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Case Report

Wilson's Disease and Nevus of Ota in a Child: A Case Report

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Keywords
Nevus of Ota · Wilson's disease · Kayser-Fleischer rings · Sunflower-type cataract

Abstract
Introduction: Wilson's disease is a rare autosomal recessive disorder that disrupts copper metabolism. It presents with distinctive ocular manifestations. Oculodermal melanosis, commonly referred to as nevus of Ota, is a painless condition characterized by hyperpigmentation in and around the eye. In this case report, we describe the unique occurrence of both conditions in this pediatric patient. ***Case Presentation:*** A 10-year-old girl exhibited classic ocular signs associated with Wilson's disease, including Kayser-Fleischer rings and sunflower-type cataracts. Additionally, she displayed unilateral confluent gray-blue hyperpigmentation consistent with a nevus of Ota. As of now, the patient remains asymptomatic, with preserved visual acuity. ***Conclusions:*** To the best of our knowledge, this case represents the first report of nevus of Ota in a child diagnosed with Wilson's disease.

Introduction

Wilson's disease is a rare autosomal recessive disorder that disrupts copper metabolism, presenting with distinctive ocular manifestations. Oculodermal melanosis, commonly referred to as nevus of Ota, is a painless condition characterized by hyperpigmentation in and around the eye. To the best of our knowledge, there is no known connection between these

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two conditions, and the chance that both will appear in a single patient is 1 in 30 million. In this case report, we describe the unique occurrence of both conditions in this pediatric patient.

Case Presentation

A 10-year-old girl was referred to the ophthalmic clinic as part of a clinical investigation into Wilson's disease, prompted by elevated liver enzymes. Additional laboratory findings revealed a low serum ceruloplasmin concentration (8 mg/dL) and a high urine output of copper (941 μg/24 h). An abdominal ultrasound disclosed a liver with a heterogeneous texture and mild splenomegaly.

Her medical history indicated an uneventful pregnancy and perinatal period, with normal growth and development. At the age of eight, she was referred to physical therapy for knee and leg pains. Additionally, she occasionally complained of headaches, and her teacher described her as easily distracted and unfocused. A pediatric neurologist found no abnormalities upon examination and recommended a brain MRI. She also underwent a cardiac examination due to intermittent palpitations, which revealed a healthy heart. Her family history included a great-grandfather who succumbed to jaundice and an undiagnosed liver disease at the age of 40.

In terms of ocular background, she had only myopia of −3.00 diopters in both eyes. Her best corrected visual acuity was 20/25 in both eyes. The left eye exhibited a confluent gray-bluish hyperpigmentation consistent with a nevus of Ota, and there was no periocular dermal pigmentation around the left eye. Both eyes displayed a Kayser-Fleischer ring, more prominent in the upper and lower parts of the peripheral cornea. Sunflower-type cataracts were present in both crystalline lenses. Intraocular pressure was measured at 15 mm Hg in both eyes, and the vitreous, retina, and optic nerves appeared normal, In addition, her eye movements and saccadic movements were all within the normal range. Images of the anterior segment are provided in Figure 1.

Following genetic counseling, sequencing of the ATP7B (NM_000053.3) gene was preformed using next-generation sequencing (NGS). The study revealed two pathogenic variants: g. chr13:52520529; c.2951C>T(het);p.(Pro984Leu) and g.chr13:52518281;c.3207C>A(het); p.(His1069Gln). Genetic testing of the parents and other sibling is pending.

The patient received a diagnosis of Wilson's disease and was recommended to adopt a low-copper diet, albeit with limited adherence. Additionally, the patient initiated treatment with zinc sulfate syrup at a dose of 75 mg three times a day under close monitoring with scheduled follow-up visits at the pediatric gastroenterology service. During her last visit, trientine was recommended.

Discussion

Wilson's disease represents a congenital disorder characterized by disrupted copper metabolism. This disease is exceptionally rare, affecting approximately 1 in 30,000 cases. While constituting less than 5% of chronic active hepatitis cases, it notably contributes to cirrhosis incidence in older children [1]. The condition stems from an autosomal recessive mutation of the gene ATP7B, positioned on the long arm of chromosome 13 (13q14. 3), with no discernible additional risk factors.

Treatment entails a low-copper diet (excluding liver, shellfish, nuts, chocolate, and mushrooms) and initiation of life long treatment such as Zinc or other chelating agents,

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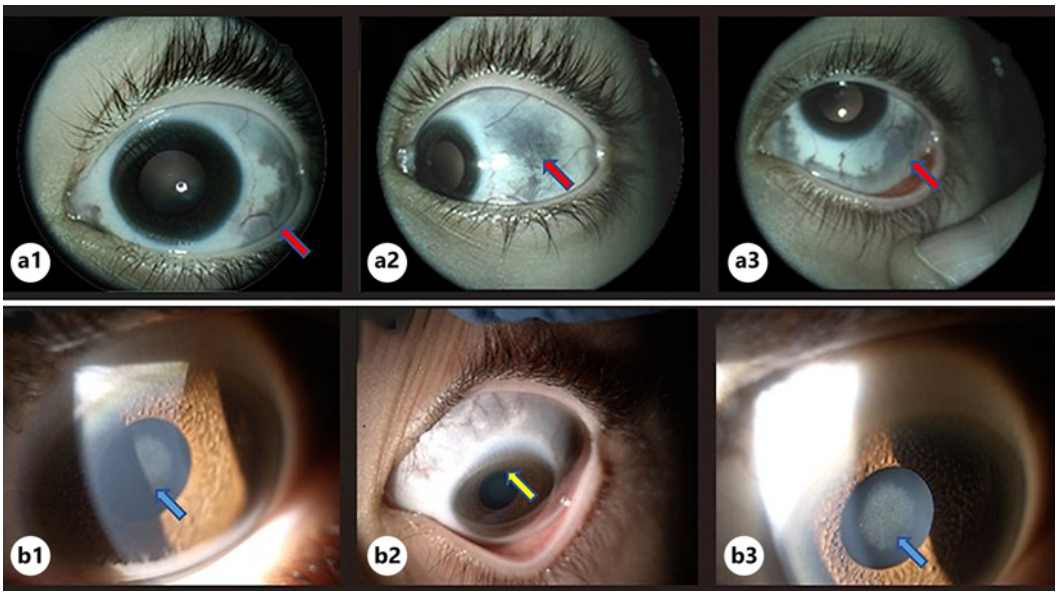

