U.S. National Library of Medicine
National Center for Biotechnology Information

NLM Citation: Verloes A, Drunat S, Pilz D, et al. Baraitser-Winter Cerebrofrontofacial Syndrome. 2015 Nov 19 [Updated 2022 Mar 24]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024.
Bookshelf URL: https://www.ncbi.nlm.nih.gov/books/

Baraitser-Winter Cerebrofrontofacial Syndrome

Alain Verloes, MD, PhD,[1] Séverine Drunat, PharmD, PhD,[2] Daniela Pilz, MD, PhD,[3] and Nataliya Di Donato, MD, PhD[4]

Created: November 19, 2015; Updated: March 24, 2022.

Summary

Clinical characteristics

Baraitser-Winter cerebrofrontofacial (BWCFF) syndrome is a multiple congenital anomaly syndrome characterized by typical craniofacial features and intellectual disability. Many (but not all) affected individuals have pachygyria that is predominantly frontal, wasting of the shoulder girdle muscles, and sensory impairment due to iris or retinal coloboma and/or sensorineural deafness. Intellectual disability, which is common but variable, is related to the severity of the brain malformations. Seizures, congenital heart defects, renal malformations, and gastrointestinal dysfunction are also common.

Diagnosis/testing

The diagnosis of BWCFF syndrome is established in a proband with suggestive findings and a heterozygous missense pathogenic variant in either *ACTB* or *ACTG1* identified by molecular genetic testing.

Management

Treatment of manifestations: Standard treatment for medical concerns in conjunction with the associated specialist; management of developmental delay and intellectual disability is tailored to the individual.

Surveillance: Routine follow up recommended for neurodevelopmental assessment in all; follow up as needed for those with seizures (neurologic evaluation), coloboma or microphthalmia (ophthalmologic evaluation), hearing loss (audiologic evaluation), cardiac defects, renal tract anomalies, and gastrointestinal dysfunction.

Genetic counseling

BWCFF syndrome is an autosomal dominant disorder. Most individuals with BWCFF syndrome reported to date have the disorder as the result of a *de novo ACTB* or *ACTG1* pathogenic variant. If a parent of the proband

Author Affiliations: 1 Université Paris Cité; Department of Genetics, APHP-Hôpital Robert Debré, Paris, France; Email: alain.verloes@aphp.fr. 2 Department of Genetics, APHP-Hôpital Robert Debré, Paris, France; Email: severine.drunat@aphp.fr. 3 Institute of Medical Genetics, University Hospital of Wales, Cardiff, United Kingdom; Email: pilzdt@cf.ac.uk. 4 Institut für Klinische Genetik, Universitätsklinikum Carl Gustav Carus, Dresden, Germany; Email: nataliya.didonato@uniklinikum-dresden.de.

has the pathogenic variant identified in the proband, the risk to the sibs of inheriting the pathogenic variant is 50%. Once the *ACTB* or *ACTG1* pathogenic variant has been identified in an affected family member, prenatal and preimplantation genetic testing for BWCFF syndrome are possible.

Diagnosis

No consensus clinical diagnostic criteria for Baraitser-Winter cerebrofrontofacial (BWCFF) syndrome have been published.

Suggestive Findings

BWCFF syndrome **should be suspected** in individuals with the following clinical and imaging findings.

Clinical findings

- Typical craniofacial features (widely spaced eyes, bulbous nose with broad nasal tip and prominent nasal bridge, congenital nonmyopathic ptosis, prominent metopic ridge, and highly arched eyebrows)
- Developmental delay / intellectual disability

Variably present findings:

- Ocular coloboma
- Wasting of the muscles of the shoulder girdle
- Sensorineural hearing loss

Imaging findings. Frontal-predominant pachygyria especially in combination with posterior-band heterotopia and enlarged perivascular spaces on brain imaging

Establishing the Diagnosis

The diagnosis of BWCFF syndrome **is established** in a proband with suggestive findings and a heterozygous pathogenic (or likely pathogenic) missense variant in either *ACTB* or *ACTG1* identified by molecular genetic testing (see Table 1).

Note: (1) Per ACMG variant interpretation guidelines, the terms "pathogenic variants" and "likely pathogenic variants" are synonymous in a clinical setting, meaning that both are considered diagnostic and both can be used for clinical decision making. Reference to "pathogenic variants" in this section is understood to include any likely pathogenic variants. (2) Identification of a heterozygous variant of uncertain significance does not establish or rule out the diagnosis of this disorder.

Molecular genetic testing approaches can include a combination of **gene-targeted testing** (multigene panel) and **comprehensive genomic testing** (exome sequencing, genome sequencing) depending on the phenotype.

Gene-targeted testing requires that the clinician determine which gene(s) are likely involved, whereas genomic testing does not. Individuals with the distinctive findings described in Suggestive Findings are likely to be diagnosed using gene-targeted testing (see Option 1), whereas those with a phenotype indistinguishable from many other inherited disorders with intellectual disability are more likely to be diagnosed using genomic testing (see Option 2).

Option 1

An intellectual disability multigene panel that includes some or all of the genes listed in Table 1 and other genes of interest (see Differential Diagnosis) is most likely to identify the genetic cause of the condition while limiting identification of variants of uncertain significance and pathogenic variants in genes that do not explain

the underlying phenotype. Note: (1) The genes included in the panel and the diagnostic sensitivity of the testing used for each gene vary by laboratory and are likely to change over time. (2) Some multigene panels may include genes not associated with the condition discussed in this *GeneReview*. (3) In some laboratories, panel options may include a custom laboratory-designed panel and/or custom phenotype-focused exome analysis that includes genes specified by the clinician. (4) Methods used in a panel may include sequence analysis, deletion/duplication analysis, and/or other non-sequencing-based tests.

For an introduction to multigene panels click here. More detailed information for clinicians ordering genetic tests can be found here.

Option 2

Comprehensive genomic testing does not require the clinician to determine which gene is likely involved. **Exome sequencing** is most commonly used; **genome sequencing** is also possible.

For an introduction to comprehensive genomic testing click here. More detailed information for clinicians ordering genomic testing can be found here.

