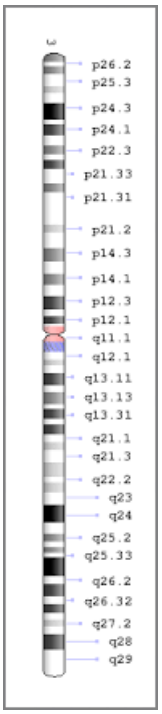
# Blepharophimosis-ptosis-epicanthus Syndrome

Blepharophimosis-ptosis-epicanthus syndrome (BPES) is essentially an autosomal dominant disorder characterized by short, horizontal palpebral fissures (blepharophimosis), drooping of the eyelids (ptosis), and vertical folds from the upper or lower eyelids towards the nose (epicanthus). BPES is caused by a mutation in the FOXL2 gene or deletions affecting this gene. Many of these mutations are either intragenic deletions or duplications that can be both in or out of the gene frame[1]. Many of these mutations are de novo and it there is a strong parental bias of the father's gamete providing this mutation.




FOXL2 is located on the long arm of chromosome 3 in band 23 (3q23) and is a forkhead domain transcription factor that controls the expression of several genes within the genome. This gene is involved in ovarian and eye development[1].

Most patients with BPES syndrome have mutations in the FOXL2 gene but there are at least 100 published patients with this syndrome who have deletions affecting this gene. These deletions differ in both size and breakpoint position. Some deletions are relatively small and affect only the FOXL2 gene, or even controlling elements located outside of the gene. In other cases, deletions may involve other genes, most of which are located distal of 3q23.

There are two types of BPES that have been categorized. Type I includes all the major eyelid features as well as infertility in females due to premature ovarian failure. Type II individuals only have the eyelid abnormalities and no other additional features[2]. It can be difficult to distinguish between type I and type II BPES in prepubertal girls due to the activity level of their ovaries being unknown. It has been suggested that using gonadotropin and steroid hormone levels can help detect the difference for this age group[3]. This early detection

can help aid families in deciding if cryopreservation of the ovary is an option they want to consider in order to preserve their child's fertility[4].

Patients with small deletions reveal typical clinical manifestations of the BPES syndrome. However, those with large deletions may not only contain FOXL2, but other neighboring genes as well. In these cases, these individuals are said to have BPES plus syndromes[2]. These patients present with various other symptoms along with the typical eye abnormalities seen in BPES patients. This includes, but is not limited to, microcephaly, heart defects, kidney defects, growth delay, developmental delays, and cognitive delays. It is thought that several of these added symptoms are due to mutations or deletions containing the ataxia- telangiectasia and Rad3-related protein (ATR) gene[5]. Many patients with deletions involving 3q24 segment have Dandy-Walker malformation which causes cerebellar defects with a posterior fossa cyst.

Individuals with BPES can grow up and lead a normal life. Some individuals will have surgery to correct their eyelids[6] but even without that, development can be normal. Many can attend school and can even grow up to have families of their own[6], however, some may require more help than others[7].

REFERENCES

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