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CLINICAL CASE

# Nystagmus secondary to albinism with ocular involvement in a female

## Nistagmo secundario a albinismo con compromiso ocular en paciente femenina

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**What do we know about the subject matter of this study?**

Infantile nystagmus is a diagnostic challenge for pediatricians. Albinism is one of its main causes and it is difficult to suspect when there is no obvious skin involvement, especially in female patients.

**What does this study contribute to what is already known?**

Based on the case of a female infant presenting nystagmus secondary to isolated ocular albinism, we discuss the clinical diagnostic approach, emphasizing the relevance of timely identification and multidisciplinary intervention.

## Abstract

Infantile nystagmus is an infrequent condition that represents a diagnostic challenge for the pediatrician. Albinism is one of its main causes, being difficult to suspect in the absence of evident cutaneous involvement, especially in female patients, due to the inheritance type of ocular albinism. **Objective:** To describe a case of nystagmus secondary to albinism with isolated ocular involvement in a female patient, in order to provide tools for pediatric approach and diagnosis. **Clinical Case**: Three-weeks-old female patient, without morbid history, referred to a pediatric neurosurgeon and ophthalmologist due to paroxysmal eye movements since 2 weeks of age. The electroencephalogram and brain images were normal. In follow-up monitoring at 3 months, iris translucency, nystagmus, and hypermetropic astigmatism were confirmed. Dermatologic evaluation ruled out cutaneous involvement. The patient developed cephalic downward inclination and coordination development delay was confirmed, the patient was handled with corrective lenses and kinesiotherapy. In follow-up monitoring at 3 years, there was an improvement in visual acuity, decreased nystagmus and normal neurodevelopment. The ophthalmological evaluation of both parents was normal and there was no history of nystagmus or albinism in the family. Upon her parents' decision, no genetic study was carried out. **Conclusion**: The diagnosis of nystagmus secondary to ocular albinism, even in the absence of cutaneous involvement, is clinical. The genetic study allows confirming the etiology, without being an essential examination, unless family planning is considered. Timely research and multidisciplinary intervention determine a better prognosis.

**Keywords:**
Nystagmus; Ocular albinism; albinism; Infantile nystagmus; congenital torticollis

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## Introduction

Nystagmus is the constant, rhythmic, involuntary, and generally conjoined ocular movement of both eyes, which can be horizontal, vertical, or oblique. It is classified as congenital or infantile if it is present at birth or develops during the first months of life and acquired if it appears after this period[1]. 87% of congenital nystagmus are diagnosed before 6 months of age[2]. Its clinical relevance lies in the visual function involvement, which makes eye contact difficult and is associated with difficulty in psychomotor development. In addition, affected individuals often adopt abnormal cervical postures or swings as a way of blocking constant eye movement and consequently reduction of nystagmus[2-4].

Nystagmus is a very rare condition. In England, it presents a prevalence of 24 per 10,000 in the general population, and 16.6 per 10,000 under 18[5], while in the United States, the reported rate is 35.3 per 10,000 in preschoolers[6].

Infantile or congenital nystagmus is associated with a wide variety of ocular pathologies such as structural defects of the eyeball, media opacity and retina alterations, and less frequent, to pathologies in the central nervous system[7,8]. It is estimated that around 10% is idiopathic or unknown cause[1]. In children, albinism is the most common individual cause[5,7,8].

Albinism is a heterogeneous group of pigment alterations, which affect the biosynthesis processes of the melanin polymer, a pigment produced by specialized ectoderm cells called melanocytes[9]. Depending on the ectodermal lineage, melanocytes are differentiated into cutaneous (clapers and skin) or extra-cutaneous (ocular and cochlear). All patients suffering from albinism in any of its forms present ophthalmological impairment, including nystagmus, photophobia, iris transillumination, decreased visual acuity, and foveal hypoplasia[10]. Oculocutaneous albinism (OCA) affects the skin and hair, while in ocular albinism (OA) only the eyes are involved[9,11,12].

