6Q25.1 DELETION

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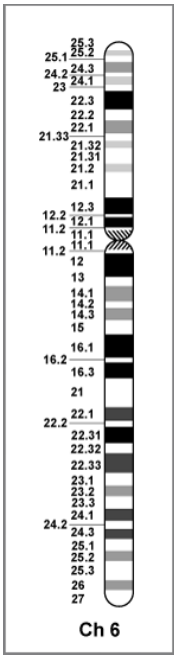

Deletions of the 6q25.1 region of the long arm of chromosome 6 constitute a specific syndrome. The main findings of this condition are defects of cardiac valves caused by the loss of the TAB2 gene, which is located in this segment. The protein encoded by the TAB2 gene stimulates a cascade of other genes that are active in the development of endocardial cushion and cardiac valves during embryonic development[1]. Due to the important role TAB2 plays in cardiac development, deletions of this gene or region are associated with non-syndromic congenital heart defects and cardiomyopathy[2].

There are a variety of congenital heart anomalies found in individuals with 6q25.1 deletions. This includes congenital valve defects in one or multiple cardiac valves such as myxomatous mitral and/or tricuspid valves (this is distinctive mark of this condition; such defects are highly unusual for other chromosomal disorders), bicuspid aortic valve, aortic stenosis, or pulmonic stenosis[1]. Atrial septal defect, ventricular septal defect, cardiomyopathy, and aortic dilation may also be seen[2]. Some individuals may present with multiple cardiac features that combine to create hypoplastic left heart syndrome. This syndrome is characterized by hypoplasia of the left ventricle and ascending aorta, an atrial septal defect, and a patent ductus arteriosus. Depending on the cardiac anomaly that is present, surgical intervention may be necessary as some of these conditions are fatal in infancy[3]. It should be noted that heart defects are an obligate finding of this deletion (all reported patients so far have been reported having these defects).

While congenital heart anomalies are the most prominent feature of 6q25.1 deletions, other features may be identified in individuals. There are several facial features such as a broad forehead, hypertelorism, ptosis, low set ears, frontal bossing, short and/or narrow palpebral fissures, and retrognathia that can be seen[1,2,4].

Other features such as short stature, intrauterine growth restriction, and hypotonia may also be seen[2]. Connective tissue abnormalities like joint laxity or hypermobility, skeletal and skin abnormalities, and pectus excavatum have also been reported[1]. Some individuals may also present with varying levels of intellectual and developmental abilities. However, the delays generally fall within the mild to severe categories[2]. Some authors suggest that patients with deletions of 6q25.1 have many manifestations in common with Noonan syndrome (a non-chromosomal genetically heterogeneous condition) such as association of heart defects, short stature and mild intellectual disability.

There is a group of patients that have mutations in TAB2 rather than deletions. Clinical manifestations in these individuals are the same as for patients with 6q25.1 deletion. This confirms the role of the TAB2 gene in the origin of these abnormalities[2].

REFERENCES

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