# ASXL1 / Bohring-Opitz Syndrome

Your Interactive Visual Aid

symptoms, concerns, and treatment options

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## Medical Disclaimer

Although children with Bohring-Opitz Syndrome often look alike, and their clinical phenotype at birth is extremely similar, each child is unique and may be affected differently. Not every child will have all the classic physical characteristics, and the variation in levels of development from one child to the next can be great. This infographic is for "information only." It is not intended to be a substitute for professional medical advice, diagnosing criteria, or treatment. Always seek the advice of your physician and/or other qualified healthcare providers for any questions you may have regarding a medical condition.

## References:

Based on published medical literature and case studies between 2006 - 2023

Bohring et al. 2006, Pierron et al. 2009, Hasting et al. 2011, Magini et al. 2012, Russell et al. 2013, Russell et al. 2015, Dangiolo et al. 2015, Arunachal et al. 2016, Kibe et al. 2018, Urreitzti et al. 2018, Bedoukian et al. 2018, Russell et al. 2018, Quintero et al. 2019, Efthymiou et al. 2019, Rohanizadegan et al. 2020, Leon et al. 2019, Zhao J. et al. 2021, Cuddapah et al. 2021, Zhao W. et al. 2021, Joshi et al. 2023, Russell et al. 2023, Ayoub et al. 2023, Patel et al. 2024

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## Bohring-Opitz Syndrome/ASXL1: Clinical Symptoms

- Feeding difficulties
- Failure to thrive
- Intrauterine growth restriction (IUGR)
- Severe/profound learning difficulties
- Recurrent infections
- Seizures
- Apneas (suspension of external breathing)

## Craniofacial – Head

- Microcephaly
- Broad, narrow, bulging, prominent forehead
- Trigonocephaly / Craniosynostosis (premature fusion of the metopic suture)
- Prominent metopic rijde
- Hypoplastic orbital ridges
- Micro/retrognathia
- Hypotonic facies with full (puffy) cheeks
- Facial asymmetry
- Long face at a later age
- Small anterior fontanel

## Eye & Vision

- High Myopia (near-sighted)
- Strabismus, Exotropia (alignment of eye)
- Nystagmoid (purposeless) movements
- Anterior chamber, Retinal, Optic nerve abnormalities, Large cup to disc ratio
- Absence of tears
- Poor visual interaction
- (Cortical) Visual impairment (vision loss)
- Prominent eyes
- Exophthalmos / Proptosis (bulging eyes)
- Hypertelorism (widely spaced eyes)
- Upward slanting palpebral fissures
- Epicanthal folds

*Corrective lenses*
*Regular follow up for vision optimization*

## ENT & Dental issues

Clinical signs and symptoms of ear, nose, mouth, and throat, as well as dental issues.

### Nose

- Depressed nasal bridge
- Wide nasal bridge
- Anteverted nares (upturned nasal tip)
- Short/long philtrum (vertical grove between nose and mouth)
- Choanal atresia (blocked nasal airway)

### Throat/Mouth

- Broad alveolar ridge, alveolar ridge overgrowth
- Abnormal (high and narrow) palate
- Unilateral and bilateral cleft/notch lip and/or palate, bifid uvula
- Buccal frenula
- Prominent palatine (tonsils) ridges
- Tongue-based airway obstruction (caused by micrognathia)
- Overproduction of salvia and mucous
- Narrow mouth
- Laryngomalacia and subglottic stenosis (narrowing of airway)

*Mandibular distraction (surgery lengthening jaw)*
*Tongue-lip adhesion*
*Referral to craniofacial team*
*Primary closure of cleft lip*

### Ear

- Low-set posteriorly rotated ears
- Overfolding helices (ear)
- Small ear canals (ear canal stenosis)
- Hearing loss
- Ear infections
- Hearing impairment

### Dental Issues

- Delayed dental eruption

- Gingival hyperplasia or hypertrophy (abnormal overgrowth of gingival tissue)
- Widely spaced teeth
- Teeth grinding

## Skin & Hair

- Nevus flammeus nevus (birth mark) on glabellar and eyelids
- Hypopigmented spot(s) on chest
- Cutis Laxa (loose skin)
- Deep palmer creases (a deep line in the palm)
- Sacral dimple (indentation in the skin on the lower back)
- Hypertrichosis (excessive hair or abnormal hair density and length)
- Low posterior hairline
- Synophrys (unibrow, abundance of  hair between the eyebrows)
- Rapid hair and nail growth
- Hirsutism dorsal (hairy back)

## Growth & Feeding

- Intrauterine growth restriction (IUGR)
- Growth retardation (postnatal growth restriction)
- Underweight
- Short stature
- (Infant) Feeding difficulties
- (Cyclic) Emesis (vomiting)
- Oral motor impairment
- Failure to thrive
- Obesity at later age

*Feeding therapy*
*Identifying and avoiding triggers for cycling vomiting*

## Gastrointestinal

- Emesis (vomiting)
- Gastro-esophageal reflux disease
- Paraoesophageal hernia
- Intestinal malrotation
- Constipation
- Inguinal hernia
- Abdominal distension

*Gastrostomy*
*Nasogastric Tube (NG Tube)*
*Nissen Fundoplication*
*Volvulus ostomy*
*Intestinal resection*
*Close monitoring of feeding intolerance*

