

An interstitial 1q duplication in a 37 week IUD detected by Microarray. A case study

George Bakirtzis, Anna Broadwell, Arriana Carpico, Mary Glancy, Linsey McCabe, Mary Shade, Andy Pearce & Eddy Maher
South East Scotland Genetic Laboratories, Western General Hospital, Edinburgh

1. Introduction

Cytogenetic analysis of tissue samples has always been time consuming and expensive with a relatively high failure rate. Recently several laboratories have started to adopt molecular techniques such as QF-PCR and MLPA. Whilst these techniques are able to detect chromosomal abnormalities in samples that may be unsuitable for culturing, they do not offer a whole genome analysis.

Our current strategy for the investigation of solid tissue samples is QF-PCR using a kit developed to detect chromosomes 13,14,15,16,18,21,22,X and Y followed where necessary by microarray analysis. The case presented here demonstrates the importance of screening using a whole genome approach.

We report the case of a recent pregnancy loss which was referred to our department for testing following an intrauterine death at 37/40 weeks of pregnancy. Post mortem analysis of the foetus revealed only cleft lip as a major external feature.

2. Materials and Methods

DNA was extracted from the tissue samples using the E21 Biorobot from Qiagen, quantitated and subsequently hybridised on the CGH array platform. The blood samples were cultured in 15 ml Starsted tubes for 48 hrs before synchronised with thymidine and cultured for further 24 hrs. The thymidine was washed and the samples were treated with colcemid for 15 min and then harvested by using standard methodology.

3a. Results (CGH Array analysis)

CGH high resolution array analysis using the Nimblegen 135k whole genome oligonucleotide platform on the tissue samples revealed a duplication of 1050 probes that map to the long arm of chromosome 1 at position q41q42 (213616838-234405852). The size of the duplication of chromosome 1 material was estimated to be a minimum of 20.79Mb. The area of the duplication is indicated with the arrow in figure 1. The case was reported as: **arr 1q41q42.3(213616838-234405852)x3**.

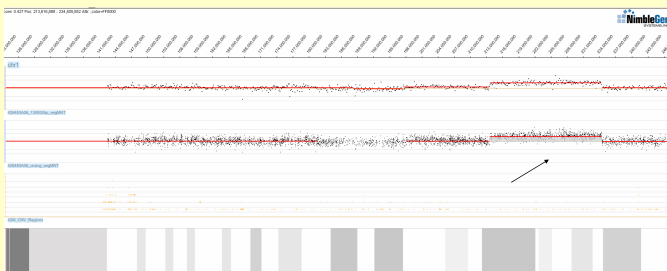


Figure 1

3b. Results (Karyotype of maternal blood sample)

Analysis of the parental blood samples indicated the presence of a complex rearrangement (insertion) involving chromosomes 1 and 10 in the maternal sample. The arrows in figure 2 indicate the area of the rearrangement (direct insertion of material from chr 1 to chr 10).



Figure 2

3c. Results (FISH analysis of maternal blood sample)

In order to further characterise and confirm the direct insertion of chromosome material from the long arm of chromosome 1 to the long arm of chromosome 10, and to investigate if any other parts of the chromosomes are involved in the rearrangement, FISH analysis was performed by using telomeric and whole chromosome paints. Figure 3 illustrates the use of telomeric paints for chromosome 1 (normal) and figure 4 shows the use of telomeric paints for chromosome 10 (normal). Figure 5 illustrates the use of whole chromosome paints for chromosomes 1 and 10. The picture confirms the direct insertion of material from chromosome 1 to chromosome 10.

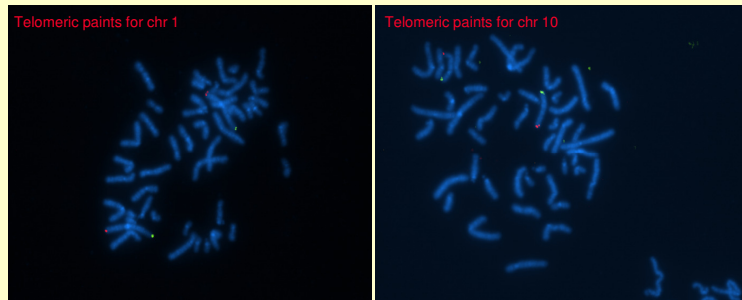


Figure 3

Figure 4

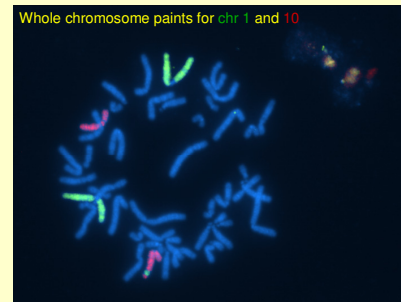


Figure 5

4. Follow up

Following the full characterisation of the chromosome abnormality and genetic counselling of the parents for any subsequent pregnancies, a CVS sample was received in our department. Cytogenetic analysis of the CVS sample showed the presence of the same chromosome abnormality as identified in the maternal blood sample (Figure 6). The arrows point the area of the rearrangement.

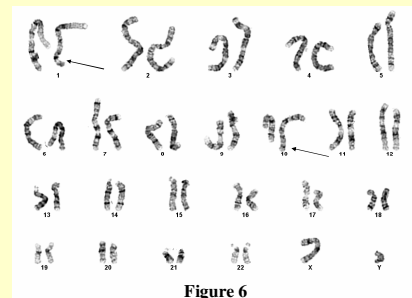


Figure 6

5. Discussion

Our case study illustrates very clearly the success and the importance of our strategy, for the analysis of tissue samples, by using a whole genome approach. This allows detailed genomic analysis of any tissue sample and guarantees a result, irrespectively of the sample's condition upon receipt, within a very short period of time. The availability of a result which explains the IUD, facilitates the process of genetic counselling and helps the parents to make more informed decisions for any future pregnancies.