Table 1. Molecular Genetic Testing Used in Baraitser-Winter Cerebrofrontofacial Syndrome

Gene [1, 2]	Proportion of BWCFF Syndrome Attributed to Pathogenic Variants in Gene	Proportion of Probands with a Pathogenic Variant [3] Detectable by Method	
		Sequence analysis [4]	Gene-targeted deletion/duplication analysis [5]
ACTB	>55%	100% [6]	NA [7, 8]
ACTG1	>35%	100% [6]	NA [7, 8]
Unknown [9]	<10%	NA	

BWCFF = Baraitser-Winter cerebrofrontofacial; NA = not applicable

1. Genes are listed in alphabetic order.
2. See Table A. Genes and Databases for chromosome locus and protein.
3. See Molecular Genetics for information on variants detected in these genes.
4. Sequence analysis detects variants that are benign, likely benign, of uncertain significance, likely pathogenic, or pathogenic. Variants may include small intragenic deletions/insertions and missense, nonsense, and splice site variants; typically, exon or whole-gene deletions/duplications are not detected. For issues to consider in interpretation of sequence analysis results, click here.
5. Gene-targeted deletion/duplication analysis detects intragenic deletions or duplications. Methods used may include a range of techniques such as quantitative PCR, long-range PCR, multiplex ligation-dependent probe amplification (MLPA), and a gene-targeted microarray designed to detect single-exon deletions or duplications.
6. Data derived from the subscription-based professional view of Human Gene Mutation Database [Stenson et al 2020]
7. Deletions and duplications of either *ACTB* or *ACTG1* do not result in the BWCFF syndrome phenotype.
8. All pathogenic variants reported to date are gain-of-function missense variants in *ACTB* or *ACTG1*; thus, testing for deletion (haploinsufficiency) or duplication (overexpression) is not indicated.
9. Estimate based on authors' experience

Clinical Characteristics

Clinical Description

Baraitser-Winter cerebrofrontofacial (BWCFF) syndrome is a multiple congenital anomaly syndrome characterized by typical craniofacial features and intellectual disability. Many (but not all) affected individuals have pachygyria that is predominantly frontal, wasting of the shoulder girdle muscles, and sensory impairment due to iris or retinal coloboma and/or sensorineural deafness. Intellectual disability, which is common but variable, is related to the severity of the brain malformations [Verloes et al 2015, Yates et al 2017]. BWCFF syndrome has been reported in fewer than 100 individuals.

Significant variation in clinical features is observed, and some individuals whose diagnosis was made through identification of a pathogenic variant on gene panel or exome analyses (rather than on clinical suspicion) are expected to show milder or incomplete phenotypes (*formes frustes*) that would not have led unambiguously to a clinical diagnosis of BWCFF syndrome.

Table 2. Baraitser-Winter Cerebrofrontofacial Syndrome: Frequency of Select Features

Feature (% of Persons w/Feature)	Comment
Dysmorphic craniofacial features (100%) incl: • Prominent metopic ridging or trigonocephaly (65%) • Widely spaced eyes (95%) • Bilateral ptosis (90%) • Highly arched eyebrows (90%) • Ocular coloboma (30%); may be assoc w/ microphthalmia (<10%) • Small ears w/↑ posterior angulation, anteverted pinnae, overfolded, thick helix, & underdeveloped antihelix (73%) • Wide, short, thick, & upturned nose, w/large, flat tip (85%) • Long, smooth philtrum (84%) • Wide mouth w/downturned corners & everted vermilion of lower lip (45%) • Cleft lip & palate (10%)	Some persons may have rather mild craniofacial features & be considered nondysmorphic.
Developmental delay / intellectual disability (>95%)	• Mild-to-moderate developmental delay w/mild intellectual disability • Delays profound if severe lissencephaly present • Rare individuals w/normal intelligence
Microcephaly (~50%)	Microcephaly may be of prenatal onset, usually mild, but may be severe w/lissencephaly (≥ -5 SD).
Brain malformation (83%) incl: • Pachygyria (frontal or predominantly central) &/or subcortical band heterotopia (61%) • Periventricular heterotopias (2%) • Corpus callosum abnormality (20%)	
Epilepsy (50%)	• Typically assoc w/structural brain anomalies • Age dependent • Manifests from 1st mos of life to 24 yrs
Neuromuscular abnormality (20%)	• Peculiar stance, joint contractures, & pterygia observed in some persons • Contractures & muscle wasting may progress w/time.
Vision abnormality (30%)	Assoc w/coloboma & microphthalmia
Sensorineural &/or conductive hearing loss (35%)	• Can be progressive • May be assoc w/inner ear malformation
Moderate short stature (44%)	
Cardiovascular abnormality (38%)	

Table 2. continued from previous page.

Feature (% of Persons w/Feature)	Comment
Genitourinary abnormality (41%)	Incl: • Hydronephrosis (23%) • Structural renal malformation (10%) • Micropenis, cryptorchidism, & hypospadias (rare)
Skeletal features (20%)	Incl pectus deformity & broad thumbs & hallux
Gastrointestinal dysfunction (41%)	• Frequent chronic constipation (requiring daily medication) & reflux disease • Occasional vomiting, diarrhea, feeding difficulties, failure to thrive • Several persons required tube feeding & PEG. • Rare anomalies incl intestinal malrotation, duodenal atresia, & bowel pseudo-obstruction
Abdominal anomaly (rare [1])	Omphalocele
Malignancy (<5%)	Lymphoma & leukemia have been reported.

PEG = percutaneous endoscopic gastrostomy
1. Zhang et al [2020]

Dysmorphic craniofacial features vary from mild to severe and evolve considerably over time. With age the facial features become significantly coarser. The face is round and flat in infancy. In those with more severe facial involvement, the widely spaced eyes are reminiscent of frontonasal dysplasia due to the degree of increased spacing and wide nose.

General craniofacial shape is characterized a flat malar region and retrognathia with a pointed chin, and often by prominent metopic ridging or trigonocephaly.

Eyes are widely spaced with bilateral ptosis, which may require surgery. Other findings:

- Long, often downslanted palpebral fissures (with or without epicanthal folds or epicanthus inversus), lagophthalmos, and euryblepharon; appearance may resemble the ocular findings in Kabuki syndrome although the gestalt is different.
- Highly arched eyebrows in continuity of the lateral edges of the nose
- Uni- or bilateral ocular coloboma that may extend from the iris to the macula, sometimes with microphthalmia

Ears are often small with increased posterior angulation, sometimes anteverted pinnae, with an overfolded, thick helix and an underdeveloped antihelix.

