# Ophtalmological Changes in Prader-Willi Syndrome: Case Report

# Alterações Oftalmológicas na Síndrome de Prader-Willi: Relato de Caso

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**Recebido/Received:** 2021-12-05 | **Aceite/Accepted:** 2022-01-17 | **Publicado/Published:** 2022-09-30


**DOI:** https://doi.org/10.48560/rspo.25964

## ABSTRACT

This work reports a case of Prader-Willi syndrome, with dyschromatopsia, its clinical characteristics and ophthalmological changes, monitoring and treatment, in a 6-year-old child. Prader-Willi syndrome is rare, being an autosomal dominant disorder caused by the exclusion of the proximal long arm of the paternal chromosome 15 (15q11-q13) or inheritance of both pairs of chromosomes 15 from the mother. Clinical manifestations include mental retardation; muscle hypotonia; hyperphagia; obesity; low; hypogonadism; strabismus; and hypersomnolence. Ophthalmological manifestations included: almond-shaped eyes, a characteristic of the syndrome, convergent strabismus, hyperopia and a dyschromatopsia. Prescribed optical correction and orthoptic treatment with occlusion and improvement of ocular deviation. After an extensive review of the literature, we found no reference to other cases of dyschromatopsia related to Prader-Willi syndrome. It evidenced the need for revision in the administration of the Brazilian public health system, highlighting the long itinerary for diagnosis and treatment covered by the patient. as well as the possibility of being assisted by telemedicine.

**KEYWORDS:** Child; Color Vision Defects; Eye Diseases/etiology; Prader-Willi Syndrome/complications; Optic Nerve/abnormalities; Strabismus.

## RESUMO

Este trabalho relata um caso de síndrome de Prader-Willi com discromatopsia, suas características clínicas e alterações oftalmológicas, acompanhamento e tratamento, em uma criança de 6 anos de idade. A síndrome de Prader-Willi é rara, sendo um distúrbio autossómico dominante causado pela exclusão do braço longo proximal do cromossoma paterno 15 (15q11-q13) ou herança de ambos os pares de cromossomas 15 da mãe. As manifestações clínicas incluem atraso mental; hipotonia muscular; hiperfagia; obesidade; baixo; hipogonadismo; estrabismo; e hiperssonolência. As manifestações oftalmológicas incluíram: olhos amendoados, característica da síndrome, estrabismo convergente, hipermetropia e discromatopsia. Prescrita correção óptica e tratamento

ortóptico com oclusão e com melhora do desvio ocular. Após extensa revisão da literatura, não encontramos referência a outros casos de discromatopsia relacionados à síndrome de Prader-Willi. Evidenciou-se a necessidade de revisão na administração do sistema público de saúde brasileiro, destacando o longo itinerário para o diagnóstico e tratamento percorrido pelo paciente., assim como a possibilidade de ser assistido por telemedicina.

**PALAVRAS-CHAVE:** Criança; Defeitos da Visão Cromática; Estrabismo; Nervo Óptico/anomalias congénitas; Oftalmopatias/etiologia; Síndrome de Prader-Willi/complicações.

## INTRODUCTION

The syndrome is named after Andrea Prader, Heinrich Willi, and Alexis Labhart who described it in detail in 1956. An earlier description occurred in 1887 by John Langdon.[1] It originates from a non-hereditary genetic disorder resulting from the absence or non-expression of genes on chromosome 15. Caused by one of three genetic mechanisms resulting in the absence of expression of imprinted genes located in the 15q11.2-q13 region. The underlying molecular mechanisms are, in order of frequency: deletion of the paternal (occurring in 65%-75% of cases), maternal uniparental disomy (UDP) (20%-30% of cases), and imprinting defects (1%-3%). Instead, genetic changes happen during ovule or sperm formation or early development. There are no known risk factors. The definitive diagnosis of PWS is made by studying the critical region methylation (PWCR) of Prader-Willi syndrome, fundamental for the selection of cases to be submitted to genetic tests.[2]

The main symptoms are: Obesity in childhood, hypotonia - delay in typical stages of psychomotor development as babies, emotional instability, hormonal changes - delayed sexual development, short stature, decreased pain sensitivity, small hands and feet, lighter than parents, small mouth with thin upper lip sloping down at the corners of the mouth, narrow forehead, eyes almonds and strabismus.

