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Case Report

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Bilateral optic atrophy as a sequela of delayed biotinidase deficiency diagnosis: a case report

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ABSTRACT

Biotinidase deficiency (BD) is a rare autosomal recessive metabolic disorder that can lead to severe neurological and ophthalmological complications if left untreated. Optic atrophy is a known but often under-recognized sequela of BD, particularly in cases with delayed diagnosis and treatment. We report the case of a 21-year-old female with a history of consanguineous parentage who presented with bilateral vision loss that was more pronounced in the left eye (OS). Her medical history revealed frequent hospitalizations in infancy due to refractory seizures, pulmonary infections, and dermatological manifestations. At the age of one, BD was diagnosed based on undetectable serum biotinidase enzyme activity (0 U/L), and biotin therapy (20 mg/day) was initiated. Despite treatment, ophthalmologic evaluation at age 21 revealed bilateral optic atrophy, decreased visual acuity (OD: 20/200, OS: counting fingers at 1 meter), and visual field defects. Visual evoked potential (VEP) testing showed a reduced amplitude in the OS, while electroretinography (ERG) remained normal. The patient was advised to continue biotin therapy and to undergo regular ophthalmologic monitoring. This case emphasizes the importance of early diagnosis and intervention in BD to prevent permanent complications, such as optic atrophy and vision impairment. We advocate universal newborn screening for BD and increased awareness among clinicians regarding its ophthalmological manifestations.

Keywords: Biotinidase deficiency, optic atrophy, newborn screening, visual impairment, metabolic disorder, consanguinity

INTRODUCTION

Biotinidase deficiency (BD) is a rare autosomal recessive metabolic disorder that impairs the body's ability to recycle biotin, an essential coenzyme for carboxylases involved in fatty acid metabolism, amino acid catabolism, and gluconeogenesis. The estimated global incidence of BD ranges from 1 in 80.000 to 1 in 100.000 live births, though higher rates have been reported in populations with a high prevalence of consanguineous marriages.[1] Early diagnosis and treatment with oral biotin supplementation can prevent most of the neurological and systemic complications associated with BD. However, delayed or missed diagnosis can result in irreversible neurological damage, including optic atrophy and visual impairment.[2]

The clinical manifestations of BD typically appear within the first few months of life, with refractory seizures being the most common presentation. Other symptoms include hypotonia, developmental delay, ataxia, sensorineural hearing loss, skin manifestations (seborrheic dermatitis, alopecia), and optic atrophy.[1] While optic atrophy is a recognized complication, its exact prevalence and pathophysiology remain unclear, and vision loss is often irreversible despite biotin supplementation.[3] This highlights the critical need for early detection, ideally through newborn screening programs that have been implemented in many countries.

In this report, we present the case of a 21-year-old female with a history of BD diagnosed at the age of one, who developed bilateral optic atrophy despite long-term biotin therapy. We emphasize the importance of early diagnosis and discuss the implications of delayed treatment on the visual outcomes.

CASE

A 21-year-old female presented to our ophthalmology clinic with progressive bilateral vision loss that was more pronounced in the left eye (OS). Her family history revealed first-degree parental consanguinity; however, no similar findings were reported in other family members.

At the age of one, the patient experienced recurrent pulmonary infections, generalized tonic-clonic seizures, and widespread erythematous exfoliation affecting both the body and scalp, requiring multiple hospitalizations. Owing to her neurological symptoms, a metabolic disorder was suspected, and biotinidase enzyme activity was measured at 0 U/L, confirming the diagnosis of profound BD. She was started on

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oral biotin therapy (20 mg/day, Gabioten), which successfully controlled her seizures and other systemic symptoms. However, her developmental milestones, hearing, and vision were not systematically assessed.

Upon presentation to our clinic, the patient's visual acuity (VA) was 20/200 in the right eye (OD) and counting fingers at 1 m in the OS. Intraocular pressure (IOP) was 18 mmHg in both eyes. Examination of the cornea and the anterior segment revealed no abnormalities. Fundus examination revealed bilateral optic atrophy, which was more pronounced in the OS (Figure 1A, 1B).