## Biliary & Metabolic System

- Gallstones
- Hyperechogenic (fatty) pancreas
- Annular pancreas

- Chronic pancreatitis
- Hepatoblastoma (liver tumor)
- Splenic cyst
- Metabolic abnormalities
- Hypothyroidism (underactive thyroid)

*Abdominal ultrasound every 3 months from birth to 8 years*
*and measurement of alpha-fetoprotein (AFP) via blood draw every three months until age 5*
*to detect the development of Hepatoblastoma*

## Cardiovascular System

- Cardiac abnormalities
- Atrial and/or Ventricular Septal Defect (congenital heart defect, hole in the wall of two heart chambers)
- Arrhythmias (irregular heartbeat)
- Bradycardia (slow heart rate)
- Cardiac hypertrophy (thickened heart muscle)
- Heart murmur
- Dilated cardiomyopathy (enlarged heart chamber)
- Congestive heart failure

## Respiratory System

- Respiratory distress (Neonatal)
- Obstructive sleep apnea
- Silent aspiration
- Dyspnea (shortness of breath)
- Pulmonary hypertension
- Recurrent infections

*Noninvasive pressure support*
*Tracheostomy*
*Polysomnography (sleep study to identify early obstructive apnea)*
*Aggressive management of chronic emesis*

## Urology & Nephrology

- Recurrent urinary tract infections (UTI)
- Renal pelvicalyceal dilatation (widening of the renal pelvis)
- Vesicoureteral reflux
- Urinary retention
- Incontinence (not toilet trained)
- Renal (kidney) abnormalities
- Horseshoe kidney
- Renal stones
- Renal cysts
- Wilms Tumors

*Renal ultrasound (every 3 months from birth to eight years to detect the development of Wilms tumor)*
*Urinalysis for possible UTI*

## Genitourinary & Puberty

- Early puberty / early onset
- Dysfunctional uterine bleeding
- Genital abnormalities
- Penile adhesions
- Hypospadias (abnormality of anterior urethral and penile development)
- Undescended testicle
- Widely spaced intermammillary nipples (the presence of an additional nipple)

## Musculoskeletal System – Muscles

- Hypotonia (low muscle tone)
- Hypertonia (high muscle tone)
- Spastic paraparesis (weakness and stiffness in the leg muscles)
- Dystonia/dystonic posturing
- Flexion contracture
- Motor delay/impairment

*Walkers and braces*

## Muscuskeletal System – Body

- BOS Posture (fixed constrictors of the upper limbs)[2]
- Scoliosis (curvature of the spine)
- Lordosis (inward curvature of the lower back)
- Thoracic kyphosis (Kelso's hunchback)
- Enlargement of vertebral foramina (dorsal and lumbar regions)
- Bony thorax abnormalities (narrow thorax, sunken chest)
- Bilateral hip dysplasia/luxation
- Segmental overgrowth

*Spinal fusion surgery*

## Musculoskeletal System – Hand & Feet

### Hand

- Ulnar deviation, flexion of wrist and fingers
- Overlapping toes and/or fingers
- Absent/single palmar crease
- Brachydactyly (short digits)
- Preaxial polydactyly (extra digit(s) are localized on the side of the thumb or great toe)
- Fetal pads
- Camptodactyly (fingers fixed in a bent position at the middle joint and cannot fully straighten)

## Feet

- Genu valgum (knock knees)
- Clubbed feet
- Small feet
- High arched feet
- Metatarsus adducts (front foot turned inward)
- Talipes valgus (deformity of the feet)
- Increased sandal gaps

## Cognitive Development

- Severe/profound learning difficulties
- Global development delay
- Cognitive disability
- Severe/profound intellectual disabilities
- Autism

*Early intervention programs*
*Individual education plans*
*Occupational therapy*
*Physical therapy*
*Medical equipment*

## Communication

- Delayed/Absence speech development
- Nonverbal
- Lack of expressive language
- Language impairment
- Decreased expressive communication

*Speech therapy*
*Augmentative and Alternative Communication (ACC) Strategies*

## Behavioral

- Stereotypic movement disorder, repetitive behavior
- Breath holding spells
- Lack of stranger anxiety
- Hypersensitivity
- Hyperactive
- Frequent tantrums
- Self-injurious behavior (eye poking)
- Pleasant and happy demeanor
- Curious, alert, and interactive

## Sleep

- (Obstructive) Apneas (suspension of external breathing)
- Sleep disturbances
- Insomnia and/or Hypersomnia
- Excessive sleepiness (narcolepsy)
- Fatigue
- Irregular sleep/wake cycle
- High sleep latency

*Severe obstructive sleep apnea may be treatable by tonsillectomy, adenoidectomy, or mandibular distraction*
*Melatonin*
*Treatment of anemia*

## Neurological

- Brain abnormalities
- Brain activity abnormalities on MRI imaging
- Hypoplasia /Agenesis corpus callosum
- Cerebral Cortex anomalies
- Delayed peripheral myelination
- Enlarged ventricles (brain)
- Bulbar dysfunction
- Dandy-Walker-Syndrome
- Epilepsy / Seizures
- Cyst on conus (spinal)
- Sacral hair patch / arachnoid cyst