Prader-Willi syndrome has no cure. During childhood, individuals should undergo therapies to improve muscle strength.[3] In recent years, GH treatment in infants has had beneficial effects on the growth and neurological development of patients diagnosed during childhood.[4] The most frequent ophthalmic changes are almond eyes, strabismus and decreased inter pupillary distance. In more than 60% of reported cases, esotropy being the most frequent. The second most frequent alteration is ametropia, astigmatism was the most observed. School-age patients had untreated strabismus or ametropia and amblyopia. Uncommon situations such as iris transillumination defect, retinal hypopigmentation, congenital uveal glaucoma associated with glaucoma may occur.[5]

After extensive literature review in databases such as PubMed, SciELO and LILACS, we did not find cases of this syndrome reported with color vision blindness or deficiency. Therefore, this study reports the first case of this syndrome associated with deuteranopia.

## CASE REPORT

DMP, 6-year-old male, after evaluation by geneticist and neuropediatrician diagnosed with Prader-Willi syndrome, was referred for ophthalmic evaluation at CDO - Ocular Diagnosis Center presenting intermittent convergent strabismus, in November 2017.

Non-consanguineous parents, uneventful pregnancy, cesarean section, good vitality at birth (APGAR 9/10). In the first hours, he presented suction difficulties remaining in hospital observation for a few hours. At neurological examination showed, hypotonia, including facial muscles (carp-shaped mouth always open) deep hypoactive reflexes (+1) with slight overall decrease in muscle strength (4+).

Encephalic magnetic resonance was normal. Due to slightly elevated serum creatine phosphokinase (CPK) levels, despite a normal electroneuromyographic study, a muscle etiology was initially suspected, and a genetic panel for myopathies and muscular dystrophies with normal results was requested suggested the presence of deletion in the 15q11.2-q12 region, which is the critical region for Prader-Willi and Angelman syndromes.

Methylation test (MS-MLPA) - methylation-sensitive binding-dependent amplification of multiple probes) was requested to identify the presence of methylation of the 15q11.2 genomic region compatible with Prader-Willi syndrome, and a definitive etiological diagnosis was established.

Ophthalmic examination;

Ectoscopy almond eyes, characteristic of PWS;

Uncorrected visual acuity, 20/40 in both eyes on Snellen chart;

Refraction over cycloplegia: +4.50 hyperopia There was an improvement in visual acuity with the prescribed correction, reporting designs with 20/25 optotypes.

The patient with Prader-Willi syndrome was evaluated with a 25-plate Ishihara Pseudoisochromatic test, which presented numbers to be observed.

He recognized the numbers in five plates, including the first of the test, which does not count for the diagnosis of color blindness.

He missed two answers, saying numbers out of the color blindness feedback answer sheet, provided by the test. On plate 4, he said that the number was 78 while a daltonic person would be expected the answer 70 and in plate 22, he said he saw only the number 7, while he was

expected the answer 2, in the case of deuteranopia and 6 in the case of protanopia.

He missed the correct answer in also other 18 plates, however in these cases he responded what a color deficiency person would answer.

On plates 23, 24 and 25 he saw only the numbers 4, 3 and 9 respectively, which indicated deuteranopia.

The test was compatible with deuteranopia due to the result of plates 23.24 and 25 and the high number of errors it presented in total (20/24).

The Ishihara test is still the most widely used worldwide for the detection of congenital dyschromatopsia. In relation to the other tests, the Farnsworth-Munsell 100-colors is a qualitative test, being also designated for cases of congenital dyschromatopsies. Leading to the dispersion of attention[6]

The child interacts well with the examiner, informing drawings and numbers, as can be seen as far as visual acuity

Retinal mapping presents slight increase in tortuosity and vascular caliber without retinal pigment change.