Fig. 1. a1–a3 Anterior segment color photography shows the nevus of Ota all around the conjunctiva (red arrow). **b1–b3** Slit camera shows sunflower cataract (blue arrow) and Kayser-Fleischer rings in the cornea (yellow arrow).

predominantly D-penicillamine [2]. Regular surveillance, including serum copper and coper excretion, ceruloplasmin, liver enzymes, international normalized ratio, complete blood count, and urinalysis during chelator usage, as well as annual physical examinations is recommended. Early diagnosis offers patients a normal life expectancy, while untreated cases are prone to the development of fulminant hepatic failure or neurological deterioration.

A classic ocular finding is the presence of corneal Kayser-Fleischer rings, indicative of copper accumulation in Descemet's membrane, and may be detected via slit lamp examination. Another ocular funding is a sunflower cataract, also known as "Bull's eye" or "central discoid" cataract. It is a distinctive opacification of the lens resembling the petals of a sunflower or a bull's eye target. The sunflower cataract's appearance is due to the deposition of copper granules within the lens fibers directly under the anterior capsule, leading to the formation of distinct circular or star-shaped opacities [3]. The central opacification may be surrounded by additional secondary opacification arranged in ray-like structures around it. This pattern resembles a sunflower, with a large central disk surrounded by petals [4]. While surgical removal of cataracts is a common treatment, addressing the underlying cause, such as managing copper levels in Wilson's disease, is essential for optimal outcomes. In our case, the patient's visual acuity was normal in both eyes, and there was an excellent view of the posterior segment. Therefore, there was no need to address the cataract surgically.

Oculodermal melanosis, also known as nevus of Ota, is a painless condition involving mesodermal melanocytes in the ophthalmic and maxillary trigeminal nerve distributions, causing hyperpigmentation of the eye and its surroundings. This hyperpigmentation appears as bluish or brownish pigmentation on the eyes, facial skin, and eyelids [5]. The prevalence of the finding varies and affects 0.03–0.1% of the population and depending on the ethnicity and race. While nevus of Ota usually manifests at birth, it can also emerge during puberty or pregnancy [5]. It is more prevalent in females, with a 5:1 ratio, and is commonly observed in individuals of Asian and African descent. No specific risk factors are known for nevus of Ota [4].

Scleral involvement occurs in over two-thirds of cases and is linked to an elevated risk of glaucoma development due to melanocyte invasion obstructing aqueous drainage [6].

Histopathologically, affected tissues exhibit excessive dendritic melanocytes, which can potentially lead to malignant melanoma development [7]. About 1 in 400 patients may develop choroidal melanoma in the affected eye, with risk factors including related cutaneous or palatal melanocytosis, scleral involvement in specific quadrants, and iris melanocytosis [8].

The definitive cause of nevus of Ota remains unclear, with several hypotheses proposed. One of them suggests that it is a result of a failure in melanocyte migration from neural crest cells to their normal location in the basal layer of the epidermis [9]. Other potential causes include past radiation exposure and hormonal factors.

Nevus of Ota is generally benign, carrying a favorable prognosis in ophthalmic and dermatologic terms. Treatment is often unnecessary unless managing increased intraocular pressure, malignant transformation of periocular skin lesions or for cosmetic purposes. Regular screenings by an ophthalmologist and dermatologist are recommended for glaucoma and malignant melanoma. Of note, a study by Shields et al. found a twofold risk of metastasis in uveal melanoma associated with nevus of Ota compared to those without melanocytosis [10]. Implementing a new definition of red, green, and blue channels can enhance the diagnosis and monitoring of these findings, thereby improving patient treatment [11].

To the best of our knowledge, this is the first report of Wilson's disease-associated ocular findings together with the presence of nevus of Ota in the same patient, and there is no evident genetic link between these conditions. According to the calculation of the prevalence of each disease separately, the probability that someone can suffer from these two diseases together is around 1 in 30 million. Currently, the patient is under follow-up at the pediatric gastroenterology and ophthalmology clinic with stable ocular findings.

At her last checkup, her liver enzymes have returned to near normal values, although her ceruloplasmin and urinary electrolytes are still abnormal, indicating her partial compliance to treatment. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material at https://doi.org/10.1159/000541119.

Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines (an official Helsinki Committee document of the hospital is attached hereto). Written informed consent was obtained from the parent of the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

A.N. and I.H.: conceptualization and writing – original draft. C.T.O. and R.S.: genetics. J.P. and M.K.: supervision and writing – review and editing.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

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