Does G band analysis still have a role in testing for Developmental Disorders?
A series of case presentations

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INTRODUCTION

Within the All Wales Medical Genetics Laboratory (AWMGL) the current diagnostic strategy for patients with intellectual disability is to perform oligonucleotide array CGH as the frontline test. Although G band analysis is no longer considered an appropriate frontline test, we are still finding that there is a requirement for this technique in order to interpret some array CGH results. Here we review cases where the use of G banding and other investigations has further interpreted the structural nature of an imbalance in patients and has informed the appropriate follow up testing strategy in their families.

AUDIT OF PREVIOUS 100 ABNORMAL ARRAY CGH CASES

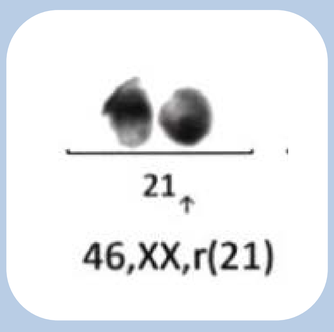
Of the last 100 abnormal array CGH reports issued, 9 have required further characterisation using techniques including G band analysis, FISH and UPD studies in order to fully interpret the complex result and inform appropriate follow up testing.

Case no.	Array CGH result	Further testing
1 & 2	Terminal copy number gain and terminal copy number loss consistent with a derived chromosome.	G banding confirmed a derived chromosome and parental samples requested to exclude a balanced translocation
3	Interstitial 46Mb gain & 1.3Mb terminal loss of chromosome 13	G banding showed a supernumerary ring chromosome 13 with inverted duplication
4	Complex pattern of copy number gain and loss on the X chromosome in a female	G banding showed a mosaic 45,X/46,X,der(X) karyotype
5		**See report**
6		**See report**
7	17.1Mb mosaic gain of 12p	G banding showed a supernumerary ring chromosome 12
8		**See report**
9	Complex pattern of both homozygous and heterozygous loss at Xp33.22 and Yp11.32 in pseudoautosomal region (PAR1) in a male	FISH testing confirmed that there was a deletion including the SHOX gene at Yp11.32. A region including SHOX regulatory regions must be deleted at Xp22.33

CASE 5

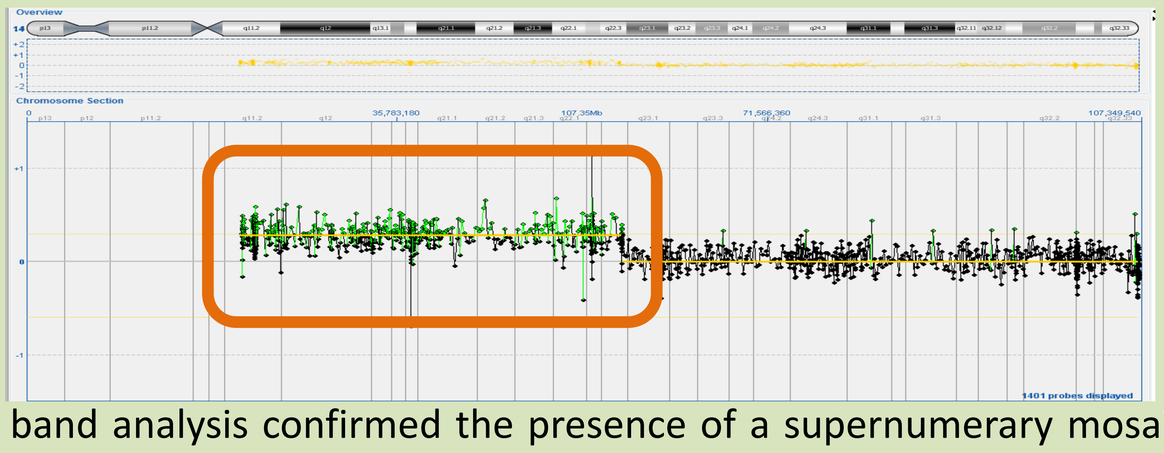
An 11 month old female was referred with faltering growth, hypertelorism, flat nasal bridge, low set ears and hypotonia. A 6.7Mb insterstitial copy number gain and a 2.3Mb terminal deletion of chromosome 21 were detected (figure below).

G band analysis showed a mosaic karyotype with 3 cell lines; one with a ring chromosome 21, one with a double ring chromosome 21 and one with a missing chromosome 21. Ring chromosomes usually arise de novo.

