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A CASE REPORT: A 11-YEARS OLD FEMALE WITH RETINITIS PIGMENTOSA

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Abstract

Retinitis pigmentosa is a hereditary retinal neurodegenerative disease with the classic presentation of night blindness (nyctalopia), with gradual degeneration of vision until blindness). This study aims to analyze a clinical case of retinitis pigmentosa (RP) in an 11-year-old female with primary symptoms of nyctalopia, progressing visual impairment, and distinctive retinal pigmentation changes identified during funduscopy. RP is a hereditary retinal degenerative condition that commonly presents as night blindness, progressing to severe vision loss or blindness. In this case, a comprehensive physical and ophthalmic examination revealed decreased visual acuity, refractive errors, and vascular attenuation, characteristic of RP, without systemic abnormalities or familial history, classifying it as a sporadic case. Given that RP is typically inherited in autosomal dominant, autosomal recessive, or X-linked patterns, sporadic cases are rarer and require careful diagnosis. This study underscores the importance of thorough ocular assessments, particularly fundus examinations, in identifying early retinal changes in RP, as well as the challenges in diagnosis without a family history. The findings emphasize that, while RP is primarily ocular, extraocular manifestations in syndromic forms also exist. RP remains a major cause of blindness worldwide, and while emerging treatments—such as gene therapy and retinal implants—offer new potential, a standardized management protocol is yet to be established. This study advocates for continued research into targeted therapeutic options to improve outcomes and quality of life for RP patients, and highlights the need for early diagnosis and ongoing monitoring to manage disease progression effectively.

Keywords: Retinitis Pigmentosa, Inherited retinal dystrophy, Night Blindness

Introduction

Retinitis pigmentosa is a hereditary retinal neurodegenerative disease, which is the most common type of inherited retinal dystrophy (IRD). This disease is characterized by progressive retinitis pigmentosa epithelium (RPE) atrophy and photoreceptors cell death (Desai & Alibhai, 2018; Bhattacharya & Chakarova, 2013). It is one of the most common cause of blindness worldwide with approximately 1 : 4.000 people affected by this disease worldwide (Fahim et al., 2023). The initial presentation of the disease includes night blindness (nyctalopia), with gradual degeneration of vision until blindness (Daiger et al., 2013). RP is a genetically heterogeneous disease in which more than 50 different genes have to be found related to RP (Bhattacharya & Chakarova, 2018; Perez-Lanzon et al., 2018) The typical presentation of RP is bilateral and symmetrical and usually begins to manifest in adolescence. However, there are also other varieties of RP cases manifest in the 30's as late as 50 years old depending on the genotype (Verbakel et al., 2018; Hamel, 2006).

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Proper diagnosis of RP requires comprehensive history taking, genetic testing, genetic genealogy, and ophthalmic evaluation. Clinical manifestations include classic triad can be observed through ophthalmoscopy (Raharja, 2022). The main goal of RP management is to prevent further progression of photoreceptor degeneration and manage complications. There are also emerging treatment options for RP patients, targeting genetic causing disease. This advancement also provides additional options for patients (Wu et al., 2023 Ludwig et al., 2019).

This study aims to analyze a clinical case of retinitis pigmentosa (RP) in an 11-year-old female with primary symptoms of nyctalopia, progressing visual impairment, and distinctive retinal pigmentation changes identified during funduscopy.

Case Report

An 11 year old female patient presented to the eye clinic at Bhayangkara Hospital Semarang with chief complaints of blurry vision in dark environments and long distance reading. About a month ago, according to the maternal parent's recollection, she began to become more aware of the patient's behavioral changes. She complained that the patient tends to bump into objects in front of her and fumble objects with her feet. These complaints were only noticed in dark environment settings, not in bright environment settings. Due to these concerns, her mother brought the patient to the hospital. Diabetes mellitus, head trauma, or similar eye condition in the family were previously denied by her mother. Previous medical history of any kind of surgery, congenital or familial eye abnormalities were also denied. Patient’s social history tends to be picky toward her food, and doesn't like eating vegetables.

Physical examination found blood pressure 70/50 mmHg, respiratory rate 18x/minute, with a regular pulse 80x/minutes, and body temperature 36,5°C. Based on systematic anamnesis, there were no abnormalities found on the heart, lungs, abdomen, urogenital, neurological, and extremintal. Refractive examination for far vision correction showed that the visual acuity of the right eye was 0.5 PH 0.6 and visual acuity of the left eye was 0.8 PH -. Best corrected vision of the right eye was 0.8 with S-0,75 Lens and the left eye did not improve.

