howard and Porteus¹ and Aarskog² described high-arched palate, hypertrichosis, low set ears, short neck and cryptorchidism. But a few features seem to occur in more than 30% of cases, namely low set ears, short neck, bulbous nose, congenital heart disease, small eyes, clinodactyly and mental retardation in all survivors.' Clinodactyly seems to be more common and is not related to a specific chromosomal loss.¹ There was no relationship between survival rate and extent of chromosomal loss, but three out of five patients with breakpoints at p36 died of congenital heart defects with respiratory distress.' These patients had inherited partial deletion of chromosome 1 by malsegregation of a familial translocation.'

Two patients with deletion of chromosome segment p22.1–p22.2 had bilateral coloboma, but there was no mention about eye examination in two other patients with deletions involving the same region.' Bilateral coloboma has been described in a number of other chromosomal deletions and duplications and is therefore non-specific.' Our case had hypertelorism.

Majority of the deletions were due to de novo deletion.' Among the 7 cases who had de novo deletions, 4 were interstitial deletions and 3 were due to malsegregation at meiosis of a familial translocation.¹ The breakpoints were distributed along the length of the short arm with clustering in p36 to the terminal region.' Ikeuchi et al⁷ described a de novo deletion involving the region between bands p22.1 and p32.1. One case was found to have deletion (1)(p21–p22.2) arising from a de novo translocation between chromosomes 1 and 2:(t(1;2)(1pter–1p22.2::2p25–2pter;2pter–2p2.5::1p21–1qter).⁶ Bene et al³ described a case of de novo deletion of chromosome 1 involving the region between bands p21 and p32. Howard and Porteus¹ reported a case of deletion of chromosome 1 involving the segment between bands p34.1 and 36.1. Peterson and Warburgh⁴ published a case of deletion of chromosome 1 involving the region between bands p22.1 and 32.1.

Congenital heart disease has been reported in 4 out of twelve cases.¹ Pulmonary atresia associated with ventricular septal defect was reported in one case.' Our case had atrial septal defect with patent ductus arteriosus.

Our case had some features of Robinow syndrome (RS). The essential features of RS include fetal facies, mesomelic brachymelia, short stature and genital hypoplasia.⁸ Other features are upturned nostrils, mesomelic or acro-mesomelic brachymelia, vertebral or costo-vertebral anomalies, distal ulnar and proximal radial hypoplasia, cleft lip and palate, crowded teeth, gingival hyperplasia, split distal phalanx of the thumbs and

partial or complete duplication of the thumb or great toe.⁹ Hypoplastic labia minora and clitoris have been reported in RS.⁹ Penile hypoplasia is nearly always present.⁹ Vera-Roman¹⁰ reported a case of RS with penile agenesis and hemivertebrae. Our case had fetal facies, mesomelic brachymelia, proximally placed thumbs, hypoplastic labia minora and absent clitoris. Many types of congenital heart defects have been reported including tetralogy of Fallots, bicuspid aortic valve, pulmonary artery stenosis, coarctation of aorta and ventricular septal defects.⁹ Our case was found to have atrial septal defect with patent ductus arteriosus. Chromosomal cultures were negative in all published cases except one, where the patient was found to have a deletion of chromosome 7(46XXdel(7)(q32 ter).¹¹ Our case had deletion of chromosome 1p.

No intracranial anomalies have been reported in deletion of chromosome 1p so far. Our patient was the first case to have absent corpus callosum. However, mental retardation, cerebellar signs including intentional tremors, incoordination with ataxia speech and psychiatric disturbances have been described in this condition.⁵

As with many conditions which do not have pathognomonic features to confirm the diagnosis, particularly when there are not enough reported cases in the literature, it becomes difficult to confirm the diagnosis. Since deletion of chromosome 1p is rare and more clinical features are added to the condition, perhaps it would be worthwhile to design a scoring system to arrive at a diagnosis.

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