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Report of a rare 16q23.1q23.2 interstitial deletion in a girl with multiple anomalies

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Introduction

Partial monosomies of chromosome 16q are uncommon[1,2]. The severity of the signs and symptoms depend on the size and localization of the deletion and genes content[1,2]. Interstitial deletions of 16q show a wide variability of clinical features[3].

The 16q23 deletion is a rare genetic condition (Jobling, 2013). Reported clinical features include growth and global developmental delays, intellectual disability, cataracts, hearing loss, hypotonia, feeding difficulties, and craniofacial anomalies[1,3,4,5,6].

Here we report a case of a 16-year-old girl referred to karyotyping due to short stature, overweight, hirsutism, myopia, syndactyly of the 2nd and 3rd toes on both feet, and suspected scoliosis. She also has mild bilateral hypoacusis, mild psychomotor developmental delay, especially language difficulties.

Methodology

The karyotype was performed as request. Additional chromosomal microarray analysis (CMA) was carried out using CytoScan HD (Affymetrix®) to characterize the chromosomal findings.

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Results

Karyotype revealed an interstitial deletion in region 16q23 (Fig. 1, Fig. 2).

CMA revealed, a 5.36 Mb interstitial deletion at 16q23.1q23.2 - arr[GRCh37] 16q23.1q23.2(75922170_81280700)x1 (Fig. 3, Fig. 4, Fig. 5).

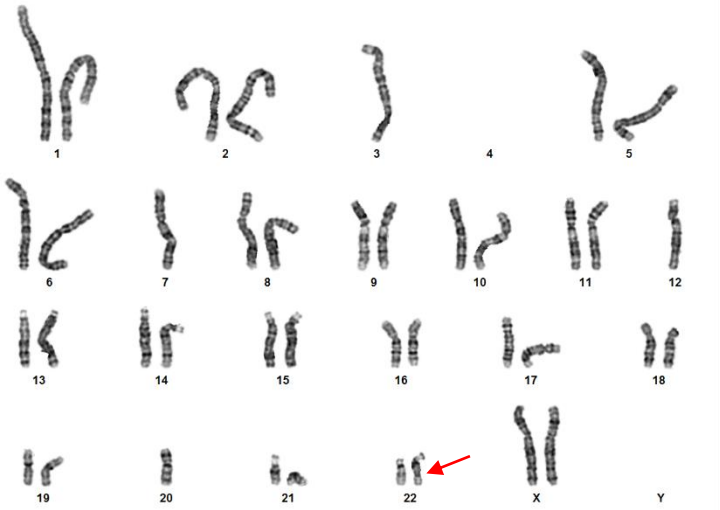

Fig. 1. karyotype showing the deletion on chromosome 16 (red arrow).

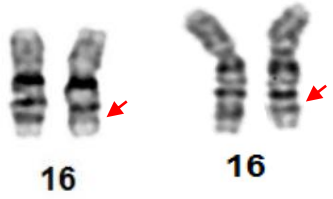

Fig. 2. Two partial karyotypes of the two chromosomes 16 showing the deletion (red arrow).

chr16: 1 - 90,354,753 (GRCh37)

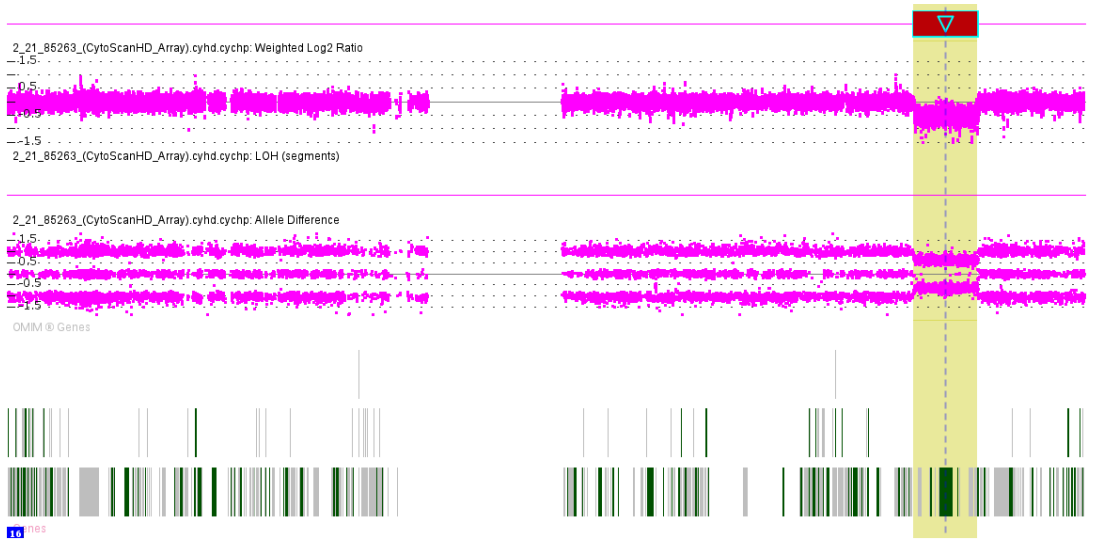

Fig. 3. Affymetrix ® CytoScan HD profile for chromosome 16, showing the interstitial loss with the oligo and SNP probes, and with OMIM genes displayed in grey and morbid genes in dark green.

