HOLOPROSENCEPHALY, OROFACIAL CLEFT, AND ORBITAL ENCEPHALOCELES: A NEW AUTOSOMAL RECESSIVE SYNDROME?

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OBJECTIVES: To investigate the genetic etiology in a patient with holoprosencephaly syndrome. CASE REPORT: A boy was born through cesarean delivery at 39 weeks (2800g) after an uneventful pregnancy, presenting microbrachicephaly, small frontonasal angle, hypotelorism, broad bilateral, two cysts in the frontonasal region, bilateral cleft lip and palate, anomalous palm folds, long fingers. He developed seizures and presents with severe developmental delay at 5 months of age. He died at 7 months. A skull MRI showed agenesis of the corpus callosum, suggestive signs of lobar holoprosencephaly, dilation of the aqueduct and bilateral endolymphatic sac, bilateral cystic cocci-vestibular malformation, expansive lesion near the ethmoid bone and the right orbital cavity, suggestive of frontonasal meningoencephalocele. G-banding karyotype and subtelomeric and microdeletion MLPA (Kits P064-C1, P036-E2 and P070-B2) were normal. Affymetrix CytoScan750K SNP-Array analysis showed large regions of homozygosity (ROH) that summed up 25,4% of the autosomal genome. CONCLUSION: The complexity of the craniofacial findings observed in our patient, including holoprosencephaly and neural tube defects, to our knowledge, is unique, suggesting a hitherto not reported new syndrome. The high rate of ROH strongly suggests a parental consanguinity and that the whole clinical picture could be attributed to the action of one or more recessive gene(s). It was obtained informed consent according to the protocols approved by the ethics committee of the HRAC-USP (CAAE 34386014.4.0000.5441)