Bannayan-Riley-Ruvalcaba syndrome

Bannayan-Riley-Ruvalcaba syndrome is a genetic condition characterized by a large head size (macrocephaly), multiple noncancerous tumors and tumor-like growths called hamartomas, and dark freckles on the penis in males. The signs and symptoms of Bannayan-Riley-Ruvalcaba syndrome are present from birth or become apparent in early childhood.

At least half of affected infants have macrocephaly, and many also have a high birth weight and a large body size (macrosomia). Growth usually slows during childhood, so affected adults are of normal height and body size. About half of all children with Bannayan-Riley-Ruvalcaba syndrome have intellectual disability or delayed development, particularly the development of speech and of motor skills such as sitting, crawling, and walking. These delays may improve with age.

About half of all people with Bannayan-Riley-Ruvalcaba syndrome develop hamartomas in their intestines, known as hamartomatous polyps. Other noncancerous growths often associated with Bannayan-Riley-Ruvalcaba syndrome include fatty tumors called lipomas and angiolipomas that develop under the skin. Some affected individuals also develop hemangiomas, which are red or purplish growths that consist of tangles of abnormal blood vessels. People with Bannayan-Riley-Ruvalcaba syndrome may also have an increased risk of developing certain cancers, although researchers are still working to determine the cancer risks associated with this condition.

Other signs and symptoms that have been reported in people with Bannayan-Riley-Ruvalcaba syndrome include weak muscle tone (hypotonia) and other muscle abnormalities, thyroid problems, and seizures. Skeletal abnormalities have also been described with this condition, including an unusually large range of joint movement (hyperextensibility), abnormal side-to-side curvature of the spine (scoliosis), and a sunken chest (pectus excavatum).

The features of Bannayan-Riley-Ruvalcaba syndrome overlap with those of another disorder called Cowden syndrome. People with Cowden syndrome develop hamartomas and other noncancerous growths; they also have an increased risk of developing certain types of cancer. Both conditions can be caused by mutations in the *PTEN* gene. Some people with Bannayan-Riley-Ruvalcaba syndrome have had relatives diagnosed with Cowden syndrome, and other individuals have had the characteristic features of both conditions. Based on these similarities, researchers have proposed that Bannayan-Riley-Ruvalcaba syndrome and Cowden syndrome represent a spectrum of overlapping features known as *PTEN* hamartoma tumor syndrome instead of two distinct conditions.

Frequency

The prevalence of Bannayan-Riley-Ruvalcaba syndrome is unknown, although it appears to be rare. Several dozen cases have been reported in the medical literature. Researchers suspect that the disorder is underdiagnosed because its signs and symptoms vary and some of them are subtle.

Genetic Changes

About 60 percent of all cases of Bannayan-Riley-Ruvalcaba syndrome result from mutations in the *PTEN* gene. Another 10 percent of cases are caused by a large deletion of genetic material that includes part or all of this gene. The protein produced from the *PTEN* gene is a tumor suppressor, which means that it normally prevents cells from growing and dividing (proliferating) too rapidly or in an uncontrolled way. If this protein is missing or defective, cell proliferation is not regulated effectively. Uncontrolled cell division can lead to the formation of hamartomas and other cancerous and noncancerous tumors. The protein produced from the *PTEN* gene likely has other important functions within cells; however, it is unclear how mutations in this gene can cause the other features of Bannayan-Riley-Ruvalcaba syndrome, such as macrocephaly, developmental delay, and muscle and skeletal abnormalities.

When Bannayan-Riley-Ruvalcaba syndrome is not caused by mutations or deletions of the *PTEN* gene, the cause of the condition is unknown.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

Other Names for This Condition

- Bannayan-Ruvalcaba-Riley syndrome
- Bannayan-Zonana syndrome
- BRRS
- BZS
- Myhre-Riley-Smith syndrome
- Riley-Smith syndrome
- Ruvalcaba-Myhre-Smith syndrome
- Ruvalcaba-Myhre syndrome

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Bannayan-Riley-Ruvalcaba syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0265326/