Nose and mouth

- Wide, short, thick, and upturned nose, with a large, flat tip, a thick columella, anteverted, thick nares, and a median grove (in the most severe cases)
- Prominent nasal bridge, flat in its middle part
- Long and smooth philtrum and thin vermilion border of the upper lip
- Wide mouth with downturned corners, everted vermilion of the lower lip
- Cleft lip and palate

Developmental delay (DD) / intellectual disability (ID) is highly variable:

- In children with normal brain structure, motor delay is common, but otherwise development is only mildly to moderately delayed. ID is usually mild. Rare individuals with normal intelligence have also been reported.
- Among those with a cortical malformation, development is always delayed. ID varied from profound in those with severe and diffuse lissencephaly to mild ID in some with anterior pachygyria or periventricular heterotopia.

Brain malformations are present in more than 80% of individuals. Findings may include:

- Frontal or predominantly central pachygyria; more rarely, severe lissencephaly or microlissencephaly [Poirier et al 2015];
- Subcortical band and/or periventricular heterotopias;
- Short, thick, or absent corpus callosum [Rossi et al 2003];
- Chiari malformation [Sandestig et al 2019].

Neurologic

- Epilepsy, of no specific type and of variable severity, is present in 50% of individuals, often in conjunction with structural cerebral anomalies.
- Variable muscular hypotonia, particularly of the upper body, is frequent and may result in progressive scoliosis beginning from age eight to 10 years.
- Many affected individuals, especially teenagers and adults, have a peculiar stance with kyphosis, anteverted shoulders, and slightly flexed elbows and knees, which may be associated with limited joint movement. Axillary and popliteal pterygia may be present at birth. A few have congenital arthrogryposis multiplex congenita.
- Increasingly difficult ambulation is seen in some adults, which may indicate a slowly progressive myopathic process with slowly progressive, generalized muscle weakness. Some adults may become dependent on a wheelchair for mobility and develop late-onset spinal deformity (kyphosis, scoliosis).

Vision abnormality. Iris and retinal coloboma and microphthalmia may severely impair vision. Ptosis may require surgical correction. An individual has been reported with congenital fibrosis of oculomotor muscles [Chacon-Camacho et al 2020]. Esotropia and refractive errors were noted.

Hearing loss. Sensorineural hearing loss of variable degree may be present and can be progressive and require hearing aids. The inner ear and auditory nerve may be malformed and hypoplastic. Several individuals have frequent otitis media resulting in conductive hearing loss especially in early childhood.

Growth

- Normal or low intrauterine growth; moderate short stature is observed in 50% of teenagers and adults.
- Head circumference is typically low normal at birth, although several individuals with severe prenatal microcephaly have been reported [Vontell et al 2019]; mild postnatal microcephaly develops in about half of individuals.

Gastrointestinal dysfunction [Authors, unpublished observations]

- Constipation (either chronic or occasional) is the most frequently observed GI finding. Rarely, bowel pseudo-obstruction occurs.
- Frequent vomiting and gastroesophageal reflux disease have been reported occasionally in newborns and small children.
- Severe feeding difficulties requiring nasogastric tube feeding with subsequent feeding tube have been reported in several children.

- Structural malformations include duodenal atresia and intestinal malrotation; one individual developed liver cirrhosis.

Other malformations

- Cardiovascular malformations such as patent ductus arteriosus, ventricular or atrial septal defects, abnormal aortic valve, aortic stenosis, mitral valve regurgitation, and tricuspid regurgitation have been identified.
- Genitourinary abnormalities can include hydronephrosis, horseshoe or ectopic kidneys, renal duplication, and hypospadias.
- Musculoskeletal features include broad thumbs and hallux (rarely, duplication of the hallux and/or thumbs).

Malignancy. Three individuals with different hematologic malignancies have been reported; causal relationship has not been demonstrated, but also cannot be reliably excluded (see Cancer and Benign Tumors).

- Cutaneous lymphoma was diagnosed at age 19 years in an individual with BWCFF syndrome and a germline *ACTG1* pathogenic variant [Verloes et al 2015].
- Precursor B-cell acute lymphatic leukemia developed at age eight years in a child with BWCFF syndrome and a germline *ACTB* pathogenic variant [Verloes et al 2015, Diets et al 2018].
- Acute myeloid leukemia, M5 subtype developed at age 21 years in an individual with BWCFF syndrome and a germline *ACTB* pathogenic variant [Cianci et al 2017].

Prognosis. Limited data have been published in adults with BWCFF syndrome; only six individuals older than age 40 years are reported in the literature [Hampshire et al 2020]. From the authors' experience, the neuromuscular involvement tends to worsen with time, with progressive muscle wasting and weakness, progressive scoliosis, osteoporosis, and loss of ambulation in the fifth decade of life. Cognitive decline was reported [Di Donato et al 2014]. Life span may be reduced; two adult individuals died in the third decade of life as a result of acute ileus, neurologic decline with feeding difficulties, and recurrent pneumonias [Authors, unpublished observations]. The oldest known individual was 62 years old at the last follow up.

Genotype-Phenotype Correlations

Although phenotypic expression of BWCFF syndrome is remarkably variable, even among unrelated individuals harboring an identical pathogenic variant, two pathogenic variants have been found in those with the most severe presentation of the BWCFF syndrome clinical spectrum, including microcephaly and pachygyria, profound intellectual disability, and epilepsy along with variable anomalies of other systems. These variants are p.Thr120Ile in *ACTB* and p.Thr203Met in *ACTG1*.

Penetrance

The penetrance of BWCFF syndrome appears to be complete, but no single clinical manifestation is constant.

Nomenclature

Cerebrofrontofacial syndrome type 1 and type 3 and Fryns-Aftimos syndrome represent the severe end of the BWCFF syndrome spectrum. As the same pathogenic variant can lead to any of those three phenotypes, those entities are not considered allelic disorders, but rather part of the phenotypic spectrum of BWCFF syndrome.

Prevalence

BWCFF syndrome is rare. Slightly fewer than 100 individuals with a molecularly confirmed diagnosis have been documented to date. However, considering the phenotypic variability, it may be underdiagnosed.

Genetically Related (Allelic) Disorders

ACTB and *ACTG1* encode cytoskeleton proteins with complex functions [Dugina et al 2021]. Other recurrent phenotypes associated with germline pathogenic variants in these genes are summarized in Table 3.

Note: Variants in *ACTB* and *ACTG1* have been identified in individuals with mild, nonrecurrent phenotypes that are not consistent with Baraitser-Winter cerebrofrontofacial syndrome or with the allelic disorders outlined in Table 3; the authors suggest the tentative designation "non-muscle actinopathies, not otherwise specified" to encompass these phenotypes.