The prevalence of albinism varies widely across ethnic groups. Globally, OCA affects 1 in 17,000 individuals in the general population, where 1 in 70 people are carrying a recessive OCA gene[13]. Studies of children in Nordic countries show higher prevalence, reaching 7 in 1,000 schoolchildren[14]. In the case of OA, the estimated frequency is 1 in 60,000 live births[15]. The difference in prevalence between these two types of albinism is due to the inheritance type where OCA is autosomal recessive while OA is generally X-linked, affecting predominantly male patients[12].

Since its low frequency and heterogeneous characteristics, the diagnosis of congenital nystagmus in pediatrics is complex, especially when there is no skin hypopigmentation. The objective of this paper is to describe a case of nystagmus secondary to albinism in a female patient in order to discuss the pediatric diagnostic approach.

## Clinical Case

Female infant, with no relevant perinatal or family history. From 2 weeks of age, the parents noted paroxysmal eye movements in drowsiness, sleep, and then also in wakefulness, thus she was evaluated by a neuro-pediatrician. To rule out epileptic syndrome, an electroencephalogram and brain ultrasound were performed which presented normal results. Due to the evolution from paroxysmal eye movements to horizontal nystagmus of moderate amplitude and frequency, she was reevaluated by an ophthalmologist, finding symmetrical bilateral iris trans-illumination, macular hypoplasia, diffuse retinal hypopigmentation, and gray optic nerves, associated with hypermetropic astigmatism (figure 1). With these findings, she was referred to dermatology, ruling out skin or hair hypopigmentation. Regarding her development, she presented a tendency towards head-down tilt associated with delayed coordination.

The ophthalmological and auto-fluorescence imaging evaluation performed on both parents ruled out the presence of ocular involvement and there were no other cases of albinism or nystagmus in the family history. In the evaluation by a geneticist, a genetic study was suggested, which was not done upon the parents' decision.

The patient was managed with corrective lenses and kinesiotherapy for cervical alignment. In the last pediatric and ophthalmologic evaluation at the age of 3, she presented a favorable ophthalmologic evolution, with an improvement of visual acuity, a decrease of nystagmus, and adequate developmental progression of coordination, fine motor skills, and posture.

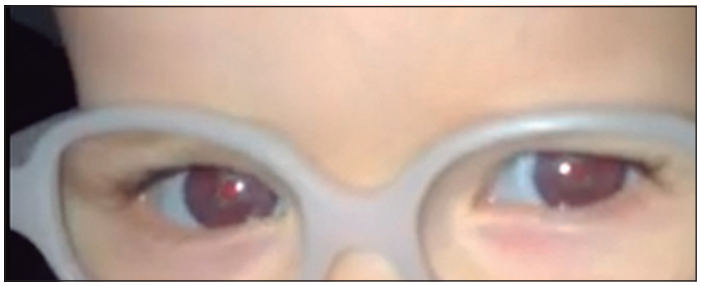

**Figure 1.** Visual evaluation: observed iris translucency.

## Discussion

Nystagmus in infants and children is an unusual cause for consultation. The initial diagnostic orientation is complex, as in our case, in which, in the first weeks of life, it was not evident that the paroxysmal eye movements corresponded to nystagmus.

In our patient, through imaging studies and electroencephalogram, we ruled out neurological involvement. Once nystagmus was identified, the objective was to define whether it was of ocular or sensorial origin, or neurological or idiopathic (figure 2). Among the causes of nystagmus, the most frequent are ocular, and among this albinism predominates[5,7,8].