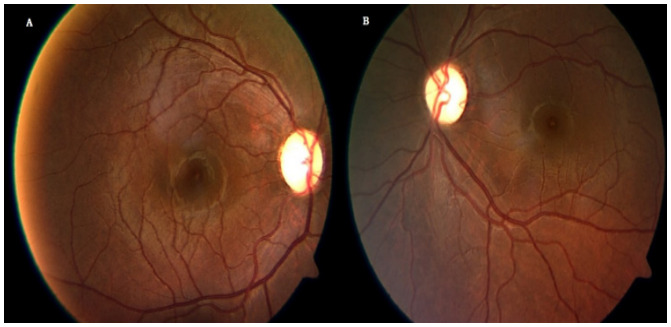

Figure 1. Fundus photography of both eyes. (**A**) Right eye (OD) showing a pale optic disc, consistent with optic atrophy. (**B**) The left eye (OS) demonstrates more pronounced optic atrophy, with significant pallor of the optic nerve head

Fundus fluorescein angiography (FFA) demonstrated a normal retinal vascular structure with normal arteriolar and venous filling and washout times (Figure 2A, 2B). Visual evoked potential (VEP) testing showed mild reduced amplitude and normal latency in the OD, whereas the OS exhibited decreased amplitude with normal latency (Figure 3A, 3B). Electroretinography (ERG) findings were normal in both eyes (Figure 4A, 4B).

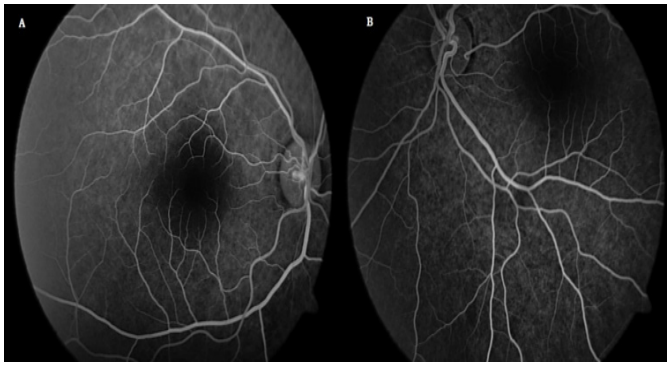

Figure 2. Fundus fluorescein angiography (FFA) in both eyes. (**A**) The right eye (OD) and (**B**) left eye (OS) show normal retinal vascular structures, with no abnormalities in arteriolar or venous filling or washout times. These findings indicate that the vascular pathology did not cause optic atrophy

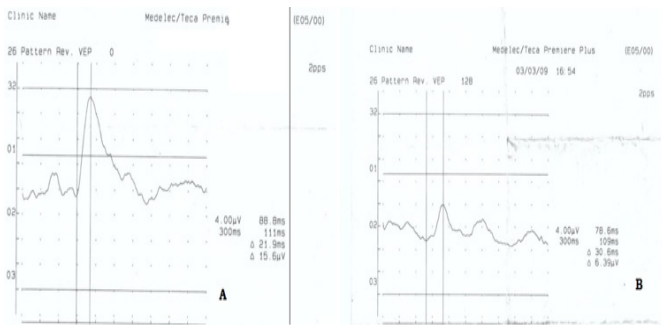

Figure 3. Visual-evoked potential (VEP) results. (**A**) Right eye (OD) showing mild reduced amplitude with normal latency, suggesting intact visual pathway function. (**B**) Left eye (OS) demonstrating a significantly reduced amplitude with normal latency, indicative of optic nerve damage and axonal loss

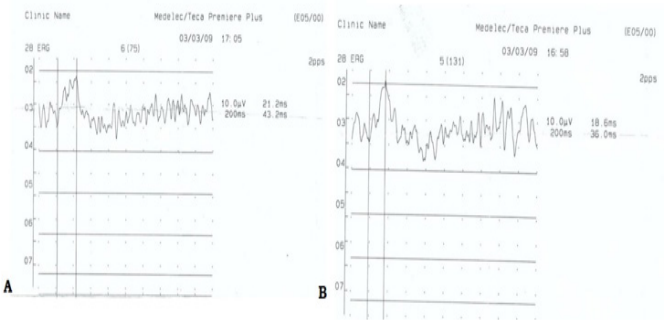

Figure 4. Electroretinographic (ERG) results. (**A**) The right eye (OD) and (**B**) the left eye (OS) showed normal responses, confirming that retinal function was preserved despite optic atrophy

On visual field testing (30-2), the OD demonstrated an enlarged blind spot, nasal step, and superior arcuate scotoma, findings consistent with inferior retinal nerve fiber layer damage (Figure 5A). The OS exhibited severe central visual field loss with marked fixation loss corresponding to total scotoma (Figure 5B).

