Prenatal detection of Turner’s syndrome in conjunction with trisomy 20 mosaicism (45,X/46, X, + 20)

SUMMARY A case of Turner’s syndrome, detected antenatally and complicated by the finding of trisomy 20 mosaicism in 50% of cells from each of two amniotic fluid cultures, is described. Cultures from seven fetal tissues in the subsequent abortus showed a predominance of 45,X cells, but nevertheless suggested the existence of a very low level of trisomy 20 mosaicism in three fetal tissues. The diagnostic dilemma in interpreting trisomy 20 mosaicism is discussed.

Much discussion has centred round the definition of mosaicism in cultured amniotic fluid cells. It is considered to be likely to exist when an identical abnormal cell line is found in more than one culture or clone. However, in some cases mosaicism has not been verified in the resultant abortus.\(^1\)\(^2\) Simola et al\(^3\) suggest that mosaicism should be ignored except where there are known severe consequences. Trisomy 20 may be in the latter category since an association with severe mental retardation has been reported.\(^4\) We report an example with monosomy X and mosaicism for trisomy 20. Counselling problems are discussed and essential procedures for confirmation are outlined.

Case report

A 40-year-old woman in her third pregnancy was referred for amniocentesis because of her age. She had had a normal delivery 7 years previously, followed by a spontaneous first trimester abortion. Amniocentesis was performed at 18 weeks.

Materials and methods

Clear amniotic fluid was obtained. Flask cultures were initiated using Ham’s F10 supplemented by 30% fetal calf serum.

Seven different tissues from the subsequent abortus (table) were taken to confirm the diagnosis. Both flask and coverslip cultures were established from each tissue using similar growth medium.

Sixty cells were analysed from each tissue to exclude 5% mosaicism to the 95% confidence limit.\(^5\)

Results

Liquor α-fetoprotein concentration was normal (14 μg/ml) while cytogenetic analysis revealed no normal karyotypes. The table shows the chromosome results for all amniotic fluid and fetal tissue cultures.

Management

The missing sex chromosome from all cells made the interpretation of the additional F-like chromosome difficult since it could have been derived from a sex chromosome, for example, iso Yq or Xp–q–. However, the G banding pattern strongly suggested identification of the F as a No 20 (fig 1).

Counselling was difficult because we could find no precedent in published reports. The parents were advised that the fetus would be likely to have the Turner phenotype but that this could be modified in one of two ways. If the F-like chromosome were a deleted X, the phenotype could even approach that of a normal female, depending on the extent of the mosaicism and its distribution in key tissues. The latter considerations also applied to the more probable explanation, namely mosaicism for trisomy 20. The paucity of information on the phenotype of trisomy 20 complicated the counselling but, by analogy, it was postulated that the fetus could be malformed and mentally retarded. Although it was a wanted pregnancy, the parents elected to have it terminated.

### Table Summary of cytogentic results

<table>
<thead>
<tr>
<th>Tissue</th>
<th>No of cells or clones</th>
<th>45,X</th>
<th>46,X,+F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amniotic fluid I</td>
<td>15</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Amniotic fluid II</td>
<td>5</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Skin</td>
<td>59</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Heart</td>
<td>60</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>60</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>59</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Cord</td>
<td>59</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Blood</td>
<td>60</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Ovary</td>
<td>60</td>
<td>0</td>
<td></td>
</tr>
</tbody>
</table>
Pathology

External examination of the fetus showed only minor abnormalities, that is, lymphoedema localised to the subcutaneous tissues behind the neck and on the dorsum of the feet.

Internally there was a lobulation defect of the right lung and a double fused kidney on the right side. The heart and aortic arch were normal. The ovaries appeared normal macroscopically but were histologically abnormal when compared with sections from the ovary of an XX female fetus of the same age (fig 2).

Discussion

Every tissue sampled had a 45,X pattern in all cells from the fetus but the trisomy 20 appears to have been verified in one cell only from three different tissues. It is puzzling that the 50% mosaicism detected antenatally was so drastically reduced. There are several possible explanations, largely depending on...
the origin of the amniotic fluid cells. In vitro origin of
the trisomy 20 cell line is possible but unlikely,
since this was the only abnormal karyotype found
in a total of 460 cells and it was found in five cul-
tures. Furthermore, the fact that trisomy 20 has been
found after repeat amniocentesis9 indicates that it is
not an artefact of the tissue culture system.

