# An autosomal dominant optic atrophy: Kjer type

## Kjer: uma atrofia óptica autossômica dominante

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## ABSTRACT

We present a case of an autosomal dominant optic neuropathy, known as Kjer's disease. The condition can manifest since childhood, presenting with bilateral symmetric optic atrophy and progressive vision loss. Genetics play a crucial role in the differential diagnosis, due to the association with the OPA-1 gene. In this report, we describe the case of a young vegan woman, initially diagnosed with optic neuropathy due to nutritional deficiency, but with laboratory tests within normal limits and a significant family history with the same findings as the patient. This case underscores the importance of comprehensive ophthalmic and genetic evaluation in patients presenting with familial patterns of vision loss.

## RESUMO

Apresentamos um caso de neuropatia óptica autossômica dominante, conhecida como doença de Kjer. A condição pode se manifestar desde a infância, apresentando atrofia óptica bilateral simétrica e perda progressiva da visão. A genética desempenha papel crucial no diagnóstico diferencial, devido à associação com o gene OPA-1. Neste relato, descrevemos o caso de uma jovem mulher, vegana, inicialmente diagnosticada com neuropatia óptica devido à deficiência nutricional, mas com exames laboratoriais dentro dos limites normais e histórico familiar significativo, com os mesmos achados da paciente. Este caso destaca a importância de uma avaliação oftalmológica e genética abrangente em pacientes que apresentam padrões familiares de perda de visão.

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## INTRODUCTION

Progressive vision loss, particularly when associated with night blindness, presents a complex diagnostic challenge for clinicians. This combination of symptoms can significantly impact a patient's quality of life and functional ability. The broad differential diagnosis for progressive vision loss includes both hereditary and acquired conditions. When a familial pattern is observed, the likelihood of an underlying genetic etiology increases, necessitating a comprehensive ophthalmic and genetic evaluation to identify the specific disorder and tailor appropriate management strategies.[1]

Hereditary optic neuropathies are a group of disorders that include conditions such as Leber's hereditary optic neuropathy (LHON) and Kjer's optic neuropathy, also known as dominant optic atrophy (DOA). Kjer's optic neuropathy is a relatively common form of hereditary optic atrophy characterized by bilateral, progressive vision loss that typically begins in early childhood and progresses gradually over time.[1] The condition is inherited in an autosomal dominant manner and is most frequently associated with mutations in the OPA1 gene. This gene encodes a dynamin-related GTPase protein crucial for mitochondrial function, which is essential for the health and function of retinal ganglion cells.[2]

Patients with Kjer's optic neuropathy typically present with a range of visual symptoms, including reduced visual acuity, color vision deficits, and central visual field scotomas.

Night blindness, or nictalopia, can also be a prominent feature, reflecting the condition's impact on cone photoreceptor function.[3] The clinical presentation and severity of symptoms can vary significantly among affected individuals, even within the same family. Ophthalmic examinations often reveal optic disc pallor, temporal atrophy of the optic nerve, and evidence of ganglion cell loss on imaging studies such as optical coherence tomography (OCT).[1] Electroretinography (ERG) can further elucidate the functional impairments, typically showing preserved rod function but significant cone dysfunction.[2] This case report was approved by the local Ethics Committee (CAAE: 84836424.0.0000.5249).

## CASE REPORT

We present a case of a 28-year-old female patient with progressive bilateral vision loss since childhood, associated with nyctalopia. She mentioned being vegan, under metabolic endocrine follow-up, and with laboratory tests within normal limits. Ophthalmological examination revealed visual acuity with correction of 20/40 -7.25 esf -2.00 cyl X 5º in the right eye and 20/25 -7.25 esf -1.75 cyl X 175° in the left eye. In addition to high myopia, the patient presented bilateral temporal optic atrophy in retinography (Figure 1A), loss of the temporal visual field (Figure 2) and altered cone function on electroretinography (ERG). Optical coherence tomography of both eyes showed diffuse thinning of the neurosensory retina and ERG with preserved rods and altered cones. The patient had a notable familial history of similar symptoms affecting her father and sister. After reporting a positive family history, genetic testing was conducted to elucidate the diagnosis. The results confirmed a homozygous mutation in the OPA1 gene, leading to the diagnosis of Kjer's optic neuropathy.

