Case report of Wolf-Hirschhorn Syndrome by Chromosomal Microarray Analysis: Importance of the Molecular Investigation for the Etiological Diagnosis of Short Stature.

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INTRODUCTION

Growth is a complex process influenced by several factors both pre and postnatal, in which 80% of the height variation is explained by genetic factors. Nevertheless, the standard medical evaluation of short stature (SS) relies upon physical examination and laboratory parameters and identifies a pathological cause of SS in 1–40% of individuals. Recent advances in genetic diagnosis are revolutionizing the clinician’s ability to obtain a molecular diagnosis for patients with growth disorders.

CASE REPORT

We report a female patient, 14 months old, presented with severe SS (-4.29 Z-Score), IUGR, neonatal jaundice, syndromic facies (microcephaly, prominent glabella, high arched eyebrow, broad nasal bridge, ocular hypertelorism, short filtrum, mouth turned down, micrognathia, malformed ears), delayed psychomotor development, intra-atrial communication and seizures. She had normal thyroid function, IGF1, Ca, P, PTH, glycemia, cortisol, renal and hepatic functions, a female karyotype, without any suggestion of chromosome alteration.

We performed the Chromosomal Microarray Analysis (CMA) on the proband and her parents (Affymetrix’s GeneChip CytoScan™ HD SNP array). CMA detected four de novo genomic imbalances, corresponding to a 3.86 Mb microdeletion (mDEL) at 4p16.3, a 1.55 Mb mDEL at 4p16.3; a 320 kbp microduplication (mDUPL) at 5p13.2 and a 4.21 Mb mDUPL at 9p24.3. The mDELS at 4p included the genes LETM1, WHSC1, WHSC2, MSXI that have been described as related to the Wolf-Hirschhorn Syndrome. The mDUPL at 5p included the NUP55 gene, and the mDUPL at 9p included KANK1 and VLDRL genes.

CONCLUSIONS

The CMA findings allowed identification of genomic cause for the clinical features of the proband. Molecular diagnosis is important because it can end the diagnostic workup for the patient, it may alert the clinician to other medical comorbidities for which the patient is at risk, and it is extremely valuable for the genetic counselling.

REFERENCES


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