

# Bilateral congenital membranous cataracts due to Glucosaminyl (N-Acetyl) Transferase 2 (GCNT2) mutation: Life-saving genetic analysis

Snehal Ganatra, Ramesh Kekunnaya,  
Virender Sachdeva

**Key words:** Cancer, GCNT-2, genetics, membranous cataract

Cataract is one of the most important causes of treatable childhood blindness.<sup>[1]</sup> Common etiologies include trauma, hereditary, intrauterine infections, maternal malnutrition, metabolic, and atopic dermatitis. Despite many possible etiologies, morphological appearance of cataract with or without associated systemic features gives clues to the underlying etiology.<sup>[2]</sup> In particular, membranous cataracts might be observed in patients with intrauterine infections, Hallermann-Streiff-François syndrome and Lowe syndrome.<sup>[3]</sup> In patients with suspected inherited cataracts, genetic markers can be helpful in identifying some forms of cataract associated with a specific mutation. We demonstrate a case of two siblings who presented with congenital membranous cataract. The morphology of the cataract initially raised suspicion of intrauterine infection, which was then ruled out through appropriate investigations.

A two-week-old female child born of non-consanguineous marriage was brought to our institute by her parents with chief complaints of white reflex in both eyes noticed at birth. Antenatal, perinatal and postnatal history was not significant. The child was born through full-term, normal delivery. On examination, the child had bilateral membranous cataract. General physical examination was normal and screening for infections like toxoplasmosis, rubella, cytomegalovirus and herpes simplex was negative. B-Scan ultrasonography (B-scan USG) was normal in both eyes. Ophthalmic evaluation of

parents was normal. Examination under anesthesia of the child was performed. She had microcornea, non-dilating pupil with posterior synechiae and white membranous cataract in both eyes [Fig. 1]. Axial length was 15 mm in both eyes. The patient underwent an uneventful bilateral lens aspiration with primary posterior capsulotomy and anterior vitrectomy (LA + PPC + AV) in the right eye (RE) followed by the left eye (LE). Intraocular lens (IOL) implantation was deferred in view of microcornea. Post-operatively, cycloplegic refraction was +23DSph in the right eye and +24DSph with -1.5DCyl @ 180 degrees in the left eye. Patient was prescribed contact lenses of appropriate power.

Genetic analysis revealed positive Glucosaminyl (N-Acetyl) Transferase 2 (GCNT2) gene mutation variant c. 1154G > A on exon 3. As this mutation has autosomal recessive inheritance, the parents were informed that the risk in the second child having the same condition would be 25%. A few years later, the second child was born with bilateral congenital membranous cataract along with microcornea. Genetic analysis revealed positive GCNT2 mutation. The child underwent uneventful LA + PPC + AV in both eyes. The child too was prescribed contact lens of appropriate power. Both the children are being followed up regularly. The older sibling, currently eight years old, has a best corrected visual acuity (BCVA) 20/40 in the RE and 20/50 in the LE. The younger sibling, currently seven months old, has a post cycloplegic refraction of +21.50D in RE and +22.0D in LE and is comfortable using contact lenses.

## Discussion

Glucosaminyl (N-acetyl) Transferase 2 (GCNT2) was originally named IGnT (I Gene). It has three tissue-specific mRNA isoforms: GCNT2A, GCNT2B, and GCNT2C (IGnTC).<sup>[4]</sup> This enzyme is important in the process of glycosylation which is a post-translational modification of proteins, glycolipids and proteoglycans. The function of GCNT2 is to branch poly-N-lactosamine chains by adding an N-acetylglucosaminyl residue via  $\beta$ -1-6 linkage to a galactosyl residue.<sup>[4]</sup> These glycolipids are expressed in red blood cells and also on the surface of most human cells, crystalline lens, milk, saliva, plasma, urine, and ovarian cyst fluid.<sup>[4]</sup> GCNT2 activity plays an essential role in lens development and hence the missense mutation in GCNT2 gene is responsible for development of congenital cataract.<sup>[4]</sup> Patients with GCNT2 mutation are reported to have non-syndromic congenital cataract.<sup>[5]</sup> Further, the morphology of cataract in patients with GCNT2 mutations is nuclear cataract.<sup>[6]</sup> Patients with mutations in GCNT2 genes might also have the rare adult i blood group.<sup>[6]</sup> The i and I antigens are carbohydrate structures on the human red blood cells (RBCs). Adult human RBCs fully express I antigens and few i antigens,