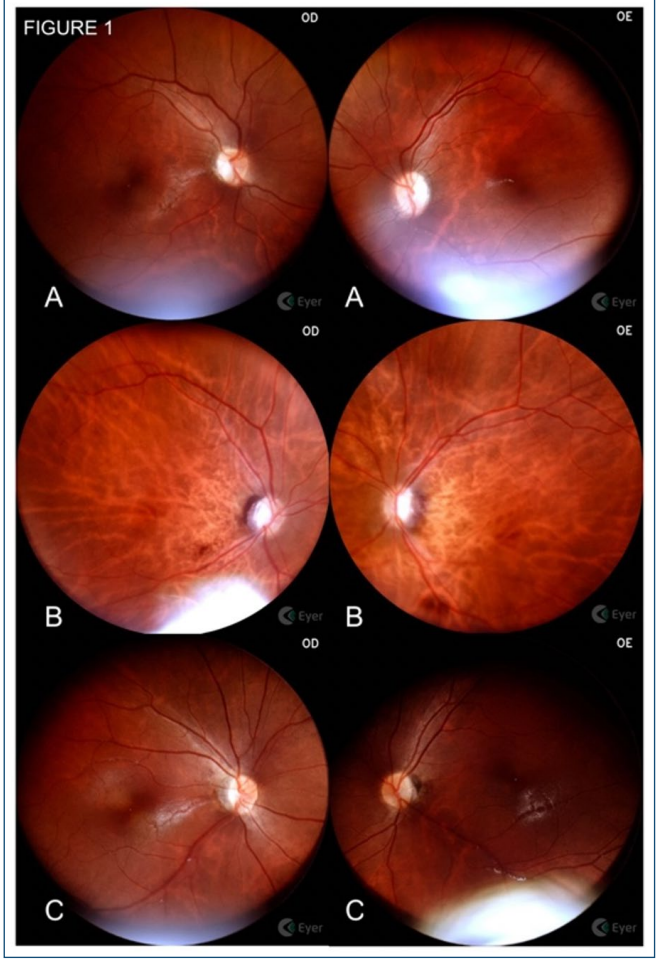


**Figure 1.** Retinography showing bilateral temporal optic atrophy of the patient (A), her father (B) and her sister (C).

## DISCUSSION

Kjer's optic neuropathy, also known as DOA, is typically considered an autosomal dominant disorder. However, in some cases, it can also exhibit autosomal recessive or

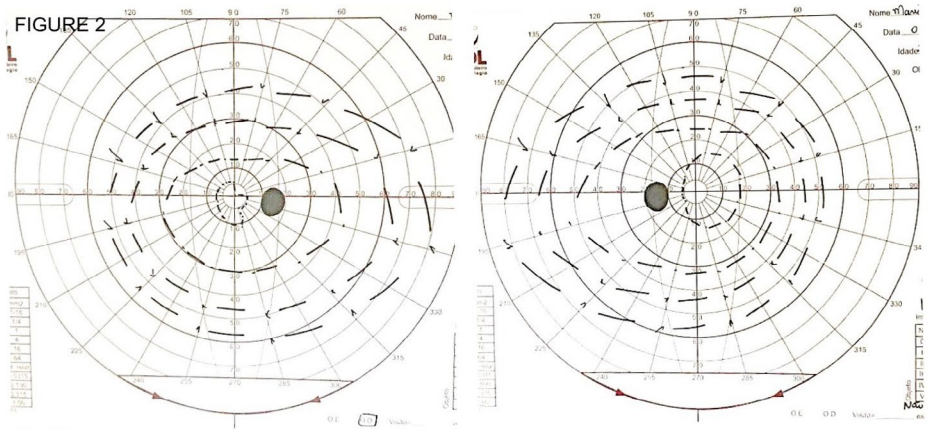


**Figure 2.** Visual field with loss of temporal vision in both eyes.

sporadic inheritance patterns. It is characterized by bilateral, symmetric vision loss that progresses over time. It often manifests in early childhood and can be associated with other symptoms such as color vision defects and central scotomas.[3,4]

