Bohring-Opitz Syndrome (BOS)

https://pubmed.ncbi.nlm.nih.gov/29446906/

Clinical characteristics:

Bohring-Opitz syndrome (BOS) is characterized by distinctive facial features and posture, growth failure, variable but usually severe intellectual disability, and variable anomalies. The facial features may include microcephaly or trigonocephaly / prominent (but not fused) metopic ridge, hypotonic facies with full cheeks, synophrys, glabellar and eyelid nevus flammeus (
simplex
), prominent globes, widely set eyes, palate anomalies, and micrognathia. The BOS posture, which is most striking in early childhood and often becomes less apparent with age, is characterized by flexion at the elbows with ulnar deviation and flexion of the wrists and metacarpophalangeal joints. Feeding difficulties in early childhood, including cyclic vomiting, have a significant impact on overall health; feeding tends to improve with age. Seizures are common and typically responsive to standard epileptic medications. Minor cardiac anomalies and transient bradycardia and apnea may be present. Affected individuals may experience recurrent infections, which also tend to improve with age.
Isolated
case reports suggest that individuals with BOS are at greater risk for Wilms tumor than the general population, but large-scale epidemiologic studies have not been conducted.

Diagnosis/testing:

The diagnosis of Bohring-Opitz syndrome (BOS) is established in a proband with suggestive clinical features and/or the identification of a constitutional heterozygous pathogenic variant in ASXL1
by molecular genetic testing.

Management:

Treatment of manifestations.

Cyclic vomiting may be managed by identification and avoidance of triggers, daily maintenance medication, and early abortive treatment; G-tubes or GJ-tubes may decrease aspiration and improve nutrition. Due to the prevalence of obstructive sleep apnea, polysomnography should be considered. Referral to a craniofacial team should be considered for those with palatal abnormalities, micrognathia, or obstructive sleep apnea. Tracheostomy may be considered for those with recurrent aspiration who develop secondary lung disease, or in those with severe sleep apnea that is not

adequately treated with noninvasive pressure support (e.g., CPAP, BiPAP) or surgical intervention (e.g., mandibular distraction). Standard management is indicated for seizures, congenital heart defects, intellectual disability, myopia, urinary tract infections, urinary retention, and renal stones.

Prevention of primary manifestations.

Adequate treatment of severe emesis can decrease hospitalizations, infectious exposures, and ascending aspiration.

Surveillance:

Renal ultrasound every three months from birth to age eight to screen for the development of Wilms tumor; frequent monitoring of growth and development; close monitoring of feeding intolerance with a gastroenterology specialist; regular follow up for vision optimization.

Agents/circumstances to avoid.

Triggers for vomiting should be avoided and managed with prophylactic antiemetics prior to the

exposure.

Genetic counseling:

Bohring-Opitz syndrome (BOS) is typically the result of a

de novo

pathogenic variant in

ASXL1

. When BOS results from a

de novo

variant, the risk to the sibs of a proband is small. No individuals with BOS have been reported to reproduce. Although the vast majority of BOS occurs as the result of a

de novo

variant in

ASXL1

, molecular genetic testing can be used to evaluate a pregnancy at theoretically increased risk as a result of constitutional and/or germline mosaicism for an

ASXL1

pathogenic variant in a clinically unaffected parent.