Table 3. Allelic Disorders

Gene	Pathogenic Variant(s)	Disorder/Phenotype	References/OMIM/ *GeneReview*
ACTB	p.Arg183Trp	Dystonia-deafness syndrome. Drug-nonresponsive dystonia & early-onset sensorineural deafness w/variable presence of dysmorphism, DD/ID, scoliosis, & epilepsy	Skogseid et al [2018], Freitas et al [2019], OMIM 607371
	LoF variants	Described in ~40 persons w/DD, ID, internal organ malformations (incl CHDs & renal tract anomalies), growth restriction, & facial dysmorphism distinct from BWCFF syndrome (interrupted wavy eyebrows, dense eyelashes, wide nose, wide mouth, prominent chin)	Cuvertino et al [2017], Baumann et al [2020]
	LoF variants (missense, small deletions, & single-base-pair insertion) clustering in 3′ region, exons 5 & 6	Syndromic thrombocytopenia. Mild DD, mild variable dysmorphism, microcephaly, & leukocytosis as well as thrombocytopenia w/platelet anisotropy (variable size incl normal & enlarged platelets). Recurrent infection, photosensitivity &/or malformations (cleft lip, CHD), arrhythmia, & periventricular nodular heterotopias may occur.	Nunoi et al [1999], Latham et al [2018], Sandestig et al [2019]
	7p22.1 microdeletions involving *ACTB*	Variable presentation, w/nonspecific DD, short stature, microcephaly, & dysmorphic traits	Shimojima et al [2016]
ACTG1	Several missense variants	Autosomal dominant nonsyndromic progressive sensorineural hearing loss (DFNA20/26)	Hereditary Hearing Loss and Deafness Overview
	p.Pro70Leu	Isolated coloboma in 2 unrelated persons	Rainger et al [2017]

BWCFF = Baraitser-Winter cerebrofrontofacial; CHD = congenital heart defect; DD = developmental delay; ID = intellectual disability; LoF = loss of function

Differential Diagnosis

Disorders to consider in the differential diagnosis of Baraitser-Winter cerebrofrontofacial (BWCFF) syndrome are summarized in Table 4.

Table 4. Selected Disorders in the Differential Diagnosis of Baraitser-Winter Cerebrofrontofacial Syndrome

Gene(s)	Disorder	MOI	Key Features
PTPN11 *SOS1* *LZTR1* *KRAS* *RAF1* *RIT1* *SOS2* *BRAF* *MAP2K1* *MRAS* *NRAS* *RRAS2* [1]	Noonan syndrome (NS)	AD (AR) [2]	Overlapping features: In BWCFF syndrome w/o brain anomalies, the facial appearance in infancy (when metopic ridge is absent), in assoc w/chest deformity & nuchal skinfolds or pterygium colli, may falsely lead to diagnosis of NS. Distinguishing features: Coloboma is rarely observed in NS & NS is not assoc w/pachygyria or muscle involvement.
SPECC1L *CDH11*	Hypertelorism, Teebi type (brachycephalofrontonasal dysplasia; OMIM PS145420)	AD	Overlapping feature: significantly widely spaced eyes
FGD1	Aarskog-Scott syndrome (OMIM 305400)	XL	Overlapping feature: significantly widely spaced eyes
SERAC1	SERAC1 deficiency	AR	Causes a combination of ID, hypotonia, early-onset dystonia, & deafness

AD = autosomal dominant; AR = autosomal recessive; BWCFF = Baraitser-Winter cerebrofrontofacial; ID = intellectual disability; MOI = mode of inheritance; XL = X-linked

1. Genes are organized first by frequency of causation of Noonan syndrome and then alphabetically. Recent reports have implicated several additional genes associated with a Noonan syndrome-like phenotype in fewer than ten individuals each, including *RRAS* and *A2ML1* (see Noonan Syndrome).

2. Noonan syndrome is most often inherited in an autosomal dominant manner. Noonan syndrome caused by pathogenic variants in *LZTR1* can be inherited in either an autosomal dominant or an autosomal recessive manner.

Management

No clinical practice guidelines for Baraitser-Winter cerebrofrontofacial (BWCFF) syndrome have been published.

Evaluations Following Initial Diagnosis

To establish the extent of disease and needs in an individual diagnosed with BWCFF syndrome, the evaluations summarized in Table 5 (if not performed as part of the evaluation that led to the diagnosis) are recommended.

Table 5. Recommended Evaluations Following Initial Diagnosis in Individuals with Baraitser-Winter Cerebrofrontofacial Syndrome

System/Concern	Evaluation	Comment
Development	Developmental assessment	• To incl motor, adaptive, cognitive, & speech/language eval • Eval for early intervention / special education
Neurologic	Neurologic eval	• To incl brain MRI • Consider EEG if brain MRI anomaly &/or seizures present.
Eyes	Ophthalmologic eval incl fundoscopy	To assess for malformation, ↓ vision, abnormal ocular mvmt, strabismus
Hearing	Audiologic eval	Assess for hearing loss
Gastroenterology	• Abdominal ultrasound &, if necessary, assess GI motility. • Assess for feeding difficulties.	To assess for gastrointestinal disorders & dysfunction & feeding difficulties

Table 5. continued from previous page.

System/Concern	Evaluation	Comment
Cardiovascular	Echocardiogram	Assess for congenital heart defects.
Genitourinary	Renal ultrasound	Evaluate for malformation of kidneys &/or ureters
Hematology	Blood count & platelet count	Baseline study given possible ↑ risk for hematologic malignancy [1]
Genetic counseling	By genetics professionals [2]	To inform affected persons & their families re nature, MOI, & implications of BWCFF syndrome to facilitate medical & personal decision making
Family support & resources	Assess need for: • Community or online resources such as Parent to Parent; • Social work involvement for parental support; • Home nursing referral.	

BWCFF = Baraitser-Winter cerebrofrontofacial; MOI = mode of inheritance
1. Note that individuals diagnosed via molecular genetic testing with a pathogenic *ACTB* variant who have only a mild BWCFF syndrome phenotype in combination with thrombocytopenia may have an allelic disorder, as BWCFF syndrome is not associated with thrombocytopenia (see Genetically Related Disorders).
2. Medical geneticist, certified genetic counselor, certified advanced genetic nurse

Treatment of Manifestations

No specific treatment for BWCFF syndrome exists. Management recommendations are detailed in Table 6. Malformations of the heart, urinary tract, and oral clefts are treated using standard procedures.