Ocular motility examination:

Normal versions and ductions;

Measurement of deviation without correction for distance: 20 prismatic diopter endotropy;

And close with 25 prismatic diopters. And with correction was orthophoric far and near, in the primary position of the eyes;

Normal near convergence point (PPC);

Fusional amplitudes: Not reported;

Stereopsy: normal with correction;

Eye dominance: Right eye;

Endotropy paralyzes 6 prismatic diopters, but does not hold, presents moments of endotropy.

The diagnostic hypothesis was accommodative endotropy with motor component (hypotonia), justified by the moments of endotropy and presumed dyschromatopsia. Total refraction (+4.50 in both eyes) was prescribed to reduce deviation and close observation. Decrease in deviation to 15 far and near prismatic diopters with prescribed correction Prescribed occlusion on alternate days (1: 1), same for both eyes, since it is not amblyopia, alternate occlusion was prescribed in an attempt to stimulate muscle strength to the primary position of the unconcluded eye, as it also is the motor component - hypotonia, characteristic of

Figure 1. No optical correction.

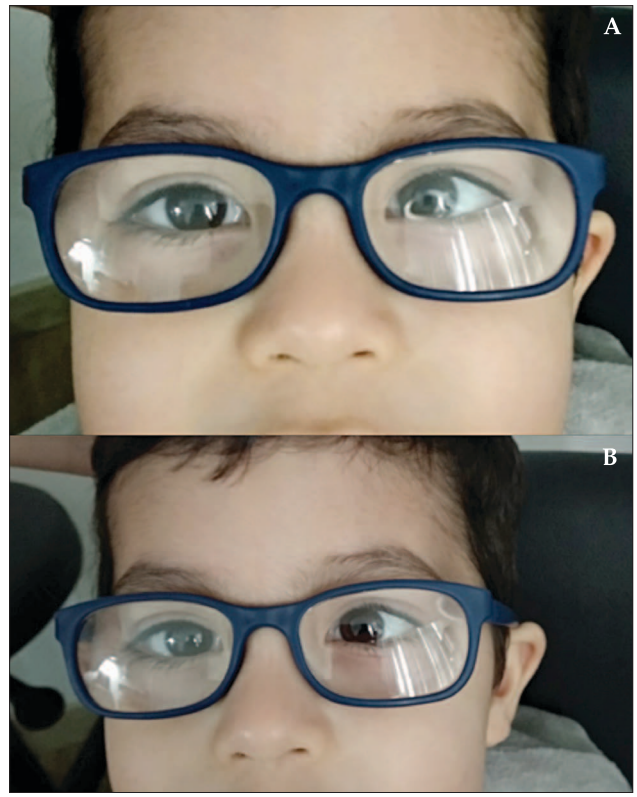


Figure 2. With optical correction (a and b).

Prader-Willi syndrome. At this age the child does not benefit from prism and can be used at school age, also helping in the motor component - hypotonia.

## DISCUSSION

Hered RW *et al* conducted a study on the ophthalmic aspects of Prader-Willi syndrome. Forty-six patients with Prader-Willi syndrome were examined to determine the incidence and character of ocular abnormalities. All patients met the clinical criteria for this syndrome.

Thirty-two patients had better corrected visual acuity between 6/6 and 6/9 in each eye. Seven patients (15%) had myopia greater than -3.75 diopters. Nineteen (41%) patients had astigmatism of 1.25 diopter or greater. Amblyopia due to strabismus or ametropia was present in 11 (24%) patients. Strabismus was present in 25 (54%) patients: 22 (48%) patients had esotropy and three (7%) had exotropy.

Nine patients received or required strabismus surgery. Thirty-three percent of the patients examined had iris transillumination defect. This study was the first major series of patients with Prader-Willi syndrome who underwent detailed ophthalmic evaluation. Recognition of this syndrome is important due to the high incidence of potentially treatable eye problems.[7]

Ophthalmologic alterations are classified in the group of minor alterations of the syndrome.