Other Diagnosis and Management Resources

- GeneReview: PTEN Hamartoma Tumor Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1488
- University of Iowa: Bannayan-Ruvalcaba-Riley Syndrome (BRRS)
  https://uihc.org/health-library/bannayan-ruvalcaba-riley-syndrome-brrs

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Encyclopedia: Colorectal Polyps
  https://medlineplus.gov/ency/article/000266.htm
- Encyclopedia: Increased Head Size
  https://medlineplus.gov/ency/article/003305.htm
- Encyclopedia: Lipoma - Arm
  https://medlineplus.gov/ency/imagepages/1209.htm
- Health Topic: Benign Tumors
  https://medlineplus.gov/benigntumors.html
- Health Topic: Developmental Disabilities
  https://medlineplus.gov/developmentaldisabilities.html

Genetic and Rare Diseases Information Center

- Bannayan-Riley-Ruvalcaba syndrome
  https://rarediseases.info.nih.gov/diseases/5887/bannayan-riley-ruvalcaba-syndrome

Additional NIH Resources

- National Institute of Diabetes and Digestive and Kidney Diseases: What I Need to Know About Colon Polyps
  https://www.niddk.nih.gov/health-information/digestive-diseases/colon-polyps

Educational Resources

- Atlas of Genetics and Cytogenetics in Oncology and Hematology
  http://atlasgeneticsoncology.org/Kprones/BannayanID10044.html
- Centers for Disease Control and Prevention: Intellectual Disability
  https://www.cdc.gov/ncbddd/actearly/pdf/parents_pdfs/IntellectualDisability.pdf
- Disease InfoSearch: Bannayan-Riley-Ruvalcaba Syndrome
  http://www.diseaseinfosearch.org/Bannayan-Riley-Ruvalcaba+Syndrome/716
- MalaCards: bannayan-riley-ruvalcaba syndrome
  http://www.malacards.org/card/bannayan_riley_ruvalcaba_syndrome
- Merck Manual Consumer Version: Polyps of the Colon and Rectum
  http://www.merckmanuals.com/home/digestive-disorders/tumors-of-the-digestive-system/polyps-of-the-colon-and-rectum
- Merck Manual Home Health Handbook: Lipomas
  http://www.merckmanuals.com/home/skin-disorders/noncancerous-skin-growths/lipomas
- My46 Trait Profile: PTEN Hamartoma Tumor Syndrome
  https://www.my46.org/trait-document?trait=PTEN%20Hamartoma%20Tumor%20syndrome&type=profile
- North American Society for Pediatric Gastroenterology, Hepatology and Nutrition: Intestinal Polyps
  http://www.gikids.org/files/documents/digestive%20topics/english/Intestinal%20Polyps%20-English.pdf
- Orphanet: Bannayan-Riley-Ruvalcaba syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=109
- University of Iowa: Bannayan-Ruvalcaba-Riley Syndrome (BRRS)
  https://uihc.org/health-library/bannayan-ruvalcaba-riley-syndrome-brrs

Patient Support and Advocacy Resources

- American Cancer Society
  https://www.cancer.org/
- GIKids
  http://www.gikids.org/
- National Organization for Rare Disorders (NORD): PTEN Hamartoma Tumor Syndrome
  https://rarediseases.org/rare-diseases/pten-hamartoma-tumor-syndrome/

GeneReviews

- PTEN Hamartoma Tumor Syndrome
  https://www.ncbi.nlm.nih.gov/books/NBK1488

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22Bannayan-Riley-Ruvalcaba+syndrome%22+OR+%22Hamartoma+Syndrome%2C+Multiple%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28Hamartoma+Syndrome,+Multiple%5BMAJR%5D%29+AND+%28%28bannayan-riley-ruvalcaba+syndrome%5BTIAB%5D%29+OR+%28bannayan-zonana+syndrome%5BTIAB%5D%29+OR+%28bannayan-ruvalcaba-riley+syndrome%5BTIAB%5D%29+OR+%28ruvalcaba-myhre-smith+syndrome%5BTIAB%5D%29+OR+%28BRRS%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+3600+days%22%5Bdp%5D

OMIM

- BANNAYAN-RILEY-RUVALCABA SYNDROME
  http://omim.org/entry/153480

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