Table 6. Treatment of Manifestations in Individuals with Baraitser-Winter Cerebrofrontofacial Syndrome

Manifestation/Concern	Treatment	Considerations/Other
Developmental delay / Intellectual disability	See Developmental Delay / Intellectual Disability Management Issues.	
Muscle wasting & joint limitation	PT may be helpful to slow progressive joint ankyloses & scoliosis.	Orthopedic monitoring during growth spurts & adolescence for early recognition & mgmt of scoliosis
Epilepsy	Standardized treatment w/ASM by experienced neurologist	• Many ASMs may be effective; none has been demonstrated effective specifically for this disorder. • Education of parents/caregivers [1]
Abnormal vision &/or strabismus	Standard treatment(s) per ophthalmologist if coloboma &/or micropthalmia is present & → poor vision	Ptosis may require surgery.
Hearing	Hearing aids may be helpful; per otolaryngologist.	Community hearing services through early intervention or school district
GI dysfunction	Osmotic laxatives were reported effective in majority of persons w/constipation.	GI eval is necessary to monitor long-term medication.

ASM = anti-seizure medication; GI = gastrointestinal; PT = physical therapy
1. Education of parents/caregivers regarding common seizure presentations is appropriate. For information on non-medical interventions and coping strategies for children diagnosed with epilepsy, see Epilepsy Foundation Toolbox.

Developmental Delay / Intellectual Disability Management Issues

The following information represents typical management recommendations for individuals with developmental delay / intellectual disability in the United States; standard recommendations may vary from country to country.

Ages 0-3 years. Referral to an early intervention program is recommended for access to occupational, physical, speech, and feeding therapy as well as infant mental health services, special educators, and sensory impairment specialists. In the US, early intervention is a federally funded program available in all states that provides in-home services to target individual therapy needs.

Ages 3-5 years. In the US, developmental preschool through the local public school district is recommended. Before placement, an evaluation is made to determine needed services and therapies and an individualized education plan (IEP) is developed for those who qualify based on established motor, language, social, or cognitive delay. The early intervention program typically assists with this transition. Developmental preschool is center based; for children too medically unstable to attend, home-based services are provided.

All ages. Consultation with a developmental pediatrician is recommended to ensure the involvement of appropriate community, state, and educational agencies (US) and to support parents in maximizing quality of life. Some issues to consider:

- IEP services:
  - An IEP provides specially designed instruction and related services to children who qualify.
  - IEP services will be reviewed annually to determine whether any changes are needed.
  - Special education law requires that children participating in an IEP be in the least restrictive environment feasible at school and included in general education as much as possible, when and where appropriate.
  - Vision and hearing consultants should be a part of the child's IEP team to support access to academic material.
  - PT, OT, and speech services will be provided in the IEP to the extent that the need affects the child's access to academic material. Beyond that, private supportive therapies based on the affected individual's needs may be considered. Specific recommendations regarding type of therapy can be made by a developmental pediatrician.
  - As a child enters the teen years, a transition plan should be discussed and incorporated in the IEP. For those receiving IEP services, the public school district is required to provide services until age 21.
- A 504 plan (Section 504: a US federal statute that prohibits discrimination based on disability) can be considered for those who require accommodations or modifications such as front-of-class seating, assistive technology devices, classroom scribes, extra time between classes, modified assignments, and enlarged text.
- Developmental Disabilities Administration (DDA) enrollment is recommended. DDA is a US public agency that provides services and support to qualified individuals. Eligibility differs by state but is typically determined by diagnosis and/or associated cognitive/adaptive disabilities.
- Families with limited income and resources may also qualify for supplemental security income (SSI) for their child with a disability.

Motor Dysfunction

Gross motor dysfunction

- Intensive and regular physical therapy is recommended to maximize mobility and to reduce the risk for later-onset orthopedic complications (e.g., contractures, scoliosis, hip dislocation).

- Consider use of durable medical equipment and positioning devices as needed (e.g., wheelchairs, walkers, bath chairs, orthotics, adaptive strollers).
- For muscle tone abnormalities including hypertonia or dystonia, consider involving appropriate specialists to aid in management of baclofen, tizanidine, Botox®, anti-parkinsonian medications, or orthopedic procedures.

Fine motor dysfunction. Occupational therapy is recommended for difficulty with fine motor skills that affect adaptive function such as feeding, grooming, dressing, and writing.

Oral motor dysfunction should be assessed at each visit and clinical feeding evaluations and/or radiographic swallowing studies should be obtained for choking/gagging during feeds, poor weight gain, frequent respiratory illnesses or feeding refusal that is not otherwise explained. Assuming that the child is safe to eat by mouth, feeding therapy (typically from an occupational or speech therapist) is recommended to help improve coordination or sensory-related feeding issues. Feeds can be thickened or chilled for safety. When feeding dysfunction is severe, an NG-tube or G-tube may be necessary.

Communication issues. Consider evaluation for alternative means of communication (e.g., augmentative and alternative communication [AAC]) for individuals who have expressive language difficulties. An AAC evaluation can be completed by a speech-language pathologist who has expertise in the area. The evaluation will consider cognitive abilities and sensory impairments to determine the most appropriate form of communication. AAC devices can range from low-tech, such as picture exchange communication, to high-tech, such as voice-generating devices. Contrary to popular belief, AAC devices do not hinder verbal development of speech, but rather support optimal speech and language development.

Social/Behavioral Concerns

Children may qualify for and benefit from interventions used in treatment of autism spectrum disorder, including applied behavior analysis (ABA). ABA therapy is targeted to the individual child's behavioral, social, and adaptive strengths and weaknesses and typically performed one-on-one with a board-certified behavior analyst.

Consultation with a developmental pediatrician may be helpful in guiding parents through appropriate behavior management strategies or providing prescription medications, such as medication used to treat attention-deficit/hyperactivity disorder (ADHD), when necessary.

Concerns about serious aggressive or destructive behavior can be addressed by a pediatric psychiatrist.

