Accommodative insufficiency in a patient with Prader–Willi syndrome and SNRPN gene mutation

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Abstract:

Accommodative insufficiency (AI) is common in children, however, has not been described in Prader–Willi syndrome (PWS). This case report presents severe AI in a child with PWS and a rare mutation on chromosome 15 (methylation at locus SNRPN). A 15-year-old boy with PWS presented with the complaint about needing to remove distance glasses while reading. The visual acuity in his right eye was 20/20 with −2.0 D, and in his left eye 20/20 with −2.75/−0.25/173°. The defocus curve manifested with severe AI, and no other abnormal ocular findings were noted. Progressive glasses were recommended. Molecular genetic analysis at the age of two years revealed altered methylation at locus SNRPN on chromosome 15. As muscular hypotonia is common in PWS, the function of smooth muscles, including the ciliary muscle might be altered, as demonstrated in this case report.

Keywords:

Accommodative insufficiency, defocus curve, Prader-Willi syndrome, SNRPN gene mutation

Introduction

Since the first description by Prader, Labhart and Willi in 1956, the Prader–Willi syndrome (PWS) has become a well recognized genetic multisystem disorder. PWS is associated with the lack of expression of paternal genes on chromosome 15q11-q13 and has an estimated prevalence between 1 in 10,000 and 1 in 20,000 births. The clinical manifestations include endocrine, respiratory, facial and developmental disorders.[1] The aim of this study is to discuss the case of a child with an atypical ocular manifestation of PWS.

Case Report

A 15-year-old boy with PWS presented with the complaint about needing to remove distance glasses while reading. His first spectacles were prescribed at the age of 12 years, and with the recent change of glasses an exacerbation of the condition was noted [Figure 1]. The visual acuity in his right eye was 20/20 with −2.0 D, and in his left eye 20/20 with −2.75/−0.25/173°. No abnormal findings in the anterior segment and eye fundus were present, and the eye position was correct. The pupil width in mesopic conditions was 7.2 mm in the right eye, and 7.1 mm in the left eye. The amplitude of accommodation was measured monocularly, using the minus lens method, and manifested severe acommodative insufficiency. The defocus curve is presented in Figure 2. Progressive glass were recommended with satisfactory results.

From birth the patient exhibited no sucking reflex, had difficulties with feeding and displayed systemic muscular hypotony. Gene testing at the age of two years revealed: 46.XY. ish15q11.2(SNRPNx2), 27 mitoses were found and 19 analyzed, deletions on chromosome 15 were excluded. Molecular analysis revealed altered methylation at locus SNRPN on chromosome 15. At the age of two he underwent orchidopexy. After the age of five he was treated with growth hormone. From the age of six, he received levothyroxine due to subclinical hypothyroidism.

Discussion

AI is common in children, nevertheless, there is a lack of adequate epidemiological studies

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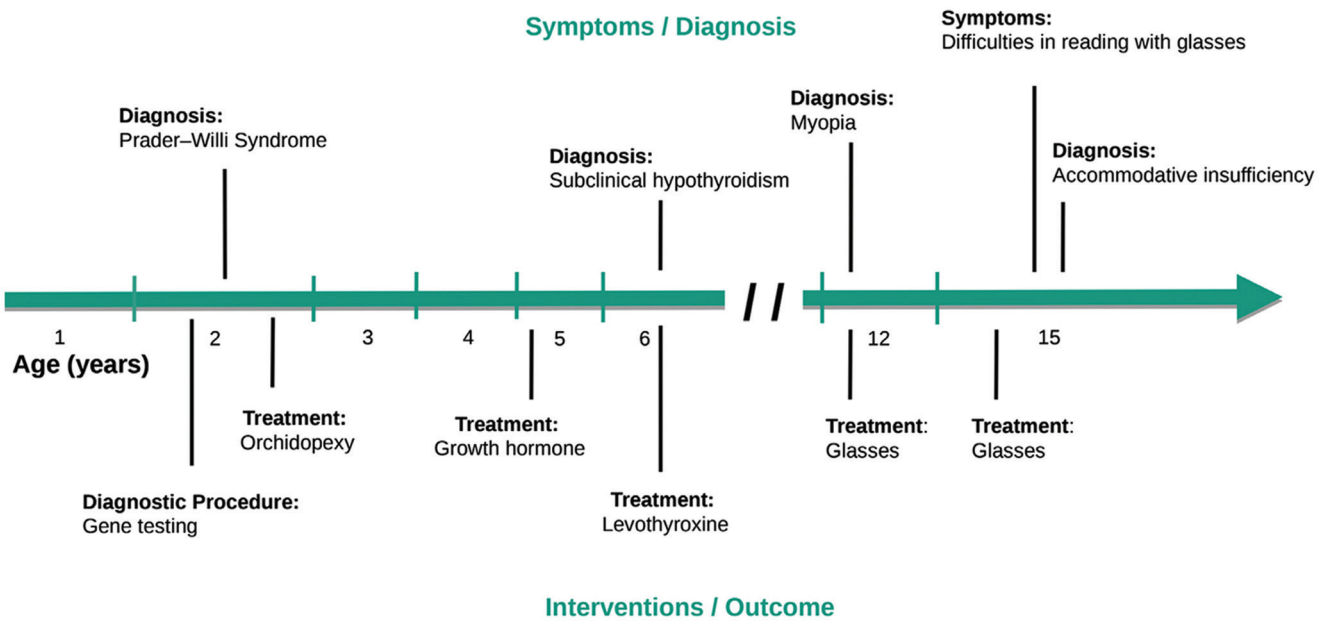

