CHARGE SYNDROME

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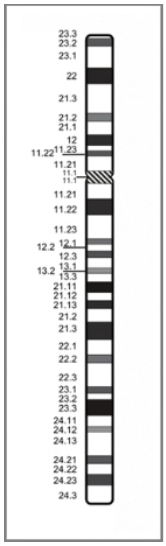

CHARGE syndrome is a rare autosomal dominant condition that is estimated to occur in 1 in every 10,000 births[1]. This syndrome is caused by mutations or deletions of the CHD7 gene, located on the long arm of chromosome 8 (8q12 segment). CHARGE syndrome is an acronym for the six key features associated with the condition. This includes coloboma (C) of the eye, heart (H) defects, atresia (A) of choanae, retardation (R) of growth and development, genital (G) hypoplasia, and ear (E) anomalies[1].

CHD7 is mutated in over 90% of those with CHARGE syndrome while deletions and genomic rearrangements account for the remaining individuals[2]. It is important to note that deletions encompassing the entire 8q12 region or small portions of CHD7 are sufficient to cause CHARGE syndrome[2]. Most cases of CHARGE syndrome are de novo[2].

While the six key features that make up the acronym of CHARGE syndrome are the most common, additional features may also be present in individuals. Specifically, extraocular features outside of bilateral or unilateral coloboma can be identified. This may include microphthalmia, cataracts, glaucoma, retinal detachments, strabismus, nasolacrimal duct obstructions[3]. Some patients have cranial nerve VII palsy[3].

Heart defects are the second portion of the acronym. Patients may present with a variety of cardiovascular malformations including patent ductus arteriosus, atrial septal defect, ventricular septal defect, or aortic stenosis[1]. As a rule, these defects are not life-threatening. As for choanal atresia, the third portion of the acronym, most individuals with this feature undergo surgical correction at some point in life[1].

Growth and development delays are frequently identified in those with CHARGE syndrome. Many males have hypogonadotropic hypogonadism resulting in cryptorchidism and/or micropenis[4]. In females, hypoplastic labia occurs in roughly 1/3 of patients and severe reproductive tract anomalies such as uterine or ovarian aplasia may occur[4]. Due to a lack of gonadotropin releasing hormones in both sexes, absent or delayed puberty is possible[4].

Ear anomalies, the sixth and final key feature of CHARGE syndrome, may manifest in a variety of ways. Low set, cup formed, and shipped off ears as well as abnormal helix shape, microtia, middle ear ossicular malformations, and inner ear defects of the cochlea may all be identified[1]. As a result, some patients may experience conductive, sensorineural, or combined hearing impairment[1].

Essentially all individuals with mutations of CHD7 gene or deletions of 8q12, which involve this gene, reveal clinical manifestations. However, not all of those with mutation of CHD7 or deletions of the 8q12 region may have all the typical features associated with CHARGE syndrome. Existing phenotypic variability may be in part due to the deletion size and location[5].

REFERENCES

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