Surveillance

Table 7. Recommended Surveillance for Individuals with Baraitser-Winter Cerebrofrontofacial Syndrome

System/Concern	Evaluation	Frequency
Development	Monitor developmental progress & educational needs.	At each visit
Neurologic	Monitor those w/seizures as clinically indicated.	
Eyes	If coloboma or microphthalmia present, ophthalmologic follow up w/ screening for intraocular hypertension & glaucoma (a known complication of colobomatous microphthalmia)	At least annually
Hearing loss	Evaluate for progression.	Annually
Cardiovascular	Monitor for complications if cardiac malformation present.	Per cardiologist
Genitourinary	Monitor for renal insufficiency if renal anomaly present.	Per nephrologist
Gastroenterology	Monitor those w/feeding difficulties & GI dysfunction.	At least annually

Table 7. continued from previous page.

System/Concern	Evaluation	Frequency
Orthopedic	Monitor for scoliosis.	At least annually; every 6 mos during growth spurts & adolescence
Family/ Community	Assess family need for social work support (e.g., palliative/respite care, home nursing, other local resources) & care coordination.	At each visit

Note: The risk of malignancies is not established for BWCFF syndrome, and thus no regular surveillance is recommended. However, screening for hematologic malignancies must be considered in case of physical deterioration or unexplained chronic fever.

Evaluation of Relatives at Risk

See Genetic Counseling for issues related to testing of at-risk relatives for genetic counseling purposes.

Therapies Under Investigation

Search ClinicalTrials.gov in the US and EU Clinical Trials Register in Europe for access to information on clinical studies for a wide range of diseases and conditions. Note: There may not be clinical trials for this disorder.

Genetic Counseling

Genetic counseling is the process of providing individuals and families with information on the nature, mode(s) of inheritance, and implications of genetic disorders to help them make informed medical and personal decisions. The following section deals with genetic risk assessment and the use of family history and genetic testing to clarify genetic status for family members; it is not meant to address all personal, cultural, or ethical issues that may arise or to substitute for consultation with a genetics professional. —ED.

Mode of Inheritance

Baraitser-Winter cerebrofrontofacial (BWCFF) syndrome is an autosomal dominant disorder.

Risk to Family Members

Parents of a proband

- Most individuals with BWCFF syndrome reported to date have the disorder as the result of a *de novo* *ACTB* or *ACTG1* pathogenic variant.
- In rare families, individuals diagnosed with BWCFF syndrome have the disorder as the result of a pathogenic variant inherited from a parent with germline mosaicism [Hampshire et al 2020] or from a heterozygous, affected parent [Yates et al 2017].
- Molecular genetic testing is recommended for the parents of the proband to confirm their genetic status and to allow reliable recurrence-risk counseling.
- If the pathogenic variant identified in the proband is not identified in either parent and parental identity testing has confirmed biological maternity and paternity, the following possibilities should be considered:
    - The proband has a *de novo* pathogenic variant.

- The proband inherited a pathogenic variant from a parent with germline (or somatic and germline) mosaicism.* Note: Testing of parental leukocyte DNA may not detect all instances of somatic mosaicism and will not detect a pathogenic variant that is present in the germ cells only.

  * A parent with somatic and germline mosaicism for an *ACTB* or *ACTG1* pathogenic variant may be mildly/minimally affected.

Sibs of a proband. The risk to the sibs of the proband depends on the genetic status of the proband's parents:

- If a parent of the proband has the pathogenic variant identified in the proband, the risk to the sibs of inheriting the pathogenic variant is 50%.
- If the proband has a known *ACTB* or *ACTG1* pathogenic variant that cannot be detected in the leukocyte DNA of either parent, the recurrence risk to sibs is slightly greater than that of the general population because of the possibility of parental germline mosaicism [Hampshire et al 2020].
- If the parents have not been tested for the pathogenic variant identified in the proband but are clinically unaffected, the risk to the sibs of a proband is presumed to be low but greater than that of the general population because of the possibility of parental germline mosaicism.

Offspring of a proband. Each child of an individual with BWCFF syndrome has a 50% chance of inheriting the *ACTB* or *ACTG1* pathogenic variant.

Other family members. The risk to other family members depends on the status of the proband's parents: if a parent has the *ACTB* or *ACTG1* pathogenic variant, the parent's family members may be at risk.

Related Genetic Counseling Issues

Family planning

- The optimal time for determination of genetic risk and discussion of the availability of prenatal/preimplantation genetic testing is before pregnancy.
- It is appropriate to offer genetic counseling (including discussion of potential risks to offspring and reproductive options) to parents of affected individuals and to young adults who are affected.

DNA banking. Because it is likely that testing methodology and our understanding of genes, pathogenic mechanisms, and diseases will improve in the future, consideration should be given to banking DNA from probands in whom a molecular diagnosis has not been confirmed (i.e., the causative pathogenic mechanism is unknown).

Prenatal Testing and Preimplantation Genetic Testing

Once the *ACTB* or *ACTG1* pathogenic variant has been identified in an affected family member, prenatal and preimplantation genetic testing for BWCFF syndrome are possible.

Differences in perspective may exist among medical professionals and within families regarding the use of prenatal testing. While most centers would consider use of prenatal testing to be a personal decision, discussion of these issues may be helpful.

Resources

GeneReviews staff has selected the following disease-specific and/or umbrella support organizations and/or registries for the benefit of individuals with this disorder and their families. GeneReviews is not responsible for the information provided by other organizations. For information on selection criteria, click here.

- **MedlinePlus**

Baraitser-Winter syndrome

Molecular Genetics

Information in the Molecular Genetics and OMIM tables may differ from that elsewhere in the GeneReview: tables may contain more recent information. —ED.

Table A. Baraitser-Winter Cerebrofrontofacial Syndrome: Genes and Databases

Gene	Chromosome Locus	Protein	Locus-Specific Databases	HGMD	ClinVar
ACTB	7p22.1	Actin, cytoplasmic 1	ACTB database	ACTB	ACTB
ACTG1	17q25.3	Actin, cytoplasmic 2	ACTG1 database	ACTG1	ACTG1

Data are compiled from the following standard references: gene from HGNC; chromosome locus from OMIM; protein from UniProt. For a description of databases (Locus Specific, HGMD, ClinVar) to which links are provided, click here.

