Deletion 14q (q22q23) associated with anophthalmia, absent pituitary, and other abnormalities

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Abstract
A fetus is described with anophthalmia, absent pituitary, hypoplastic adrenal glands and kidneys, absent left horn of the uterus, underdeveloped genitalia, and clinodactyly, with a deletion of 14q(q22q23). A review of published reports found no similar deletion cases.

Although deletions of small chromosomal segments are relatively common, there are only a few instances reported of deletions involving the long arm of chromosome 14. Furthermore, most of these are terminal; there appear to be only four published cases of interstitial deletions. We describe a fetus with an interstitial deletion of 14q and an unusual combination of clinical features.

Case report
This was the fourth pregnancy of unrelated Caucasians, the mother and father being 31 and 29 years old, respectively. The first pregnancy was ectopic, the second ended as a spontaneous abortion at 12 weeks, and the third resulted in a normal appearing stillbirth at 22 weeks owing to placenta praevia. In the fourth pregnancy, ultrasound examination at 21 weeks showed an unusually shaped fetal head, small orbits with the absence of eye lenses, loose skin at the back of the neck, and possible polydactyly. In view of these findings, the couple opted for termination of the pregnancy.

The female fetus was markedly dysmorphic (figure). There was bilateral anophthalmia, confirmed by histology, and short, widely spaced palpebral fissures. The nose had a high bridge and antverted and flared nares. The upper lip markedly overrode the lower and the lower jaw was receding. The ears were fleshy, angular, and low set. There was brachycephaly with an abrupt vertical occiput, and the forehead was high and prominent. There was excess skin around the posterior neck. On both hands the fifth fingers were incurved with short middle phalanges and the thumbs were flexed. The external genitalia were underdeveloped.

Internally, the left uterine horn was absent, the kidneys were somewhat small, and the adrenal glands markedly hypoplastic. Histologically, the kidneys appeared hypoplastic and the adrenal glands had a reduced fetal cortical layer, similar to that seen in anencephaly. There were abnormalities of the cranium and brain. The cranial floor was short in the anterior and posterior direction and the pituitary fossa

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was absent. The optic nerves, chiasma and tracts, the
geniculate bodies, pituitary stalk and gland were
absent; the cerebellum was small.

Tissue from the fetus was cultured and showed a
small deletion of the long arm of chromosome 14,
karyotype 46,XX,del(14q22q23). Both parents had
normal chromosomes.

Discussion
The four other cases of interstitial deletions of 14q had
breakpoints more distal than those of the present
case (table). There is no consistent clinical picture in
these four patients, although all were dysmorphic,
with overdeveloped eyebrows, a small, bulbous nose,
micrognathia, developmental delay, and mental
retardation. One (case 1) had a horseshoe kidney and
an atrial septal defect (ASD), another (case 2) was
said to have Holt–Oram syndrome with reduction
deformities of the forearms and thumbs and an ASD,
and yet another (case 3) also had a cleft palate.

Two chromosome aberrations involving regions of
14q more proximal than our case have been reported.
One was a complex translocation involving chromo-
somes 3, 11, and 14 which included an interstitial
deletion of 14q at q13q22. The child had bilateral cleft
lip, complete cleft palate, and congenital glaucoma.
The other resembled our case in one respect; the
child had bilateral anophthalmia, but also unilateral
macrostomia, preauricular skin tags, and cervical
hemivertebrae, and was associated with a translocation
between chromosomes 4 and 14, with the breakpoint
on 14q at q11.

The combination of defects found in our fetus is
unusual. A search of the London Dysmorphology
Database and McKusick’s *Mendelian inheritance in
man* has shown no similar case.

Primary anophthalmia (no eye tissue in the orbit)
with no other associated features is an autosomal
recessive condition. Anophthalmia in conjunction
with other defects can be found in Fraser syndrome,
Goldenhaar syndrome, and anophthalmia (type
Waardenberg), but in these there is no pituitary
abnormality. Absent pituitary gland can be seen in
holoprosencephaly, but this is not associated with
anophthalmia. There is, however, a report of five
mentally retarded adults with microphthalmia or
anophthalmia and hypogonadism with low gonado-
trrophin levels, which suggests a hypothalamic or
pituitary deficit. Their chromosomes were said to be
normal.

This combination of abnormalities in our case
appears to be unique, and the additional finding of a
specific minute chromosomal deletion suggests that
this region of the genome on 14q, q22q23, could be
important for normal eye, pituitary, craniofacial, and
uterine development.

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