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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.

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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 μ g/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 cytogenetic results

Tissue	No of cells or clones	
	45,X	46,X,+F
Amniotic fluid I	15	15
Amniotic fluid II	5	5
Skin	59	1
Heart	60	0
Liver	60	0
Lung	59	1
Cord	59	1
Blood	60	0
Ovary	60	0

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FIG 1 Trisomy 20 cell from amniotic fluid (46,X,+20).

FIG 2 (a) Ovary of normal female fetus at 22 weeks. Prominent primordial germ cells cuffed by true granulosa cells. (b) Ovary of 45,X fetus at 22 weeks. Increased cellularity resulting from an increase in stromal and pregranulosa cells. Occasional immature primordial germ cells.

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

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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 cultures. Furthermore, the fact that trisomy 20 has been found after repeat amniocentesis⁶ 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 al*⁷ 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 authors^{1 2 6 8 9} 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 physically normal although cytogenetic follow-up was inadequate in the majority of cases. Three pregnancies 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 al*⁸ suggest that trisomy 20 is a phenomenon similar to tetraploidy, arising spontaneously 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 al*¹ 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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JESSIE L WATT, DAVID A COUZIN,
ALAN W JOHNSTON, VIJAY JANDIAL,
AND ELIZABETH S GRAY

*Departments of Genetics, Obstetrics, and Pathology,
University of Aberdeen,
Foresterhill, Aberdeen AB9 2ZD*

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Requests for reprints to Dr Jessie L Watt, Department of Genetics, University of Aberdeen, University Medical Buildings, Foresterhill, Aberdeen AB9 2ZD.