Table B. OMIM Entries for Baraitser-Winter Cerebrofrontofacial Syndrome (View All in OMIM)

102560	ACTIN, GAMMA-1; ACTG1
102630	ACTIN, BETA; ACTB
243310	BARAITSER-WINTER SYNDROME 1; BRWS1
614583	BARAITSER-WINTER SYNDROME 2; BRWS2

Molecular Pathogenesis

ACTB encodes the cytoplasmic protein beta-actin (β-actin; actin, cytoplasmic 1), consisting of 375 amino acids. β-actin interacts with multiple cytoplasmic proteins. *ACTG1* encodes the cytoplasmic protein gamma-actin (γ-actin; actin, cytoplasmic 2) and is almost identical to β-actin, also consisting of 375 amino acids. Primary sequences of γ-actin and β-actin differ only by four amino acid residues; however, the two proteins have distinct post-translational modifications. Both cytoplasmic actins are essential for cell survival, but they perform various functions in the interphase and cell division, and the actin ratio depends on the cell type. The β- and γ-actins coexist in most cell types as components of the cytoskeleton and as mediators of internal cell motility, and play a role in sarcomere assembly. They have both cooperative interactions and partially nonredundant functions.

ACTB protein plays a role in a wide variety of cellular functions such as cell growth, cell division, cell motility, immune response, maintenance of cell stability, and cytoskeletal formation.

ACTG1 protein functions in non-muscle cells and is abundant in the auditory hair cells. It is responsible for the cellular plasticity and motility and essential for the shape and function of stereocilia of hair cells of the cochlea [Dugina et al 2019, Dugina et al 2021].

Mechanism of disease causation. Pathogenic variants in *ACTB* and *ACTG1* leading to BWCFF syndrome have a gain-of-function effect.

Table 8. Baraitser-Winter Cerebrofrontofacial Syndrome: Notable Pathogenic Variants by Gene

Gene [1]	Reference Sequences	DNA Nucleotide Change	Predicted Protein Change	Comment [Reference]
ACTB	NM_001101.5 NP_001092.1	c.359C>T	p.Thr120Ile	Assoc w/severe phenotype [Di Donato et al 2014]

Table 8. continued from previous page.

Gene [1]	Reference Sequences	DNA Nucleotide Change	Predicted Protein Change	Comment [Reference]
ACTG1	NM_001614.5 NP_001605.1	c.608C>T	p.Thr203Met	Assoc w/severe phenotype [Vontell et al 2019, Chacon-Camacho et al 2020]

Variants listed in the table have been provided by the authors. *GeneReviews* staff have not independently verified the classification of variants.
GeneReviews follows the standard naming conventions of the Human Genome Variation Society (varnomen.hgvs.org). See Quick Reference for an explanation of nomenclature.
1. Genes from Table 1 in alphabetic order

Cancer and Benign Tumors

Sporadic, isolated tumors (including hepatocellular carcinoma, melanoma, ovarian cancer, leukemia, and B-cell lymphoma) frequently harbor somatic pathogenic variants in *ACTB* and *ACTG1* that are not present in the germline.

A recent study using data available in the cBioPortal database have shown that somatic variants in *ACTB* and *ACTG1* were rare events in 174 cancer studies covering multiple cancer subtypes. However, *ACTB* and *ACTG1* were more frequently mutated in hematologic cancers, specifically in lymphoid and not in myeloid malignancies [Witjes et al 2020]. Whether somatic variants in *ACTB* and *ACTG1* merely represent passenger variants or have a driver effect remains unclear.

Chapter Notes

Revision History

- 24 March 2022 (ha) Comprehensive update posted live
- 19 November 2015 (me) Review posted live
- 9 March 2015 (av) Original submission

References

Literature Cited

Baumann M, Beaver EM, Palomares-Bralo M, Santos-Simarro F, Holzer P, Povysil G, Müller T, Valovka T, Janecke AR. Further delineation of putative ACTB loss-of-function variants: a 4-patient series. Hum Mutat. 2020;41:753–8. PubMed PMID: 31898838.

Chacon-Camacho OF, Barragán-Arévalo T, Villarroel CE, Almanza-Monterrubio M, Zenteno JC. Previously undescribed phenotypic findings and novel ACTG1 gene pathogenic variants in Baraitser-Winter cerebrofrontofacial syndrome. Eur J Med Genet. 2020;63:103877. PubMed PMID: 32028042.

Cianci P, Fazio G, Casagranda S, Spinelli M, Rizzari C, Cazzaniga G, Selicorni A. Acute myeloid leukemia in Baraitser-Winter cerebrofrontofacial syndrome. Am J Med Genet A. 2017; 2017;173:546–9. PubMed PMID: 27868373.

Cuvertino S, Stuart HM, Chandler KE, Roberts NA, Armstrong R, Bernardini L, Bhaskar S, Callewaert B, Clayton-Smith J, Davalillo CH, Deshpande C, Devriendt K, Digilio MC, Dixit A, Edwards M, Friedman JM, Gonzalez-Meneses A, Joss S, Kerr B, Lampe AK, Langlois S, Lennon R, Loget P, Ma DYT, McGowan R, Des Medt M, O'Sullivan J, Odent S, Parker MJ, Pebrel-Richard C, Petit F, Stark Z, Stockler-Ipsiroglu S, Tinschert S, Vasudevan P, Villa O, White SM, Zahir FR, Study DDD, Woolf AS, Banka S. ACTB loss-of-function

mutations result in a pleiotropic developmental disorder. Am J Hum Genet. 2017;101:1021–33. PubMed PMID: 29220674.

Di Donato N, Rump A, Koenig R, Der Kaloustian VM, Halal F, Sonntag K, Krause C, Hackmann K, Hahn G, Schrock E, Verloes A. Severe forms of Baraitser-Winter syndrome are caused by ACTB mutations rather than ACTG1 mutations. Eur J Hum Genet. 2014;22:179–83. PubMed PMID: 23756437.

Diets IJ, Waanders E, Ligtenberg MJ, van Bladel DAG, Kamping EJ, Hoogerbrugge PM, Hopman S, Olderode-Berends MJ, Gerkes EH, Koolen DA, Marcelis C, Santen GW, van Belzen MJ, Mordaunt D, McGregor L, Thompson E, Kattamis A, Pastorczak A, Mlynarski W, Ilencikova D, van Silfhout AV, Gardeitchik T, de Bont ES, Loeffen J, Wagner A, Mensenkamp AR, Kuiper RP, Hoogerbrugge N, Jongmans MC. High yield of pathogenic germline mutations causative or likely causative of the cancer phenotype in selected children with cancer. Clin Cancer Res. 2018;24:1594–603. PubMed PMID: 29351919.

Dugina VB, Shagieva GS, Kopnin PB. Biological role of actin isoforms in mammalian cells. Biochemistry (Mosc). 2019;84:583–92. PubMed PMID: 31238858.