Genetic testing helps identify the specific genetic mutations responsible for Kjer's disease in affected individuals. The majority of cases of Kjer's disease is associated with mutations in the OPA1 gene, which encodes a protein essential for mitochondrial function.

Other genes, such as OPA3 and OPA8, are also associated with similar optic neuropathies. Understanding the genetic basis of the disease provides valuable insights into its pathogenesis and potential therapeutic targets.[1]

Furthermore, genetic testing allows for accurate risk assessment and genetic counseling for affected individuals and their families. It helps determine the likelihood of passing on the disease to offspring and enables informed family planning decisions. Additionally, identifying carriers of the mutated gene within the family facilitates early intervention and monitoring for those at risk of developing the disease.[1]

In the literature, Kjer's optic neuropathy is described as the most common form of hereditary optic atrophy, with an estimated prevalence of 1 in 12,000 to 1 in 50,000. It should be considered as a diagnosis of exclusion. Its main differential diagnoses are nutritional optic neuropathy (NON), LHON, toxic optic neuropathy, ischemic optic neuropathy, among others. Distinguishing between these conditions requires a thorough clinical evaluation, including history, examination, and often additional investigations such as neuroimaging and genetic testing.[2]

Patients often present with insidious onset of visual loss, typically becoming symptomatic in the first decade of life. This correlates with the patient's history of progressive vision loss since childhood. Studies, such as those by Yu-Wai-Man et al., have shown that disease progression can be variable, with some individuals experiencing rapid decline in visual acuity, while others have a more gradual loss.[1]

Electrophysiological testing, including ERG, often reveals abnormal cone function, as seen in our patient. This is consistent with the findings reported by Votruba et al., who noted that cone dysfunction is a common feature in patients with OPA1 mutations. Furthermore, Votruba et al. also described additional features such as optic disc pallor and temporal atrophy, which were not specifically documented in this patient's initial examination but should be considered in future follow-ups.[2]

The patient's symptoms and findings are indicative of Kjer's optic neuropathy, a hereditary retinal dystrophy affecting cone function. The significant refractive error and the results of the ERG are consistent with this diagnosis. Genetic testing confirmed the condition, which has a notable familial pattern. The patient's father and sister also exhibit symptoms of progressive vision loss and night blindness, suggesting a strong hereditary component.[4]

Management of Kjer's optic neuropathy primarily focuses on supportive care and symptomatic treatment. There is currently no cure, but low vision aids and rehabilitative strategies can significantly improve the quality of life for affected individuals. Genetic counseling is essential to inform patients and their families about the inheritance pattern and potential risks to offspring.[5]

Recent studies have explored potential therapeutic approaches for managing conditions related to OPA1 mutations, including gene therapy and idebenone treatment. Sarzi et al. demonstrated that OPA1 gene therapy

prevents retinal ganglion cell loss in a mouse model of dominant optic atrophy, highlighting the promise of gene therapy in treating OPA1-related conditions.[6] Regarding idebenone treatment, Romagnoli et al. reported that idebenone increases the chance of stabilization or recovery of visual acuity in patients with OPA1-dominant optic atrophy, suggesting its potential as a therapeutic option. [7]

However, a placebo-controlled trial by Smith et al. (2016) evaluated the therapeutic efficacy of idebenone in a mouse model of OPA1-related optic atrophy, revealing a limited therapeutic effect on retinal ganglion cells. [8] Similarly, Yu-Wai-Man et al. investigated idebenone and its analogues in the context of mitochondrial optic neuropathies, including those related to OPA1 mutations, suggesting that while idebenone shows some promise, its efficacy may be limited and further research is needed to fully understand its potential benefits.[1]

In this case, the patient's vegan diet necessitates careful nutritional monitoring to prevent deficiencies that could potentially worsen her condition. Ensuring adequate intake of nutrients such as vitamin B12, which is crucial for optic nerve health, is particularly important. The role of nutritional support in managing hereditary optic neuropathies has been highlighted in several studies, emphasizing the need for a multidisciplinary approach in patient care.[9]

This case highlights the importance of considering genetic factors in the evaluation of patients with progressive vision loss and a familial pattern of ocular disease.

