

Case Report

A rare presentation of autosomal recessive proximal renal tubular acidosis

Aishwarya Ajit Godbole¹, Farhad Fareedbhai Mansuri¹, Avantika Netraprakash Gaur¹, Purvi Raj Bhagat²

¹Department of Ophthalmology, M&J Western Regional Institute of Ophthalmology, Civil Hospital, ²Glaucoma Clinic M&J Western Regional Institute of Ophthalmology, Ahmedabad, Gujarat, India.

ABSTRACT

Proximal renal tubular acidosis (pRTA) is characterised by an inability of the kidneys to reabsorb bicarbonate from the proximal convoluted tubule leading to urinary loss of bicarbonate ions causing metabolic acidosis. It can present as an isolated pRTA or be associated with Fanconi syndrome. Isolated inherited pRTA is exceedingly rare. The inheritance can be autosomal dominant, autosomal recessive (AR), or sporadic. The AR form is linked to a SLC4A4 (NBCe1) mutation and is associated with glaucoma, cataract, band keratopathy, mental and growth retardation requiring lifelong alkali therapy and ocular care. The prognosis is good although extra-renal symptoms may persist and ocular abnormalities may progress with age. Here, we report a rare case of congenital glaucoma associated with cataracts, band keratopathy, growth retardation, and mental retardation in a young female having isolated AR pRTA with SLC4A4 gene mutation.

Keywords: Proximal renal tubular acidosis, Autosomal recessive, SLC4A4, Glaucoma, Band Keratopathy, Metabolic acidosis

INTRODUCTION

Proximal renal tubular acidosis (pRTA) is a disease affecting the proximal tubule function resulting in metabolic acidosis. Inherited isolated pRTA is rare and the age of presentation is variable. The inherited isolated form is more commonly autosomal recessive (AR), with the SLC4A4 gene encoding basolateral sodium-bicarbonate cotransporter (NBCe1). Its mutation leads to reduced activity and/or trafficking, thus disrupting the normal bicarbonate (HCO₃⁻) reabsorption in proximal tubules, leading to pRTA, severe growth retardation, mental retardation, migraine, calcification of basal ganglia, and ocular abnormalities such as glaucoma, band keratopathy, and cataracts.^[1-4] NBCe1 found on corneal endothelium transports sodium (Na⁺) and HCO₃⁻ from the corneal stroma into the aqueous humour, defects which would lead to increased stromal HCO₃⁻ facilitating calcium deposition and band-shaped keratopathy formation. It is also thought to play a similar role in the maintenance of lens transparency explaining cataract formation, nevertheless, the role of NBCe1 in the pathogenesis of glaucoma remains unclear.^[5] Ocular abnormalities as seen in this patient are typical of inherited isolated pRTA and can prove to be diagnostic clinchers for a disease as rare. Inherited pRTA requires lifelong bicarbonate

replacement therapy in large doses. A mixture of sodium and potassium (bicarbonate or citrate) salts may be supplemented to prevent hypokalemia. Thiazide diuretics can also be given to enhance HCO₃⁻ reabsorption.^[6] Ocular manifestations such as band-shaped keratopathy can be managed by giving topical ethylene diamine tetra acetic acid (EDTA) eye drops and glaucoma can be managed medically by the use of topical intraocular pressure (IOP) lowering drugs and surgically by methods such as trabeculectomy and goniotomy. With proper treatment, the prognosis of acidosis is good, although extra-renal symptoms do not resolve with alkali treatment and ocular abnormalities may show progression with age.^[7]

CASE REPORT

An 11-year-old female was clinically diagnosed to have inherited isolated pRTA and presented to our tertiary care centre in March 2023 for ophthalmic evaluation. The patient had come with the genetic study report which confirmed the presence of c.1170G>C; p.R390S of SLC4A4 gene in homozygous state in AR form [Figure 1].

On evaluation, the visual acuity was found to be 6/60, and counting fingers 2 m in the right and the left eye, respectively,

*Corresponding author: Aishwarya Ajit Godbole, Department of Ophthalmology, M&J Western Regional Institute of Ophthalmology, Civil Hospital, Ahmedabad, Gujarat, India. aishwaryagodbole7@gmail.com

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DISCUSSION

Inherited pRTA is rare and is commonly AR. The SLC4A4 gene encodes three basolateral sodium-bicarbonate cotransporter (NBCe1) variants: NBCe1-A, NBCe1-B, and NBCe1-C.^[6] NBCe1-A mutation leads to pRTA and ocular abnormalities such as band keratopathy, increased corneal opacity, glaucoma, or at least elevated IOP and cataracts.^[7-9] NBCe1-B mutation leads to intestinal abnormalities and NBCe1-C mutation leads to neurological abnormalities.^[10]

The management of pRTA is alkali therapy to treat acidosis. A Jewish-Georgian woman having normal intelligence, short stature, deformed teeth, and no perception of light had a history of being diagnosed with bilateral glaucoma in early childhood for which she was treated with oral acetazolamide from the age of 6 years and had undergone several operative procedures for control of the high IOP. The patient had developed bilateral cataracts and band keratopathy over the coming years and lost all her vision by the age of 16 years. Metabolic acidosis was first noted when the patient was 33 years of age and she tested positive for a novel mutation of NBCe1 (SLC4A4) with pRTA.^[8] Demirci *et al.* identified a novel, homozygous, missense SLC4A4 mutation in 27 years male Caucasian having pRTA, short stature, enamel hypoplasia, migraine, transient hemiparesis attacks, ataxia, and bilateral ocular manifestations such as cataracts, glaucoma, and band keratopathy.^[5] The patient first had disturbances in his vision during his kindergarten years but his eye examination then was completely normal. He later developed progressive myopia, corneal fine granules, and minute lenticular snowflake-type opacities. Gradually, cataracts and band-shaped keratopathy became more evident and he was also diagnosed with bilateral open-angle glaucoma which was initially treated with topical medication but eventually required surgical interventions. EDTA chelation was also advised for the band keratopathy but eventually, the patient lost his eyesight by the age of 27 years.

In both the above cases, the presenting features were ocular abnormalities that progressed with age. The glaucoma was initially treated medically but eventually, surgical treatment was required, despite which both the patients lost their eyesight. This makes counselling of such patients with regard to the visual prognosis of paramount importance.

In our case too, the patient first presented with ocular symptoms, and a similar pattern of progression of ocular symptoms was seen in our patient. Glaucoma in this patient was managed medically as the parents refused any surgical intervention when the visual prognosis, need for multiple surgeries and risk of general anaesthesia was explained. Considering the morbidity of this condition, it is imperative to have regular long-term follow-ups, monitoring of systemic parameters, and aggressive counselling of parents.

CONCLUSION

Ocular manifestations such as glaucoma, band keratopathy, and cataracts may be the presenting features of rare familial disorders such as inherited AR pRTA. Prompt recognition of ocular and systemic features can lead to early diagnosis and can provide an opportunity for efficient treatment. A multidisciplinary approach and parental counselling are also vital for overall management.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Conflicts of interest

Dr.Purvi Raj Bhagat is on the editorial board of the Journal.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The author(s) confirms that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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