A complete eye examination should be done. This in-

cluded visual acuity in each eye obtained from the current correction, an external examination, ocular motility assessment, stereo cuteness determination by the Titmus test, an anterior segment biomicroscopic examination, a cycloplegic refraction, and a fundus examination.[8]

No revised article found in the medical literature included color vision tests.

Visual problems in SPW include strabismus and ametropia. Strabismus includes both esotropia, which is more common, and exotropia. Treatment is based on correction of refractive errors, better eye correction and / or surgical correction of eye muscle dysfunction. Generally, treatment is most successful if started in the early years of life. Amblyopia, or reduced vision due to disuse of one eye during development, results from improperly treated strabismus. Myopia and hyperopia are also common findings in children with PWS. Periodic examinations with a pediatric ophthalmologist are recommended throughout childhood. Type 2 oculo-cutaneous albinism has been associated with region 15q11-q13 - individuals with PWS due to exclusion in this area may also have signs of depigmentation.[9]

Retinal vessel tortuosity, can also be congenital, sometimes accentuated, considering this finding, the diagnostic value and pathological implication should be evaluated sparingly.[10]

Color blindness can be inherited. It is most commonly inherited from mutations on the X chromosome but the mapping of the human genome has shown there are many causative mutations—mutations capable of causing color blindness originate from at least 19 different chromosomes and 56 different genes (as shown online at the Online Mendelian Inheritance in Man (OMIM) database at Johns Hopkins University). Two of the most common inherited forms of color blindness are protanopia, and deuteranopia. One of the common color vision defects is the red-green deficiency which is present in about 8 percent of males and 0.5 percent of females of Northern European ancestry.

Dyschromatopsia is usually of genetic cause. It may be just an associated finding, but it may also indicate a manifestation of the syndrome not yet reported by the absence of color tests performed in ophthalmologic evaluation in patients.

## CONCLUSION

No reports of color assessment in Prader-Willi syndrome patients were found in the literature. Therefore, chromatic evaluation should be considered for all holders of this syndrome.

The diagnosis of genetic diseases has become more common in all medical fields and has demanded from experts more knowledge about the implications of these diseases in relation to their specialty. The geneticist, or other specialist, should recognize the importance of the ophthalmologist in the diagnosis and clinical follow-up of these patients, increasing the diagnostic accuracy and preventing or treating common complications in these diseases. The ophthalmologist should be aware of all these aspects, as his intervention in these cases is very important and decisive.

Rare genetic diseases are an important public health problem.

The experience of users of the Brazilian Public Health service with genetic diseases includes:

The debilitating and disabling nature of the disease, practical, administrative and bureaucratic problems.

It highlights the long itinerary for the diagnosis and treatment traveled by the patient.

This itinerary is often composed of care in the private health network until patients can access geneticist from the Brazilian public health system.

We conclude the necessity a review in the administration of the Brazilian public health system, to receive and treat properly these rare cases, which has high cost, often hindering the low-income patient.[11]

## CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO:

All authors declare that they had a substantial and direct intellectual contribution in the design and elaboration of this article, that they participated in the analysis and in- terpretation of the data, in the writing of the manuscript, in the revision of versions and critical revision of its content and in the approval of the final version, agreeing who are responsible for the accuracy and completeness of all work.

## RESPONSABILIDADES ÉTICAS

**Conflitos de Interesse:** Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.

**Fontes de Financiamento:** Não existiram fontes externas de financiamento para a realização deste artigo.

**Confidencialidade dos Dados:** Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.

**Consentimento:** Consentimento do doente para publicação obtido.

**Proveniência e Revisão por Pares:** Não comissionado; revisão externa por pares.

## ETHICAL DISCLOSURES

**Conflicts of Interest:** The authors have no conflicts of interest to declare.

**Financing Support:** This work has not received any contribution, grant or scholarship.

**Confidentiality of Data:** The authors declare that they have followed the protocols of their work center on the publication of data from patients.

**Patient Consent:** Consent for publication was obtained.

**Provenance and Peer Review:** Not commissioned; externally peer reviewed.

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