Comprehensive ophthalmic and genetic evaluations are critical for early diagnosis and intervention, which can help in managing symptoms and improving the quality of life for affected individuals.

In conclusion, Kjer's optic neuropathy represents a challenging diagnostic entity within the spectrum of hereditary optic neuropathies. As demonstrated in the presented case, its clinical manifestations, including bilateral progressive vision loss and night blindness, require a comprehensive evaluation to distinguish it from other conditions with overlapping symptoms. With its autosomal dominant inheritance pattern and association with OPA1 gene mutations, genetic testing plays a pivotal role in confirming the diagnosis and providing valuable prognostic information for affected individuals and their families.

While management strategies for Kjer's optic neuropathy primarily focus on supportive care and symptomatic treatment, ongoing research holds promise for future therapeutic interventions targeting mitochondrial dysfunction, including gene therapy and idebenone treatment.

In summary, advancing our understanding of Kjer's optic neuropathy and refining diagnostic and therapeutic strategies are crucial steps toward improving outcomes and enhancing the quality of life for individuals affected by this rare hereditary disorder.

Through collaborative efforts in research, clinical practice, and patient advocacy, we can strive to mitigate the impact of Kjer's disease and provide optimal care for affected individuals and their families.

## REFERENCES


1. Yu-Wai-Man P, Griffiths PG, Chinnery PF. Mitochondrial optic neuropathies disease mechanisms and therapeutic strategies. Prog Retin Eye Res. 2011;30(2):81-114.
2. Votruba M, Moore AT, Bhattacharya SS. Clinical features, molecular genetics, and pathophysiology of dominant optic atrophy. J Med Genet. 1998;35(10):793-800.
3. Meire FM, Delleman JW, Bleeker-Wagemakers LM, Luyendijk L, van Schooneveld MJ. Clinical and genetic studies on 12 large, unrelated kindreds with dominant optic atrophy. Arch Ophthalmol. 2011;99(8):1377–84.
4. Thiselton DL, Alexander C, Taanman JW, Brooks S, Rosenberg T, Eiberg H, et al. A comprehensive survey of mutations in the OPA1 gene in patients with autosomal dominant optic atrophy. Invest Ophthalmol Vis Sci. 2002;43(6):1715-24.
5. Newman NJ, Biousse V. Hereditary optic neuropathies. Eye (Lond). 2004;18(11):1144-60.
6. Sarzi E, Seveno M, Piro-Mégy C, Elzière L, Quilès M, Péquignot M, et al. OPA1 gene therapy prevents retinal ganglion cell loss in a Dominant Optic Atrophy mouse model. Sci Rep. 2018;8(1):2468.
7. Romagnoli M, La Morgia C, Carbonelli M, Di Vito L, Amore G, Zenesini C, et al. Idebenone increases chance of stabilization/recovery of visual acuity in OPA1-dominant optic atrophy. Ann Clin Transl Neurol. 2020;7(4):590-4.
8. Smith TG, Seto S, Ganne P, Votruba M. A randomized, placebo-controlled trial of the benzoquinone idebenone in a mouse model of OPA1-related dominant optic atrophy reveals a limited therapeutic effect on retinal ganglion cell dendropathy and visual function. Neuroscience. 2016;319:92-106.
9. Milea D, Cassoux N, LeHoang P. Blindness in a strict vegan. N Engl J Med. 2000;342(12):897-8.