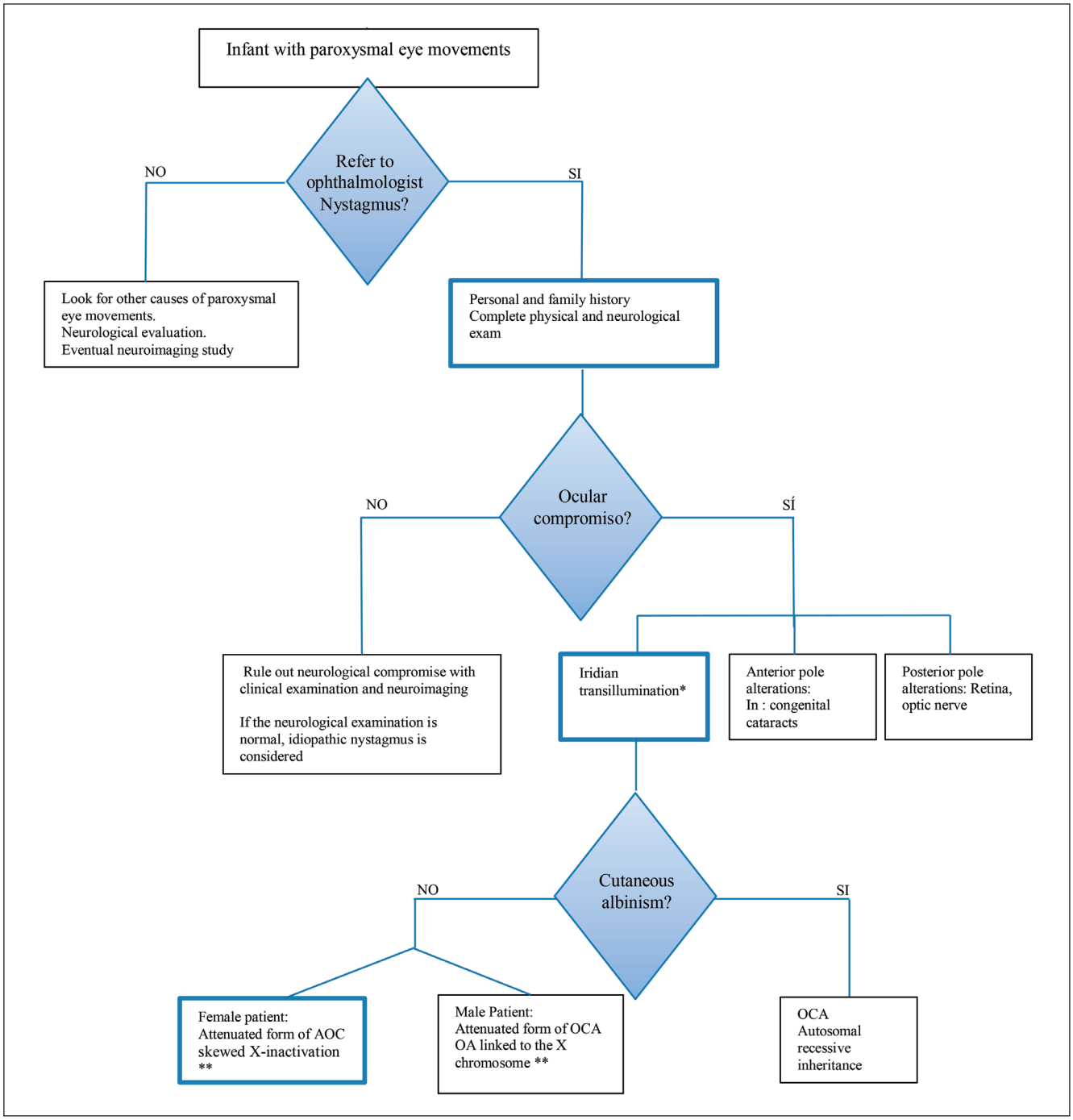


**Figure 2.** Algorithm proposed for the initial diagnostic approach of congenital nystagmus. OCA = oculocutaneous Albinism; AO = ocular Albinism *The ophthalmologist performs the differential diagnosis of transillumination, considering other pathologies such as uveitis, trauma, anterior segment dysgenesis or others.**In a syndromic context, consider "pigmentary dilution" syndromes such as Hermansky- Pudlak syndrome, Sd. Chédiak-Higashi syndrome and Griscelli Syndrome.

The diagnosis of ocular involvement in albinism is clinical, based on the triad consisting of nystagmus, iris trans-illumination, and foveal hypoplasia[10]. The ophthalmological examination usually also shows a reduction in visual acuity, refractive errors, iris alterations, macular hypoplasia, nerve alterations, and optic chiasm[1]. As opposed to a typical eye examination, no additional tests are required. The general physical examination usually shows appendages and skin hypopigmentation, a condition that is not always present since there are types of albinism that have exclusively ocular manifestations[12].