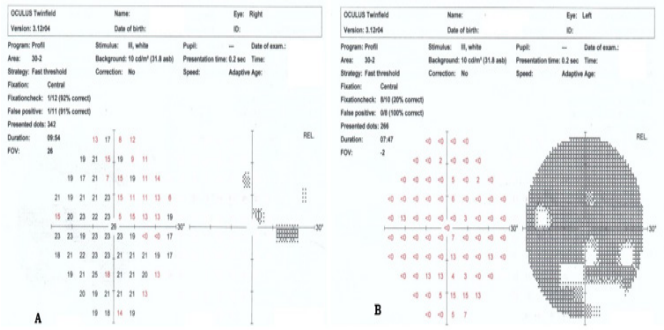

Figure 5. Visual Field testing (30-2). (**A**) Right eye (OD) demonstrating an enlarged blind spot, nasal step, and superior arcuate scotoma corresponding to inferior retinal nerve fiber layer damage. (**B**) The left eye (OS) exhibited severe central visual field loss with marked fixation loss, indicative of total scotoma

The patient was advised to continue the biotin supplementation (20 mg/day). Given the irreversible nature of optic atrophy, the primary goal of management is vision preservation through regular ophthalmologic follow-ups and possible low-vision rehabilitation strategies.

DISCUSSION

BD is a rare but treatable inherited metabolic disorder that, if undiagnosed or untreated, can lead to irreversible neurological and ophthalmic complications.[1] The disorder follows an autosomal recessive inheritance pattern and is more prevalent in populations with high consanguinity rates.[2] Early diagnosis and lifelong biotin supplementation (5–40 mg/day) effectively prevent most symptoms, but delayed treatment often results in permanent sequelae, particularly optic atrophy and sensorineural hearing loss.[3]

Optic atrophy in BD is attributed to progressive axonal degeneration due to prolonged metabolic stress and mitochondrial dysfunction, leading to retinal ganglion cell damage and visual impairment.[4] Our patient, despite receiving biotin therapy since infancy, developed bilateral optic atrophy and severe visual field loss, likely due to a late diagnosis at one year of age. Studies suggest that while metabolic and dermatologic symptoms improve rapidly with biotin therapy, neurological deficits, particularly optic and auditory damage, may remain irreversible if treatment is not

initiated within the first few weeks of life.[5] This underscores the critical importance of newborn screening, which has been implemented in several countries to enable early intervention before irreversible damage occurs.

In our case, neuro-ophthalmologic evaluation revealed bilateral optic atrophy with significant visual field defects, which were more pronounced in the OS. VEP testing confirmed decreased amplitude in the OS, further supporting optic nerve dysfunction. Despite continued biotin therapy at 20 mg/day, no visual improvement was observed, reinforcing previous findings that optic nerve damage in BD is largely irreversible. Given the progressive nature of BD-related optic atrophy, regular ophthalmologic monitoring is essential for assessing disease stability and visual function over time.

This case highlights the long-term visual consequences of delayed diagnosis of BD and emphasizes the urgent need for universal newborn screening programs. In many countries, BD is included in newborn screening panels, allowing for early diagnosis and immediate biotin supplementation. However, in regions where newborn screening is not widely implemented, cases such as ours may continue to occur, leading to preventable, but permanent vision loss.

CONCLUSION

Our case highlights the devastating effects of delayed BD diagnosis, particularly its association with irreversible optic atrophy and severe visual impairment. While biotin supplementation remains the cornerstone of BD treatment, it does not reverse established optic nerve damage. Therefore, early detection through newborn screening is essential for preventing permanent neurological and ophthalmic sequelae. We strongly advocate the inclusion of BD in newborn screening programs worldwide, particularly in populations with high rates of consanguinity. Additionally, clinicians should maintain a high index of suspicion for BD in infants presenting with refractory seizures, dermatological manifestations, or developmental delay, ensuring prompt diagnosis and treatment.

ETHICAL DECLARATIONS

Informed Consent

The patient signed and free and informed consent form.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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