The trisomy 20 may have been present in higher
proportions in the extraembryonic tissues or
urinary tract. In retrospect, it is unfortunate that
these tissues were not cultured since Priest et al7
suggest that the most common type of cell in
amniotic fluid may be from fetal membranes.

Finally, it is conceivable that the small number of
trisomy 20 cells in the cultured fetal tissues did not
in fact originate from those tissues per se but were
stray cells from the amniotic fluid contaminating
the sampling area.

Mosaicism for trisomy 20 in amniotic fluid has
been reported by several authors1 2 6 8 9 10 and it is
interesting that there appears to be a significant sex
bias, since only a single male fetus has been reported.1
The majority of fetuses were consequently aborted
and in only one was the trisomy 20 mosaicism
weakly verified, in a single cell cultured from
placenta.1 All but two aborted fetuses were physi-
cally normal although cytotgenetic follow-up was
inadequate in the majority of cases. Three preg-
nancies were allowed to continue despite advised
risk of mental handicap and surprisingly the babies
were apparently normal in all respects.

However, true trisomy 20 mosaicism has been
reported in subjects with severe mental retardation4
and partial trisomy 20 may cause mild to severe
mental retardation.10

Thus, in vitro trisomy 20 poses a most difficult
prenatal diagnostic problem. Repeat amniocentesis
is thought to be of little value in the majority of
cases since true mosaicism may be missed,11 while
verification is not necessarily indicative of fetal
abnormality.1

Rodriguez et al8 suggest that trisomy 20 is a
phenomenon similar to tetraploidy, arising sponta-
eneously in amniotic fluid cells. However, if this
aneuploidy reflects a peculiar propensity to particular
non-disjunction, one might expect to find increasing
incidence of trisomy 20 in older cultures, as is true of
tetraploidy, unless predisposition to this non-
disjunction already exists in vivo.

Rudd et al12 suggest that the family be advised of
a risk of mental handicap although this is no longer
generally accepted.6 Furthermore, since our findings
indicated the unique combination of trisomy 20 and
Turner’s syndrome, we were able to predict positively
the presence of one abnormality and add to this the
possibility of another. However, the mosaicism
found in the fetus was of such a low level that it is
difficult to predict what effect, if any, this might have
had on the child.

It is essential that full follow-up is performed on
all present and future cases of trisomy 20 whether
aborted or liveborn. This should include stringent
methods of detection of low level mosaicism and
examination of as many fetal and extraembryonic
tissues as possible. Only then will the significance
of mosaicism for trisomy 20 in amniotic fluid be
resolved.

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References

1. Rudd NL, Gardner HA, Worton RG. Mosaicism in
amniotic fluid cell cultures. Birth Defects 1977;XIII:
No 3D:249-58.
2. Kardon NB, Lieber E, Davis JG, Hsu LYF. Prenatal
267-72.
3. Simola K, Aula P, Ryvainen M, von Koskull H. In-
complete prenatal diagnosis of G-trisomy mosaicism.
4. Pallister PD, Herrmann J, Meisner LF, Inhorn SL,
Opitz JM. Trisomy 20 syndrome in man. Lancet 1976;1:
431.
5. Hook EB. Exclusion of chromosomal mosaicism:
tables of 90%, 95% and 99% confidence limits and comments
6. Mascarello JT, Chadwick DL, Moyers TG. Trisomy 20
mosaicism in amniotic fluid cells. Lancet 1980;i:1089.
7. Priest JH, Priest RE, Sgoutas DS. Production of hormone
by cells cultured from human amniotic fluid. Am J Hum
Genet 1977;29:88A.
8. Rodriguez ML, Luthy D, Hall JG, Norwood TH, Hoehn
H. Amniotic fluid cell mosaicism for presumptive trisomy
10. de Grouchy J, Turleau C. Clinical atlas of human chromo-
11. Milunsky A, Atkins L. The frequency of chromosomal
abnormalities diagnosed prenatally. In: Hook EB,
Porter IH, eds. Population cytogenetics. Studies in

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