Eye movement examination revealed normal results with good eye movement in all directions. Confrontational examination for visual field testing also revealed no visual loss. Anterior examination using a slit lamp, the results were within normal limits. Fundus examination using indirect ophthalmoscopy showed on the right and left eye with clear media images, well defined round optic disc, physiological cup to disc ratio, physiological artery to venous ratio, fundus reflex (+), macula reflex (+), attenuation of blood vessel, and found Hyperpigmentation spots in the form of bone spicules peripherally indicates retinitis pigmentosa. Intraocular pressure examination revealed right eye and left eye were 16 mmHg and 15 mmHg respectively.

The patient was diagnosed with bilateral retinitis pigmentosa with OD myopia and OD astigmatism. The management of this patient was educated about the disease, symptoms, risk factors, prognosis, and prevention for complications. The patients was also educated to reduce sunlight exposure. Non-pharmacological management was prescription of corrective glasses for myopia and astigmatism.

Results and Discussion

Retinitis pigmentosa is a hereditary retinal neurodegenerative disease, which is the most common type of inherited retinal dystrophy (IRD). RP is a genetically heterogeneous disease which encompasses wide variations genetic mutations with

reportedly more than 50 different genes.(2,5) RP can be inherited in autosomal dominant (adRP,15–25%), autosomal recessive (arRP, 5–20%), and X-linked RP(x-RP, 10–15%) (Liu et al., 2022). However, the remaining cases with no family history or inheritance are termed as sporadic case. In general, patients with X-linked RP exhibit more severe disease phenotypes than those with arRP, whereas patients with adRP have the best prognosis with preserved central vision (Liu et al., 2022).

The prevalence of RP worldwide was approximately 1 : 4.000. However, this prevalence also varies depending on the geographic location. In the US and Europe, its reported the prevalance of RP was 1 : 3.500-4.000 and in study in Singapore reported six cases for every 10.000 above 40 years old adults in multi-ethnicity Asian Population (Teo et al., 2022)

As a genetically heterogeneous disease, the pathogenesis of retinitis pigmentosa are involved with multiple genetically directed mechanisms which leads to progressive photoreceptors death and RPE atrophy. Rods or cones photoreceptors cells both can be the cause retinitis pigmentosa (Newton & Megaw, 2020). However, most cases of RP are caused by defects in rods specific mutation. Initially, the genetic mutation cause primary degeneration of rod cells which responsible for the initial presentation of RP. Then, The primary degeneration of rods cells can cause degeneration of cone receptors as well through oxidative stress, impaired glucose transport into cone cells, and activation of microglial cells causing inflammation. Phototoxic mechanism also can accelerate degeneration of rod and cone photoreceptors, including alternation in retinol metabolism, acceleration of oxygen consumption, and increasing of light exposure (Liu et al., 2022; Campochiaro et al., 2018; Cross et al., 2022).

The classic symptoms of RP are initially starting by nyctalopia (reduced night vision), difficulty adapting to changes in light or dim light, followed by progressive loss of vision and gradually narrowing visual field in a concentric pattern, until total blindness (Kamde & Anjankar, 2023). In this case, the most prominent of RP symptoms are nyctalopia were complained about by patient's mother approximately a month ago. Most RP cases also begin in adolescence and progressively more apparent. There are also other varieties of RP cases manifest in the 30's as late as 50 years old depend on the genotype (Verbakel et al., 2018; Hamel, 2006).

The clinical manifestation appearance in RP based on ophthalmoscopy examination are the presence of bone spicule pigmentation, vascular attenuation, and optic disc "waxy" pallor (Tsang, 2018). The exact mechanism or cause for pigmentation and attenuation were not fully understood yet but there are some suggestions for the findings. Pigmentation of retina are due to melanin pigment in retinal pigment epithelial cells, which detach and migrate to peripheral location in the retina. A study by Giansanti *et al.,* suggests vascular attenuation and rarefaction in RP were due to death of large numbers of photoreceptors causing decrease in metabolic demand or alternation in choroid (Giansanti et al., 2022). Formation of glial cells covers optic disc and increases reflectivity making waxy pallor appearance (Lu et al., 2021).

Other than ocular symptoms, Approximately 20-30% of RP also reported having extra-ocular abnormalities (Verbakel et al., 2018) This manifestation categorized RP into two categories, Syndromic or Non-syndromic RP, which based on occurance systemic symptoms or not (Newton & Megaw, 2020). Usher syndrome is the most common form of syndromic RP, which is accompanied by neurosensory hearing loss and vestibular dysfunction (Tatour & Ben-Yosef, 2022). Bardet-Biedl syndrome also is another well recognized syndromic RP with more complex presentation. Patients with Bardet-Biedl

syndrome reported with mental impairment, obesity, polydactyly, renal dysfunction, and obesity (Melluso et al., 2023).