OA is a rare condition that does not affect the skin. Due to its X-linked inheritance, this condition predominates in male patients[12,16]. Females have a random X-inactivation, with the 'healthy remnant' being enough to prevent major clinical manifestations of OA, however, heterozygous females may have some degree of pigment mosaicism seen in the ocular fundus and a characteristic auto-fluorescence pattern[17-20].

The most common form of OCA is that associated with OCA1 gene mutation, which affects significantly the skin, however, there are other forms in which skin pigmentation can be virtually normal, such as that associated with the OCA2 gene. Both presentations are autosomal recessive. Also, part of the differential diagnosis of OA is Hermansky-Pudlak syndrome and Chédiak-Higashi syndrome, where albinism is associated with a syndromic spectrum disorder[13].

In our case, where we ruled out skin involvement, there was no family history of albinism or nystagmus, and clinical examination and auto-fluorescence were normal in both parents. Therefore, an X-linked OA was considered as an alternative, with phenotypic characteristics that could be due to a skewed X-inactivation or an attenuated form of OCA.

There are few reported cases of OA in female patients in the literature[21,22]. Genetic testing would have helped to identify the differential diagnosis and future family planning, which was not necessary according to her parents, who understood albinism as a non-disabling condition with a non-progressive course. Authors state that genetic screening has a performance rate lower than 50%[23]. In the future, the test's cost-effectiveness could vary given advances in sequencing techniques and the progressive decrease in its costs.

Early multidisciplinary intervention in patients with nystagmus due to albinism, allows to decrease complications and improve quality of life. Although there is no curative treatment to date[11], management focuses on the correction of ophthalmological and skin comorbidities and developmental alterations secondary to difficulties in eye contact and abnormal cervical postures[3,4]. In our case, we managed the patient with glasses use and kinesiotherapy, highlighting the improvement in visual acuity, head posture, and coordination skills, with normal neurodevelopment at the age of three. Our patient's favorable evolution is in line with follow-up reports of children with albinism. Dijkstra, et al. showed that binocular vision improved during the school stage[24], while Kutzbach, et al. reported that most carriers would have normal neurological development and academic performance, regardless of visual difficulties and the higher prevalence of attention-deficit/hyperactivity disorder (ADHD)[25].

## Conclusions

Congenital nystagmus often represents a diagnostic challenge, since it is not always evident at birth and can appear as paroxysmal eye movements, as in this case. Nystagmus secondary to albinism where there is no skin involvement, especially in female patients, represents an additional challenge, due to the predominant type of inheritance in the OA that is X-linked, considering the very attenuated forms of OCA as a differential diagnosis. Although the diagnosis is clinical, the genetic study allows confirming the etiology which, in the authors' opinion, is not an essential test[23]. Timely identification and multidisciplinary intervention determine a better prognosis.

## Ethical Responsibilities

**Human Beings and animals protection:** Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

**Data confidentiality:** The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

**Rights to privacy and informed consent:** The authors have obtained the informed consent of the parents (tutors) of the patients and/or subjects referred to in the article. This document is in the possession of the correspondence author.

## Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

## Financial Disclosure

Authors state that no economic support has been associated with the present study.

