*There are roughly 200 known cases worldwide as of 2022.

**Therapies to consider:**
- Visual services and/or vision therapy, especially focused on CVI.
- Physical therapy.
- Occupational therapy.
- Speech therapy, consideration of sign language and alternative communication devices.
- ABA therapy if a diagnosis of autism spectrum disorder is made (can also be considered for ADHD)
- Music therapy.
- Hippotherapy.

**Clinical Course over time:**
BBSOAS is a neurodevelopmental disorder, which is present at the time of birth and has the course of a static encephalopathy. There is no known regression seen in this syndrome. Importantly, there is no progression of the eye phenotype known, including no known progression of optic atrophy.

Most individuals with BBSOAS will require intensive therapies throughout their lifetime. They will continue to make progress, and they will reach many milestones, but the expected functioning level is still in the intellectual disability range. Some individuals with BBSOAS live semi-independently, some have become parents. The majority of individuals with BBSOAS will still require assistance when they are adults.

There is no major limitation to life expectancy in individuals with BBSOAS.

**Clinical Exams/Tests recommended for children with BBSOAS:**
A developmental assessment to identify areas of impairment and allow for early intervention.
- A comprehensive psychological evaluation for autism. *ADI-R and ADOS testing performed by a certified clinical psychologist.
- EEG if seizures are suspected.
- Brain MRI, recommended at age three years or older.
- Full, dilated eye examination by an ophthalmologist every two years.
- Full hearing evaluation every two years.

**Treatment:**
Currently there is no treatment for BBSOAS. However, there are treatments for some of the symptoms:
- Anti epileptic drugs (AEDs) for seizures/epilepsy.
- ACTH or vigabatrin (Sabril TM) for infantile Spasms.
- ADHD medications (guanfacine and clonidine preferred for patients with epilepsy.)

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Medical Providers Guide to BBSOAS
Bosch-Boonstra-Schaaf Optic Atrophy Syndrome

December 7th is our worldwide awareness day. Show support by wearing teal, coral, or stripes.
Your Patient has or may have BBSOAS—now what?

BBSOAS stands for Bosch-Boonstra-Schaaf Optic Atrophy Syndrome which is an ultra-rare neurodevelopmental disorder. BBSOAS is an autosomal dominant condition caused by mutation of the NR2F1 gene. The NR2F1 gene (also called COUP-TF1), located at 5q15, encodes for a conserved orphan nuclear receptor protein and transcriptional regulator that plays a role in cortical patterning, neurogenesis, guidance of thalamocortical axons, arborization, and neurodevelopment of the eye and optic nerve. NR2F1 works as a homodimer and contains a DNA-binding domain (DBD) formed by two zinc-finger domains as well as a ligand-binding domain (LBD). Loss-of-function variants in NR2F1 are associated with Bosch-Boonstra-Schaaf optic atrophy syndrome and the phenotypic presentation.

Inheritance:
The majority of cases are De Novo. BBSOAS is passed on through an autosomal dominant inheritance pattern. There is currently 1 case of mosaicism. An individual with BBSOAS has a 50% chance of passing the mutation/deletions onto any children they may have. Parents with one child with BBSOAS have a less than 3% chance of having another child with BBSOAS. Cases may be caused by a mutation of the entire gene, or by point mutations in the ligand binding domain or DNA binding domain within the NR2F1 gene.

Phenotypic Spectrum:
The phenotypic spectrum of Bosch-Boonstra-Schaaf optic atrophy syndrome (BBSOAS) is broad and variable. There are five major impairments or disorders associated with BBSOAS. The most well-established characteristics include developmental delay/intellectual disability and visual impairment (including optic nerve atrophy, optic nerve hypoplasia, and cortical visual impairment). Learning to recognize the symptoms of each is very helpful not only for a diagnosis, but also for determining the areas where an individual needs specific intervention such as a variety of therapies or potential medications.

1. Autism Spectrum Disorder (ASD) – Over 80% of individuals diagnosed with BBSOAS are also diagnosed with or exhibit features of an autism spectrum disorder. Symptoms may include: Social impairments, cognitive impairments, communication difficulties, repetitive behaviors.

2. Speech and Language Impairment – One of the most common features of BBSOAS is language or speech impairment, with 99% diagnosed with a speech delay. Types of Speech & Language Disorders: Apraxia of Speech; Expressive Language Disorder; Receptive Language Disorder; Other Common Speech and Language Disorders: Stuttering (stammering), Dysarthria (slurred speech), Lisp, Spasmodic Dysphonia (causes the voice to break or sound strained), Muteness and Selective Mutism.

3. Vision impairment – Vision problems are very common among those diagnosed with Bosch-Boonstra-Schaaf optic atrophy syndrome, as about 90% have some form of visual problem. Common visual impairments among individuals with BBSOAS include optic atrophy (82%), alacrima (78%), manifest latent nystagmus (52%), optic nerve hypoplasia (49%), and cortical vision impairment (68%).

4. Epilepsy and/or Seizures – About half of everyone diagnosed with BBSOAS has also been diagnosed with epilepsy or a seizure disorder. Some common types of seizures seen in individuals with BBSOAS are infantile spasms, focal seizures, absence seizures, generalized clonic-tonic seizures, atonic seizures, and myoclonic seizures.

Other symptoms can include:
- Developmental/Cognitive Impairment
- Extreme love of music
- High pain tolerance
- Oromotor dysfunction
- Repetitive behavior not associated with ASD
- Attention-deficit hyperactivity disorder
- Hearing impairment
- Spasticity
- Mild and inconsistent dysmorphic facial features
- Thin corpus callosum on brain MRI

5. Hypotonia – Hypotonia, or low muscle tone, is seen in over 90% of those with BBSOAS, and can cause its own set of problems:
- Decreased muscle tone; muscles feel soft and doughy
- Ability to extend limb beyond its normal limit (extreme flexibility)
- Failure or delay in acquiring motor-related developmental milestones
- Problems with feeding (inability to suck or chew for prolonged periods)
- Shallow breathing Under-active gag reflex