DELETIONS 3Q21

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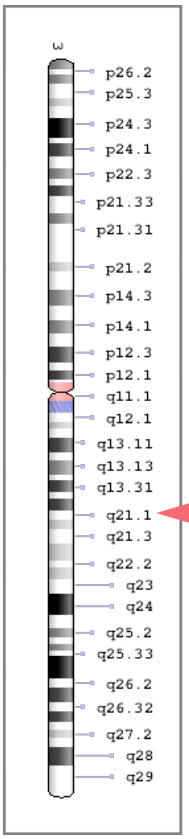

The chromosomal segment 3q21 includes a very important GATA2 gene. This gene creates a transcription factor that is typically expressed in hematopoietic pro-genitor cells like mast cells, megakaryocytes, early erythroid cells, and is critical for hematopoiesis (generation of blood cells)[1]. Malfunction or absence of this gene leads to the myelodysplastic syndrome (MDS). MDS occurs as a result of disruption of the production of blood cells who fail to become mature. It is a precancerous condition which may lead to some forms of blood cancers (leukemias[2]). MDS is a common finding in patients having mutations in the GATA2 gene. Similar manifestations may be found in individuals having deletions of this chromosomal segment. Although mutations of 3q21 may be inherited from the parents[2], all known patients with deletions of this area occurred de novo.

MDS is an almost obligatory finding in patients with 3q21 deletions affecting the GATA2 gene. There are only 2 patients with the deletion where abnormalities of blood cells were not reported. In combination with blood disorders and cancers, abnormal function of blood cells, which in normal conditions participate in immune responses, may lead to infections due to bacteria or viruses. The deletion may also lead to an absence of several kinds of cells that participate in an immune defense[3].

Individuals with relatively small deletions involving the GATA2 gene may have no other manifestations aside from MDS. However, almost all patients with 3q21 deletions reveal an involvement of several neighboring genes. These additional genes can have a wide variety

of effects on the individuals who have them. This can include not only blood disorders or related immunological problems, but also cognitive and developmental disabilities, facial dysmorphism, and congenital defects.

Cognitive and developmental delays are also common with patients with 3q21 deletions. These individuals may experience speech apraxia, gross motor delays, or speech delays[1,4].

3q21 deletion patients may present with a wide range of facial dysmorphism which can include features like low-set ears, hypoplastic ears, asymmetric skull and face[4]. In addition to these facial dysmorphisms, other physical abnormalities may be present as well. There are several reports of preaxial limb defects (preaxial polydactyly [additional thumb] or underdeveloped thumbs), heart and kidney defects, agenesis of the corpus callosum[1].

Blood defects may be not obvious, especially in infants or toddlers. Therefore, detailed blood examinations seem to be necessary for all kids where deletion in the 3q21 area was found, even if indication to their cytogenetic examination was unrelated to hematological problems[1].

REFERENCES

[1]Greenmyer JR, Thompson WS, Hoppman NL, et al. (2022). 3q21 deletion affects GATA2 and is associated with myelodysplastic syndrome. Brit J Haematol v. 196, 1120–1123.

[2]Kazenwadel J, Secker GA, Liu Y J, et al. (2012). Loss-of-function germline GATA2 mutations in patients with MDS/AML or MonoMAC syndrome and primary lymphedema reveal a key role for GATA2 in the lymphatic vasculature. Blood v. 119, 1283–1291.

[3]Vinh DC, Palma L, Storring J, et al. (2018). GATA2 Deficiency due to de novo complete monoallelic deletion in an adolescent with myelodysplasia. J Pediatr Hematol/Oncol v. 40, e225–e228.

[4]Callier P, Faivre L, Marle N, et al. (2009). Detection of an interstitial 3q21.1-q21.3 deletion in a child with multiple congenital abnormalities, mental retardation, pancytopenia, and myelodysplasia. Amer J Med Genet v. 149, 1323–1326.