To establish diagnosis, patients with suspect RP are required to undergo a series of ophthalmological examinations to ascertain the presence, severity, and progression of the disease. A complete history taking and genetic genealogy of the family should be taken to construct a detailed pedigree of history to determine the genetic involvement in the disease and variant of RP. Additionally, a review of possible infectious disease or toxin which can help to exclude possible disease. Ophthalmologic examination is needed, including fundoscopy and retinal examination to diagnose and determine the progression of disease (Raharja, 2022). In this patient, ocular symptoms and early age were found to be fitting the profile of inherited retinal dystrophy (IRDs) with progressive nyctalopia in both eyes. History of infectious disease or toxin also denied in this patient.

Funduscopic examination, revealing the "classic triad" as mentioned before which is fundamental in diagnosing RP. Visual acuity assessment serves as a standard measure for evaluating visual function, with better vision preservation in the early stages and subsequent vision deterioration in advanced stages of RP. Visual field assessment through kinetic perimetry function to determine peripheral vision loss (Chang, 2023). Color vision assessment such as ishihara test is essential in detecting presence and progression of dyschromatopsia. Dyschromatopsia in RP is often observed in advanced stage of RP due to degression of cone receptor involvement (Hamel, 2006). Both visual field and dyschromatopsia were not reported in this case which indicate an early stage of disease. Moreover, Electroretinograms (ERGs) aid in detecting early RP, quantifying the severity of the disease and also tracking the progression. Electroretinograms evaluate the entire retina and identify anomalies before the clinical manifestation such as nyctalopia and fundoscopic abnormalities (Zhang, 2016).

Recent years have witnessed significant progress in understanding the genetic causes of retinitis pigmentosa (RP) and the development of novel treatments. While the focus is on targeting specific disease-causing genes and preventing cone photoreceptor degeneration, a standardized treatment for RP is still lacking. In current practices, Vitamin A or DHA, alone or combine, has been prescribed for RP patients to supposedly stop the progressive degeneration of retinal photoreceptors (Fahim, 2018). Administration age adjusted (5.000-15.00 IU/d) of Vitamin A has shown to delay progression of RP in children which claimed by Berson et al. (2018). However, a study conducted by Schwartz et al has concluded no clear evidence for the benefit for vitamin A or DHA, or both for RP patients (Kamde & Anjankar, 2023). Hence, The effectiveness of treatments involving vitamin A or DHA, alone or combined, remains uncertain. In our case, we educated patients regarding the eye condition and recommended to consumpt food high in Vitamin A content.

Six current treatment strategies for RP include neuroprotective agents, gene therapy, optogenetics, stem cell treatment, retinal prosthesis, and photochemical switch (Ludwig et al., 2019). In early stages, gene therapy for replacing disease-causing genes, and optogenetics or photosensitive protein before advanced retinal degeneration (Newton, 2020). Cell replacement and retinal prosthesis implantation offer further options, but their success diminishes in later stages. In addressing RP complications, cataracts are treated with phacoemulsification and intraocular lens implantation, while macular edema is managed using carbonic anhydrase inhibitors like acetazolamide sodium (Liu et al., 2022; Cross et al., 2022). A comprehensive, multifaceted approach is crucial in managing RP and its associated complications.

Conclusion

In conclusion, retinitis pigmentosa (RP) stands as a complex and genetically heterogeneous hereditary retinal neurodegenerative disease, encompassing a spectrum of manifestations. With over 50 identified genes contributing to its genetic diversity, RP can be inherited in autosomal dominant, autosomal recessive, or X-linked patterns. The disease, prevalent worldwide but with varying incidence, leads to progressive photoreceptor death and retinal pigment epithelium atrophy. Clinical manifestations include a classic triad observed through ophthalmoscopy, often accompanied by extra-ocular abnormalities categorizing RP into syndromic or non-syndromic forms. Diagnosis involves detailed ophthalmological examinations, genetic analysis, and consideration of familial history to ascertain the presence, severity, and progression of the disease. Prognosis of RP patients is dependent on the initial symptoms and pattern of inheritance. Current treatments, including Vitamin A supplementation and emerging strategies like gene therapy and optogenetics. However, the standardized approach remains unclear. This comprehensive understanding underscores the need for continued research and a multifaceted approach to manage RP and its associated complications effectively.

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