

Introduction

Invasive prenatal diagnosis is advised for high risk pregnancies identified by serum screening and abnormal ultrasound scan. We report a case referred for an abnormal scan including an increased nuchal translucency, hydrops, oligohydramnios and mild pericardial effusion. Conventional cytogenetic analysis was undertaken. We demonstrate here the importance of using conventional cytogenetics along with molecular cytogenetic techniques to interpret complex rearrangements.

Prenatal results

G-banded analysis on the amniotic fluid showed an unbalanced rearrangement resulting in trisomy for the distal region of chromosome 2 (breakpoint 2q21) and monosomy for the distal region of chromosome 13 (breakpoint q32) (see figure 1). Due to poor sample growth, the analysis was limited to one coverslip culture only.

Karyotype: 46,XX,der(13)t(2;13)(q21;q32)

Parental blood samples were requested urgently, which were normal. The pregnancy continued to term.



Figure 1:
der(13)(2;13)(q21;q32)

Postnatal cytogenetic results

A postnatal blood sample was received. The referral reasons being: nuchal skin folds, normal heart sounds, poor feeding, head circumference and weight <0.4th centile, flat nasal bridge and occiput, anterior anus. Further assessment by the Clinical Genetics team also identified long fingers, microcephaly, bitemporal narrowing and a broad nasal root (photo 1). The patient was noted to have good posture, tone and movements and was quite reactive.



Photo 1:
skin folds,
microcephaly

Karyotype: 46,XX,r(2)(p?25q?21.1),der(13)t(2;13)(q21.1;q32).ish r(2)(p?25q?21.1)(RP11-11G20+,2pter-,2qter-),der(13)t(2;13)(q21.1;q32)(RP11-480K16-,13qter-,2qter+)dn (see figures 2, 3, 4, 5)

Additional screening showed that some cells did not contain the ring chromosome 2, whilst other cells contained 2 copies. This is a frequent finding with ring chromosomes and is a result of their inherent instability.

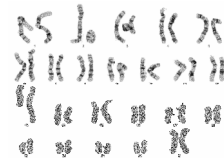


Figure 2: Postnatal karyotype

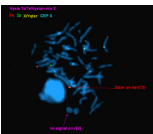


Figure 3: FISH image showing loss of 2p and 2q from the ring chromosome

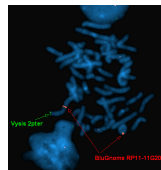


Figure 4: FISH image showing the presence of 2q14.3 on the ring chromosome

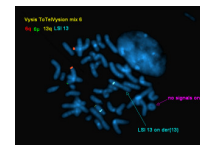


Figure 5: FISH image showing loss of 13q from the derivative chromosome 13

Array CGH result

Array CGH, using the BlueGnome CytoChip ISCA 8x60K (NCBI build 36), showed the net imbalance of the rearrangements identified cytogenetically were: deletions of the terminal regions of 2p and 13q and an interstitial deletion of the distal region of chromosome 13 (see figures 6 - 9). Although numerous genes within the deleted regions had OMIM entries none had associations with the clinical phenotype described. Overlapping regions, however, have been reported with developmental delay/mental retardation. Developmental delay is likely to be a phenotypic feature in this patient in the future.

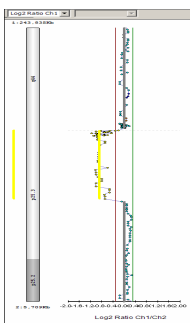


Figure 6: Array analysis showing a deletion of 2.28-2.37Mb of 2p25.3

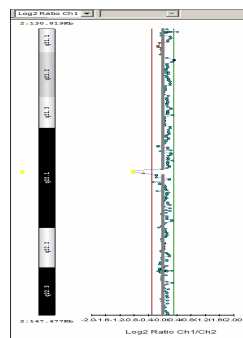


Figure 7: Array analysis showing a deletion of 164-256kb of 2q22.1

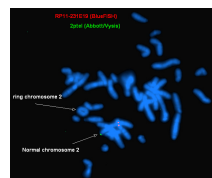


Figure 8: FISH image showing the deletion of 2q22.1

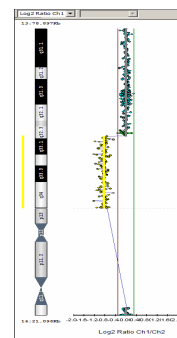


Figure 9: Array analysis showing a deletion of 14.08-14.14Mb of 13q32.3-q34

Conclusion

Postnatal karyotyping demonstrated a different, but related, result to that found prenatally. The findings were complex and could not be fully resolved using G-banding and fluorescent *in situ* hybridisation alone. This case illustrates the importance of using an integrated approach, using a variety of techniques, to elucidate complex rearrangements.

Reference

<http://decipher.sanger.ac.uk/>