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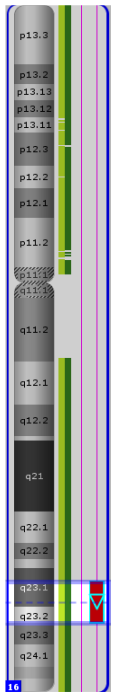

Fig. 4. Chromosome 16 ideogram showing the loss at 16q23.1q23.2 (red segment).

chr16: 72,560,464 - 84,642,406 (GRCh37)

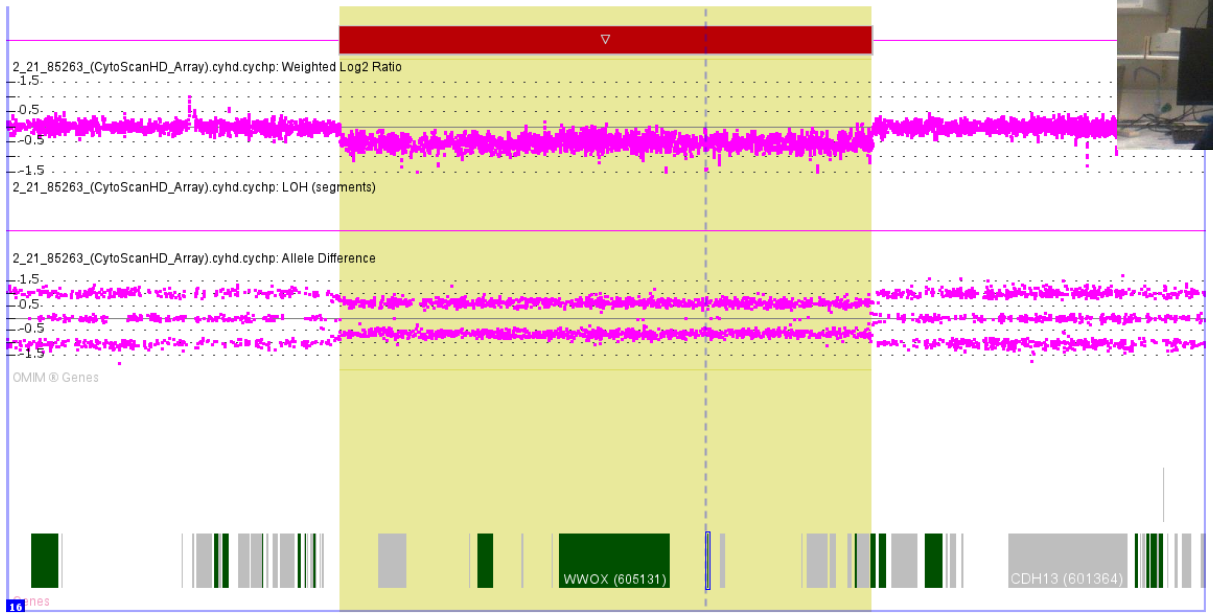

Fig. 5. Affymetrix ® CytoScan HD profile for chromosome 16q deleted region, with the oligo and SNP probes showing the interstitial loss and with OMIM genes displayed in grey and morbid genes in dark green.

Discussion

The deleted region, classified with a pathogenic clinical significance[7,8] encompasses 16 OMIM genes including 5 morbid genes of which *MAF* and *BCO1* are associated to pathologies with an autosomal dominant inheritance.
Specific heterozygous mutations in *MAF* are causal for Aymé-Gripp syndrome (AYGRPS) and most reported cases about this region are described in the context of this syndrome[3,9,10].

Discussion (cont.)

AYGPRS is classically defined as the triad of bilateral early cataracts, sensorineural hearing loss, and characteristic facial features[9,11]. It may also include developmental delay/intellectuall disability, behavioral disorders, seizures, postnatal short stature, brachycephaly, and cardiac and skeletal anomalies[9,10,11]. Some of these features overlap with those present in our patient, like the short stature, hearing loss, and intellectual disability, whereas cataract and the distinctive facial face are not present. Skeletal abnormalities have also been seen in affected individuals including scoliosis[9,12]. Foot anomalies may also be present, but syndactyly has not been reported. However, there are no large deletions encompassing these gene reported in AYGRPS patients and hence no direct correlation is possible.

Larger deletions in 16q23, like in our case, are rarely described in the literature and presentation of the clinical features shows variability[3,4,5] including short stature, some degree of psychomotor developmental delay, language difficulties, eye and skeletal anomalies, as some are in our patient. Nonetheless overweight and hirsutism have not been describe to date.

In our case it is expected that the phenotype will result from the complexity of the genetic factors involved and not just the *MAF*. Other genes, within or outside the deleted region, or their interaction, may contribute to the observed phenotype.

It is worth of note that recent information was given on the family history and our patient´s sister exhibits cognitive delay, epilepsy, polycystic ovarian syndrome/hyperandrogenism, scoliosis and overweight. CMA studies in the sister revealed a similar loss in 16q23 but parental studies are still pending. We are looking forward to the possible full study of this family.

References

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