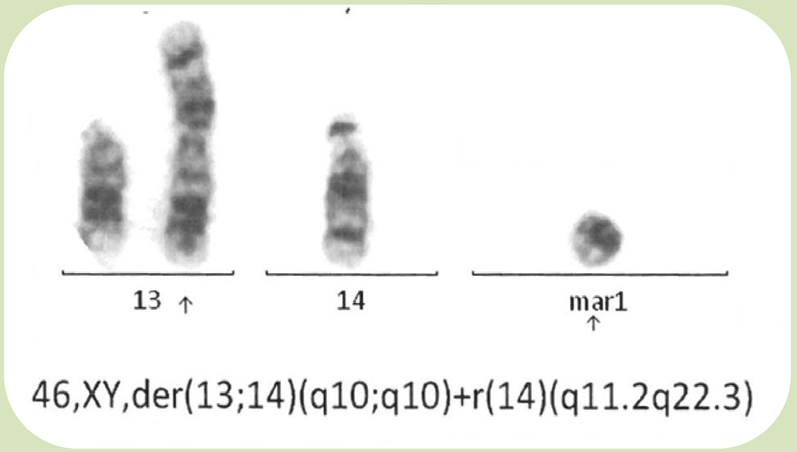


CASE 6

A 20 month old male was referred with gross motor and speech delay, mild myopathic facies, axial hypotonia, mild proximal weakness and significant small stature. A 26.8Mb mosaic copy number gain from 14q11.2 to q22.3 was detected (figure below).



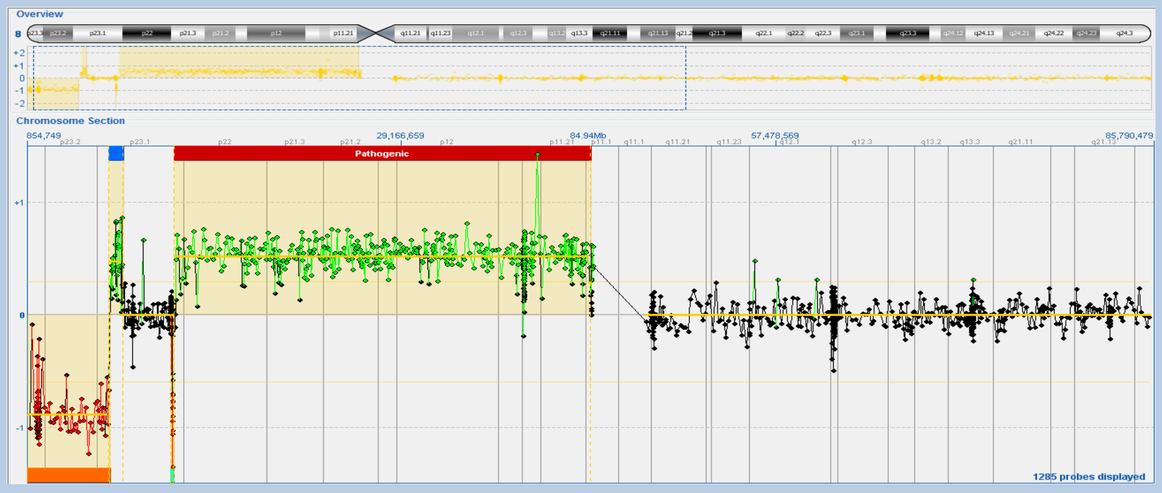
G band analysis confirmed the presence of a supernumerary mosaic ring chromosome 14 and, in addition, showed a balanced Robertsonian translocation between chromosomes 13 and 14.



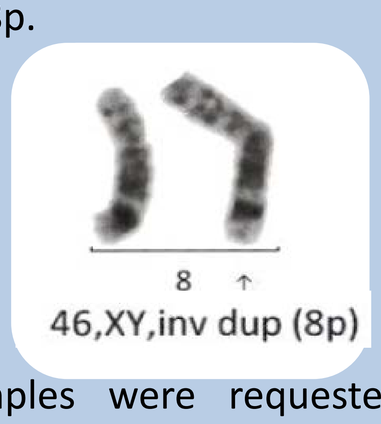
UPD testing identified that the child had maternal UPD 14 and therefore a diagnosis of Temple Syndrome.

CASE 8

An 11 month old male was referred with faltering growth, developmental delay, tracheal tag and stridor. A 6.7Mb terminal copy number loss from 8p23.3 to p23.1 and a 31.3Mb interstitial copy number gain from 8p23.1 to p11.1 were detected (figure below).



G band analysis showed a complex derivative chromosome 8, consisting of an inverted duplication of nearly the whole of 8p with a terminal deletion of 8p.



Parental blood samples were requested to investigate if the imbalance was due to a balanced parental rearrangement.

CONCLUSION

G band analysis still has a role to play in diagnostic genetics. My experience as a trainee Clinical Scientist has been that although it is possible to develop skills and expertise in a technique that is used as a frontline test with sufficient throughput e.g. array CGH, it is much more difficult to acquire and maintain the same skills for a test that, although vital, is much less frequently used.