Figure 1: Clinical Timeline. Accommodative insufficiency in a 15-year-old boy with Prader-Willi syndrome

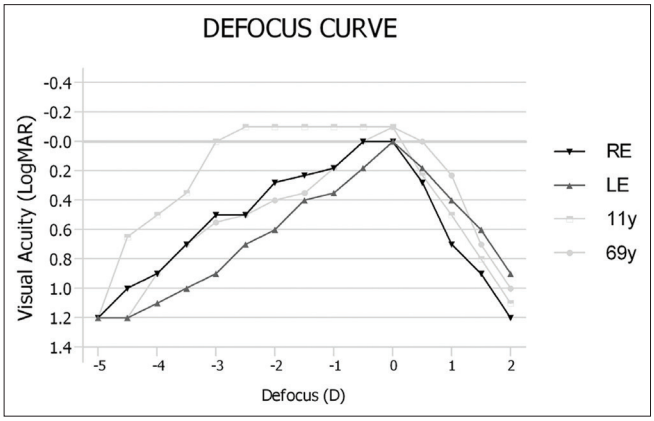

Figure 2: Defocus curve of the right eye (RE) and left eye (LE) of the patient with Prader-Willi syndrome. For comparative purposes a defocus curve of a healthy 11-year-old girl is presented (11y), as well as of a presbyopic patient (69y). Manifest refraction is marked as defocus 0 D

dealing with the prevalence of accommodative disorders in paediatrics.[2] The wide discrepancies in prevalence rates are due to both a small sample population and the lack of uniformity in diagnostic criteria and methods for AI evaluation. Different methods can be used to assess the subjective amplitude of accommodation (AOA). The four common clinical techniques include push-up, push-down, defocus curve with minus lenses, and modified push-up. An increased AOA may be achieved via pharmacological stimulation with topical pilocarpine.[3] Nevertheless, the minus lens method exhibits the best repeatability, least mean difference and coefficient of repeatability.[2] AI has not previously been described in a patient with PWS.

Typically, patients with PWS manifest several ophthalmic disorders. The most common manifestations are strabismus (range from 40 to 95%, mainly esotropia) and ocular hypopigmentation.[4] Other frequent findings include depressed visual acuity or amblyopia, moderate to high refractive error and astigmatism.[5,6] Less common features include ocular fibrosis, diabetic retinopathy or congenital ectopia of uvea. On the other hand, Fox *et al*.[7] noted an overall similarity between PWS and control groups on all measures except for myopia and stereopsis.

Muscular hypotonia is common in PWS. It is believed to be caused by a central nervous system abnormality. Nevertheless, muscular fiber immaturity, abnormal muscle fiber distribution and sarcolemmal aggregates of mitochondria are observed in PWS patients. PWS patients present a lack of necdin during their developmental period, which is required for smooth muscle differentiation in mesoangioblast stem cells.[8] Subsequently, the function of smooth muscles, including the ciliary muscle responsible for accommodation, could be altered.[9] It should be underlined that in most cases of PWS deletion on 15q11-q13 or maternal uniparental disomy of chromosome 15 can be found. Interestingly, gene mutations of the 15q11-q13 region, as found in this case, are responsible for less than 1% of cases of PWS.[10]

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Conflicts of interest
There are no conflicts of interest.

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