Branchiootorenal/branchiootic syndrome

Description

Branchiootorenal (BOR) syndrome is a condition that disrupts the development of tissues in the neck and causes malformations of the ears and kidneys. The signs and symptoms of this condition vary widely, even among members of the same family. Branchiootic (BO) syndrome includes many of the same features as BOR syndrome, but affected individuals do not have kidney abnormalities. The two conditions are otherwise so similar that researchers often consider them together (BOR/BO syndrome or branchiootorenal spectrum disorders).

"Branchio-" refers to the second branchial arch, which is a structure in the developing embryo that gives rise to tissues in the front and side of the neck. In people with BOR/BO syndrome, abnormal development of the second branchial arch can result in the formation of masses in the neck called branchial cleft cysts. Some affected people have abnormal holes or pits called fistulae in the side of the neck just above the collarbone. Fistulae can form tunnels into the neck, exiting in the mouth near the tonsil. Branchial cleft cysts and fistulae can cause health problems if they become infected, so they are often removed surgically.

"Oto-" and "-otic" refer to the ear; most people with BOR/BO syndrome have hearing loss and other ear abnormalities. The hearing loss can be sensorineural, meaning it is caused by abnormalities in the inner ear; conductive, meaning it results from changes in the small bones in the middle ear; or mixed, meaning it is caused by a combination of inner ear and middle ear abnormalities. Some affected people have tiny holes in the skin or extra bits of tissue just in front of the ear. These are called preauricular pits and preauricular tags, respectively.

"Renal" refers to the kidneys; BOR syndrome (but not BO syndrome) causes abnormalities of kidney structure and function. These abnormalities range from mild to severe and can affect one or both kidneys. In some cases, end-stage renal disease (ESRD) develops later in life. This serious condition occurs when the kidneys become unable to filter fluids and waste products from the body effectively.

Frequency

Researchers estimate that BOR/BO syndrome affects about 1 in 40,000 people.

Causes

Mutations in three genes, *EYA1*, *SIX1*, and *SIX5*, have been reported in people with BOR/BO syndrome. About 40 percent of people with this condition have a mutation in the *EYA1* gene. *SIX1* gene mutations are a much less common cause of the disorder. *SIX5* gene mutations have been found in a small number of people with BOR syndrome, although researchers question whether mutations in this gene cause the condition. Some affected individuals originally reported to have *SIX5* gene mutations were later found to have *EYA1* gene mutations as well, and researchers suspect that the *EYA1* gene mutations may be the actual cause of the condition in these people.

The proteins produced from the *EYA1*, *SIX1*, and *SIX5* genes play important roles in development before birth. The EYA1 protein interacts with several other proteins, including SIX1 and SIX5, to regulate the activity of genes involved in many aspects of embryonic development. Research suggests that these protein interactions are essential for the normal formation of many organs and tissues, including the second branchial arch, ears, and kidneys. Mutations in the *EYA1*, *SIX1*, or *SIX5* gene may disrupt the proteins' ability to interact with one another and regulate gene activity. The resulting genetic changes affect the development of organs and tissues before birth, which leads to the characteristic features of BOR/BO syndrome.

Some people with BOR/BO syndrome do not have an identified mutation in any of the genes listed above. In these cases, the cause of the condition is unknown.

Learn more about the genes associated with Branchiootorenal/branchiootic syndrome

- EYA1
- SIX1
- SIX5

Inheritance

BOR/BO syndrome is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In about 90 percent of cases, an affected person inherits the mutation from one affected parent. The remaining cases result from new mutations in the gene and occur in people with no history of the disorder in their family.

Other Names for This Condition

- BO syndrome
- BOR
- BOR syndrome
- BOS
- Branchio-oto-renal syndrome

- Branchio-otorenal dysplasia
- Branchio-otorenal syndrome
- Branchiootic syndrome
- Branchiootorenal dysplasia
- Branchiootorenal spectrum disorders
- Branchiootorenal syndrome
- Melnick-Fraser syndrome

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Branchiootic syndrome 3 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1842124/)
- Genetic Testing Registry: Branchiootorenal syndrome 2 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1970479/)
- Genetic Testing Registry: Branchiootic syndrome 1 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C1865143/)
- Genetic Testing Registry: Branchiootorenal syndrome 1 (https://www.ncbi.nlm.nih.gov/gtr/conditions/C4551702/)

Genetic and Rare Diseases Information Center

- BOR syndrome (https://rarediseases.info.nih.gov/diseases/10147/index)
- Branchiootic syndrome (https://rarediseases.info.nih.gov/diseases/10148/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Catalog of Genes and Diseases from OMIM

- BRANCHIOOTORENAL SYNDROME 1; BOR1 (https://omim.org/entry/113650)
- BRANCHIOOTIC SYNDROME 2; BOS2 (https://omim.org/entry/120502)
- BRANCHIOOTIC SYNDROME 1; BOS1 (https://omim.org/entry/602588)
- BRANCHIOOTIC SYNDROME 3; BOS3 (https://omim.org/entry/608389)
- BRANCHIOOTORENAL SYNDROME 2; BOR2 (https://omim.org/entry/610896)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28%28branchiootorenal%5BTIAB%5D%29+OR+%28branchio-oto-renal%5BTIAB%5D%29+OR+%28branchio-otorenal%5BTIAB%5D%29+OR+%28branchio-otic%5BTIAB%5D%29+OR+%28branchiootic%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1800+days%22%5Bdp%5D)

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