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## References

1. Papageorgiou E, McLean R, Gottlob I, Nystagmus in Childhood. Pediatr Neonatolo 2014; 55: 341-51.
2. Abadi V, Bjerre A, Motor and sensory characteristics of infantile nystagmus. BR J Ophthalmol 2002;86:1152-60.
3. Noval S, González-Manrique M, Rodríguez-Del Valle JM, Rodríguez-Sánchez JM. Abnormal Head Position in Infantile Nystagmus Syndrome. ISRN Ophthalmol. 2011;1-7.
4. Hertle RW, Zhu X. Oculographic and clinical characterization of thirty-seven children with anomalous head postures, nystagmus, and strabismus: the basis of a clinical algorithm. J AAPOS. 2000;4(1):25-32.
5. Sarvananthan N, Surendran M, Roberts EO, et al. The Prevalence of Nystagmus: The Leicestershire Nystagmus Survey. Invest Ophthalmol Vis Sci 2009;50(11):5201-6.
6. Repka MX, Friedman DS, Katz J, Ibironke J, Giordano L, Tielsch JM. The prevalence of ocular structural disorders and nystagmus among preschool-aged children. J AAPOS 2012;16:182-4.
7. Bertsch M, Floyd M, Kehoe T, Pfeifer W, Drack A. The clinical evaluation of infantile nystagmus: What to do first and why. Ophthalmic Genet 2017;38:(1):22-33.
8. Lazcano-Gómez G, Fuentes-Cataño C, Villanueva-Mendoza C. Etiología del nistagmo congénito o infantil. Ruta diagnóstica. Rev Mex Oftalmol 2010:84(1):49-54.
9. Kamaraj B, Purohit R. Mutational Analysis of Oculocutaneous Albinism: A Compact Review. BioMed Res Int 2014;905472.
10. Preising MN, Forster H, Gonser M, Lorenz B, Screening of *TYR*, *OCA2*, *GPR143*, and *MC1R* in patients with congenital nystagmus, macular hypoplasia, and fundus hypopigmentation indicating albinism. Mol Vis 2011;17:939-48.
11. Hertle R, Albinism: Particular Attention to the Ocular Motor System. Middle East Afr J Ophthalmol 2013;20(3):248-55.
12. Lewis RA. Ocular Albinism, X-Linked. 2004 [Updated 2015 Nov 19]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2019. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1343/ [accedido el 11.11.2019].
13. Grønskov K, Ek J, Brondum-Nielsen K. Oculocutaneous albinism, Orphanet J Rare Dis 2007;2:43
14. Ohlsson J, Villarreal G, Sjöström A, Abrahamsson M, Sjöstrand J. Visual acuity, residual amblyopia and ocular pathology in a screened population of 12–13-year-old children in Sweden. Acta Ophthalmol Scand 2001;79(6):589-595.
15. Rosenberg T, Schwartz M. X-linked ocular albinism: prevalence and mutations-a national study. Eur J Med Genet. 1998;6(6):570.
16. Bassi MT, Schiaffino MV, Renieri A, et al. Cloning of the gene for ocular albinism type 1 from the distal short arm of the X chromosome. Nat Genet 1995; 10:13-9.
17. Falls HF. Sex linked ocular albinism displaying typical fundus changes in the female heterozygote. Am J Ophthalmol 1951; 34:41-50.
18. Schiaffino MV, Bassi MT, Galli L, et al. Analysis of the OA1 gene reveals mutations in only one third of patients with X-linked ocular albinism. Hum Mol Genet 1995;4:2319-25.
19. Mauri L, Manfredini E, Del Longo A. Clinical Evaluation and molecular screening of a large consecutive series of albino patients. J Hum Genet 2017;62(2):277-90.
20. Rodanant N, Bartsch DU, Bessho K, Freeman WR. Autofluorescence image in ocular albinism. Retina. 2003;23(2):265-6.
21. Scialfa A. Ocular albinism in a female. Am J Ophthalmol 1972;73(6).
22. Pearce WG, Johnson GJ, Gillan JG. Nystagmus in a female carrier of ocular albinism. J Med Genet. 1972;9(1):126-9.
23. O'Gorman L, Norman CS, Michaels L, et al. A small gene sequencing panel realises a high diagnostic rate in patients with congenital nystagmus following basic phenotyping. Scientific reports. 2019;9(1):1-8.
24. Dijkstal JM, San Cooley S, Holleschau AM, King RA, Summers CG. Change in visual acuity in albinism in the early school years. Journal of pediatric ophthalmology and strabismus. 2012;49(2):81-6.
25. Kutzbach BR, Summers CG, Holleschau AM, MacDonald JT. Neurodevelopment in children with albinism. Ophthalmology. 2008;115(10):1805-8.