Dugina VB, Shagieva GS, Shakhov AS, Alieva IB. The cytoplasmic actins in the regulation of endothelial cell function. Int J Mol Sci. 2021;22:7836. PubMed PMID: 34360602.

Freitas JL, Vale TC, Barsottini OGP, Pedroso JL. Expanding the phenotype of dystonia-deafness syndrome caused by ACTB gene mutation. Mov Disord Clin Pract. 2019;7:86–7. PubMed PMID: 31970217.

Hampshire K, Martin PM, Carlston C, Slavotinek A. Baraitser-Winter cerebrofrontofacial syndrome: Report of two adult siblings. Am J Med Genet A. 2020;182:1923–32. PubMed PMID: 32506774.

Latham SL, Ehmke N, Reinke PYA, Taft MH, Eicke D, Reindl T, Stenzel W, Lyons MJ, Friez MJ, Lee JA, Hecker R, Frühwald MC, Becker K, Neuhann TM, Horn D, Schrock E, Niehaus I, Sarnow K, Grützmann K, Gawehn L, Klink B, Rump A, Chaponnier C, Figueiredo C, Knöfler R, Manstein DJ, Di Donato N. Variants in exons 5 and 6 of ACTB cause syndromic thrombocytopenia. Nat Commun. 2018;9:4250. PubMed PMID: 30315159.

Nunoi H, Yamazaki T, Tsuchiya H, Kato S, Malech HL, Matsuda I, Kanegasaki S. A heterozygous mutation of beta-actin associated with neutrophil dysfunction and recurrent infection. Proc Natl Acad Sci U S A. 1999;96:8693–8. PubMed PMID: 10411937.

Poirier K, Martinovic J, Laquerrière A, Cavallin M, Fallet-Bianco C, Desguerre I, Valence S, Grande-Goburghun J, Francannet C, Deleuze JF, Boland A, Chelly J, Bahi-Buisson N. Rare ACTG1 variants in fetal microlissencephaly. Eur J Med Genet. 2015;58:416–8. PubMed PMID: 26188271.

Rainger J, Williamson KA, Soares DC, Truch J, Kurian D, Gillessen-Kaesbach G, Seawright A, Prendergast J, Halachev M, Wheeler A, McTeir L, Gill AC, van Heyningen V, Davey MG, FitzPatrick DR, et al. A recurrent de novo mutation in ACTG1 causes isolated ocular coloboma. Hum Mutat. 2017;38:942–6. PubMed PMID: 28493397.

Rossi M, Guerrini R, Dobyns WB, Andria G, Winter RM. Characterization of brain malformations in the Baraitser-Winter syndrome and review of the literature. Neuropediatrics. 2003;34:287–92. PubMed PMID: 14681753.

Sandestig A, Green A, Jonasson J, Vogt H, Wahlström J, Pepler A, Ellnebo K, Biskup S, Stefanova M. Could dissimilar phenotypic effects of ACTB missense mutations reflect the actin conformational change? Two novel mutations and literature review. Mol Syndromol. 2019;9:259–65. PubMed PMID: 30733661.

Shimojima K, Narai S, Togawa M, Doumoto T, Sangu N, Vanakker OM, de Paepe A, Edwards M, Whitehall J, Brescianini S, Petit F, Andrieux J, Yamamoto T. 7p22.1 microdeletions involving ACTB associated with developmental delay, short stature, and microcephaly. Eur J Med Genet. 2016;59:502–6. PubMed PMID: 27633570.

Skogseid IM, Røsby O, Konglund A, Connelly JP, Nedregaard B, Jablonski GE, Kvernmo N, Stray-Pedersen A, Glover JC. Dystonia-deafness syndrome caused by ACTB p.Arg183Trp heterozygosity shows striatal

dopaminergic dysfunction and response to pallidal stimulation. J Neurodev Disord. 2018;10:17. PubMed PMID: 29788902.

Stenson PD, Mort M, Ball EV, Chapman M, Evans K, Azevedo L, Hayden M, Heywood S, Millar DS, Phillips AD, Cooper DN. The Human Gene Mutation Database (HGMD®): optimizing its use in a clinical diagnostic or research setting. Hum Genet. 2020;139:1197–207. PubMed PMID: 32596782.

Verloes A, Di Donato N, Masliah-Planchon J, Jongmans M, Abdul-Raman OA, Albrecht B, Allanson J, Brunner H, Bertola D, Chassaing N, David A, Devriendt K, Eftekhari P, Drouin-Garraud V, Faravelli F, Faivre L, Giuliano F, Guion Almeida L, Juncos J, Kempers M, Eker HK, Lacombe D, Lin A, Mancini G, Melis D, Lourenço CM, Siu VM, Morin G, Nezarati M, Nowaczyk MJ, Ramer JC, Osimani S, Philip N, Pierpont ME, Procaccio V, Roseli ZS, Rossi M, Rusu C, Sznajer Y, Templin L, Uliana V, Klaus M, Van Bon B, Van Ravenswaaij C, Wainer B, Fry AE, Rump A, Hoischen A, Drunat S, Rivière JB, Dobyns WB, Pilz DT. Baraitser-Winter cerebrofrontofacial syndrome: delineation of the spectrum in 42 cases. Eur J Hum Genet. 2015;23:292–301. PubMed PMID: 25052316.

Vontell R, Supramaniam VG, Davidson A, Thornton C, Marnerides A, Holder-Espinasse M, Lillis S, Yau S, Jansson M, Hagberg HE, Rutherford MA. Post-mortem characterisation of a case with an ACTG1 variant, agenesis of the corpus callosum and neuronal heterotopia. Front Physiol. 2019;10:623. PubMed PMID: 31231230.

Witjes L, Van Troys M, Verhasselt B, Ampe C. Prevalence of cytoplasmic actin mutations in diffuse large B-cell lymphoma and multiple myeloma: a functional assessment based on actin three-dimensional structures. Int J Mol Sci. 2020;21:3093. PubMed PMID: 32349449.

Yates TM, Turner CL, Firth HV, Berg J, Pilz DT. Baraitser-Winter cerebrofrontofacial syndrome. Clin Genet. 2017;92:3–9. PubMed PMID: 27625340.

Zhang K, Cox E, Strom S, Xu ZL, Disilvestro A, Usrey K. Prenatal presentation and diagnosis of Baraitser-Winter syndrome using exome sequencing. Am J Med Genet A. 2020;182:2124–8. PubMed PMID: 32588558.

License