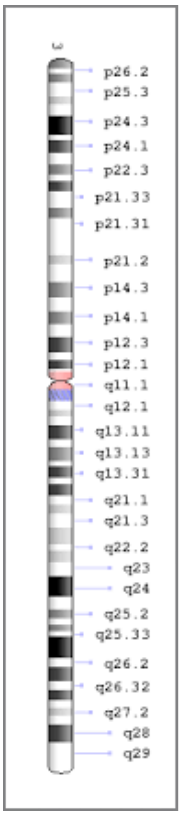
LAMB-SHAFFER SYNDROME

Lamb-Shaffer Syndrome

In 2012 Lamb et al.[1] reported several patients with deletions of a relatively small segment in the short arm of chromosome 12 (12p12.1) who had developmental delay, behavioral problems and facial dysmorphism. All these deletions included the SOX5 gene. It was shown that physical breaks of the SOX5 gene due to reciprocal translocations or mutations, resulting in haploinsufficiency, produced the same clinical picture. Most of these mutations are sporadic but it is possible for the mutation or small deletion to be passed on from a parent. The term "Lamb-Shaffer syndrome", which was coined for this condition, is currently used both for patients with deletions of 12p12.1 and for the patients with mutations of the SOX5. The ratio between patients with deletions and mutations is unknown but at least 40 patients with this syndrome caused by deletion involving 12p12.1 have been so far reported. SOX5 encodes an important transcription factor that plays vital roles in the development of chondrocytes, oligodendrocytes, and neurons.



Individuals with the disorder can be clinically characterized by their intellectual, developmental and speech delays, behavioral abnormalities, and some dysmorphic features. Occasionally, ophthalmologic and skeletal abnormalities are also seen in patients.

Intellectual, developmental, and speech delays are seen in almost all patients with Lamb-Shaffer Syndrome. However, the severity of those affected ranges widely. Patients are frequently delayed in their gross motor skills as well as their age of sitting on their own and walking independently[2]. Speech is also frequently delayed but again, varies widely. Some individuals by the age of three years or older can use full sentences[3], while others are not able to begin putting words

together to formulate small sentences until the age of five[2]. Although these developmental and speech delays have the potential to be severe, it is possible that they can be managed through continuous speech and occupational therapy[4].

Lamb-Shaffer Syndrome may also cause some individuals to have behavioral abnormalities. Some patients may eventually be diagnosed with autism spectrum disorder based on what these abnormalities are. Other observed behavioral abnormalities include stereotypes, isolation, tantrums, or hyperactivity[3]. Some other individuals with the syndrome may also have aggressive behaviors, some self-injurious behaviors, or ADHD[1].

Dysmorphic features are often seen among many individuals with Lamb-Shaffer Syndrome. This includes a broad or full nasal tip, thin upper lip or full lips, small jaw or chin, long face, or epicanthal folds[3]. Others have reported
down-slanting palpebral fissures, a broad nasal bridge, accentuated and
prominent philtrum ridges, and an open mouth appearance[2].

Ophthalmologic issues are seen in about half of patients (54.8%) with Lamb-Shaffer syndrome. This includes abnormalities like strabismus, refractive errors such as myopia and astigmatism, optic nerve abnormalities, and optic atrophy or pallor[4].

Occasionally, individuals with Lamb-Shaffer will also have skeletal abnormalities. Conditions like butterfly vertebrae and scoliosis can be observed[1].

REFERENCES

[1]Lamb A.N., Rosenfeld J.A., Neill N.J., et al. Haploinsufficiency of SOX5 at 12p12.1 is associated with developmental delays with prominent language delay, behavior problems, and mild dysmorphic features. Hum Mutation 2012, v. 33, 728-740.

[2]Schanze I., Schanze D., Bacino C.A., et al. Haploinsufficiency of SOX5, a member of the SOX (SRY-related HMG-box) family of transcription factors is a cause of intellectual disability. Eur J Med Genet 2013, v. 56, 108-113.

[3]Zawerton A., Mignot C., Sigafoos A., et al. Widening of the genetic and clinical spectrum of Lamb-Shaffer syndrome, a neurodevelopmental disorder due to SOX5 haploinsufficiency. Genet Med 2020, v. 22, 524-537.

[4]Mahmud H., Gustainis D., Jackson-Cook C., et al. Ophthalmic manifestations of Lamb-Shaffer syndrome: a case presentation and literature review. J Amer Assoc Pediatr Ophthalm Strabismus 2022, online ahead of print.