HEIDELBERG UNIVERSITY HOSPITAL

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Dear Doctor,

You are seeing a patient with Bosch-Boonstra-Schaaf optic atrophy syndrome (BBSOAS), a rare neurodevelopmental disorder. In this letter we summarize what we know about this condition, and what may be relevant to understanding the symptoms in this patient.

BBSOAS is an autosomal dominant condition caused by mutation of the *NR2F1* gene. The *NR2F1* gene encodes for a protein that plays an important role in the development of the central nervous system and the eye. Mutations in this gene cause BBSOAS features.

List of features

- Developmental delay/intellectual disability

- Visual impairment

  - Optic nerve atrophy
  - Optic nerve hypoplasia
  - (and/or) Cortical visual impairment (CVI)
  - Alacrima
  - Manifest latent nystagmus

- Hypotonia (low muscle tone)

- Oromotor dysfunction (swallowing problems)

- Repetitive behavior

- Autism spectrum disorder

- Seizures, including infantile spasms and febrile seizures

- Attention-deficit hyperactivity disorder

- Hearing impairment

- Spasticity

- Mild and inconsistent dysmorphic facial features

- Thin corpus callosum on brain MRI

The clinical features of BBSOAS are variable, and not every individual manifests all features necessarily. Also, the severity of the condition varies from one individual to the next. Individuals with point mutations in the DNA-binding domain of the gene have a somewhat more severe phenotype compared to those with whole-gene deletions

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

- 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

Therapeutic approaches to be considered

- Visual therapy, 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

- Anti-convulsive treatment if epilepsy is present

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 and much support when they are grown up to be adults.

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

Thank you for helping this individual with BBSOAS and his/her family.

Feel free to contact me for more information.

With kind regards,

Christian Schaaf