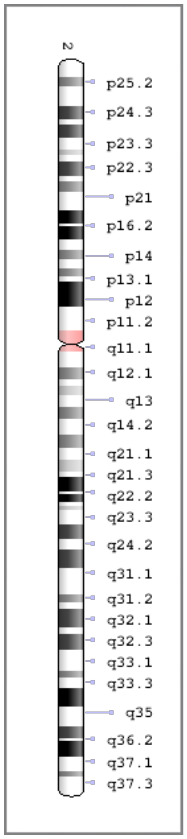
DELETION 2P24
FEINGOLD SYNDROME 1

Deletion 2p24 (Feingold Syndrome 1)



Feingold syndrome 1 (FS-1) is an autosomal dominant disorder caused by mutations or deletions of the MYCN gene located on the distal portion of the short arm of chromosome 2 (segment 2p24). These mutations and deletions have the potential to be de novo, but others are passed on from parent to child. The term FS-1 is necessary because there is a Feingold syndrome-2 caused by deletions of a segment on chromosome 13 (13q31.3).

Patients with FS-1 may have a wide variation of possible mutations. Most of individuals with FS-1 have a point mutation within the MYCN gene and 10% have chromosomal deletions that encompass the entirety of the gene locus[1].

Feingold syndrome 1 can be identified clinically through a variety of different manifestations. This includes microcephaly, duodenal and/or esophageal atresia, digital anomalies, heart defects, hearing problems and kidney defects.

Microcephaly is the most common feature associated with FS-1. An analysis of 38 known patients with FS-1 caused by whole gene mutations showed that 25 of them microcephaly. Many patients also have abnormalities of internal organs. This includes frequent atresia or stenosis of the esophagus or duodenum. In the same analysis of 38 patients, 10 exhibited duodenal abnormalities (sometimes caused by annular pancreas) and another 2 had esophageal atresia. It should be mentioned that duodenal defects are highly unusual for patients with chromosomal disorders (except trisomy 21).

Patients with FS-1 also commonly present with digit anomalies. Short middle phalanges of the second and fifth fingers, syndactyly 2-3 or 4-5

toes, fifth finger clinodactyly, and hypoplastic thumbs are some of the features that have been reported[2]. Others have also reported a large space between the first and second toes, called a sandal gap[3].

Although less frequent, congenital heart defects are also significant. Ventricular septal defect, atrial septal defect, and patent ductus arteriosus were identified in 7 of 38 identified individuals mentioned above. However, cardiac defects are typically described in only 15% of patients[2].

Hearing loss or hearing impairment have about the same frequency in prevalence with them being found around 10% of patients[2]. It's possible that these defects may actually be even more frequent: in the group of patients with FS-1 caused by deletions hearing problems were reported in 8 out of 38 patients, although several of these patients have not been tested by hearing acuity.

A significant portion of individuals with deletions had agenesis of one kidney with agenesis of both kidneys being reported in several fetuses. At the same time, there are no reports of renal cysts or renal dysplasia which are more common for patients with chromosomal disorders.

There has been no consensus on how to achieve a specific clinical diagnosis, but it is recommended that minimal criteria include microcephaly and some of the described digital anomalies. Genetic examinations conforming mutations in the MYCN gene or deletions of this area are necessary for the final diagnosis of this condition[1].

REFERENCES

[1]Tedesco MG, Lonardo F, Ceccarini C et al. (2021). Clinical and molecular characterizations of 11 new patients with type 1 Feingold syndrome: Proposal for selecting diagnostic criteria and further genetic testing in patients with severe phenotype. Amer J Med Genet v. 185, 1204–1210.

[2]Burnside RD, Molinari S, Botti C et al. (2018). Features of Feingold syndrome 1 dominate in subjects with 2p deletions including MYCN. Amer J Med Genet v. 176, 1956-1963.

[3]Chen CP, Lin SP, Chern SR et al. (2012). A de novo 4.4-Mb microdeletion in 2p24.3 → p24.2 in a girl with bilateral hearing impairment, microcephaly, digit abnormalities and Feingold syndrome. Eur J Med Genet v. 55, 666-669.