Access this article online	
Quick Response Code:	Website: www.ijo.in
	DOI: 10.4103/ijo.IJO_2271_21

Department of Pediatric Ophthalmology, Strabismus and Neuro-Ophthalmology, L.V. Prasad Eye Institute, Andhra Pradesh, India

**Correspondence to:** Dr. Virender Sachdeva, Consultant, Pediatric Ophthalmology, Strabismus and Neuro-Ophthalmology, Child Sight Institute, Nimmagadda Prasad Children's Eye Care Centre, L V Prasad Eye Institute (LVPEI), GMR Varalakshmi Campus, Visakhapatnam, Andhra Pradesh - 530 040, India. E-mail: vsachdeva@lvpei.org

Received: 31-Aug-2021

Revision: 25-Nov-2021

Accepted: 18-Jan-2022

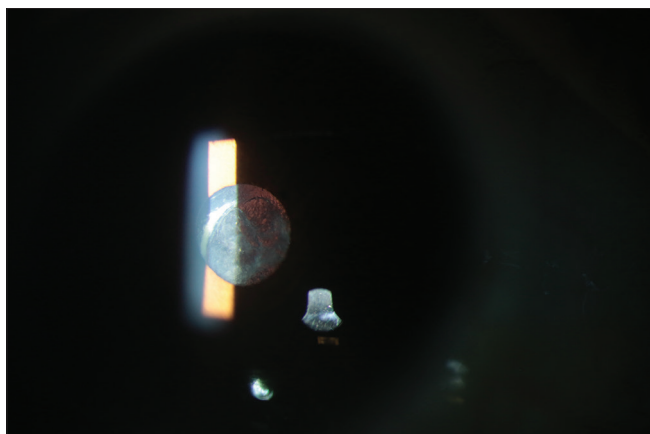
Published: 30-Jun-2022

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**For reprints contact:** WKHLRPMedknow\_reprints@wolterskluwer.com

**Cite this article as:** Ganatra S, Kekunnaya R, Sachdeva V. Bilateral congenital membranous cataracts due to Glucosaminyl (N-Acetyl) Transferase 2 (GCNT2) mutation: Life-saving genetic analysis. Indian J Ophthalmol 2022;70:2622-3.





**Figure 1:** Representative slit lamp image of a child with membranous cataract

which predominate in fetal and neonatal RBCs.<sup>[7]</sup> The rare adult *i* phenotype results from lack of I-branching transferase activity and has been associated with congenital cataracts in Asians.<sup>[8]</sup>

In our case, both siblings with congenital membranous cataract had a homozygous missense variation in exon 3 of the GCNT2 gene (chr6:g. 10626785G > A; Depth: 166x) that resulted in the amino acid substitution of Histidine for Arginine at codon 385. Increased GCNT2 expression is a common feature in metastatic breast cancer, prostate cancer, colon cancer, and adrenal adenomas.<sup>[9]</sup> In breast cancer cell lines, high GCNT2 mRNA expression increases the ability of cells to detach and migrate, endothelial cell adhesion, invasion, and pulmonary metastasis. Similar findings are reported in prostate and colon cancer.<sup>[9]</sup> Hypomethylation of GCNT2 has also been implicated in adrenal adenomas.<sup>[9]</sup> Since GCNT2 mutation predisposes the patient to other epithelial cancers, it is important to make the parents aware of the possibility of breast, prostate, and colon cancers which can help in early and life-saving diagnosis in the future.

This case highlights the importance of genetic analysis in patients with congenital cataract. To our knowledge, the GCNT2 mutation with *I* blood group phenotype is uncommon and has not been reported in the Indian population. Morphology of the cataract may not always help us in diagnosis of the cause of the cataract, just like in our case where the initial impression was membranous cataract secondary to intrauterine rubella infection. However, different causes of cataract can have overlapping morphologies. This

is where genetic analysis in patients with congenital cataract can be useful and prove genetic basis which can be useful in monitoring other manifestations in the future. We would like to reiterate to consider possible GCNT2 mutations in patients with membranous cataracts and monitoring the children for other expressions.

#### Author's contribution

All persons designated as authors qualify for authorship, and all those who qualify are listed. Each author has participated sufficiently in the work to take public responsibility for appropriate portions of the content.

#### Financial support and sponsorship

Nil.

#### Conflicts of interest

There are no conflicts of interest.

## References

1. Foster A, Gilbert C, Rahi J. Epidemiology of cataract in childhood: A global perspective. *J Cataract Refract Surg* 1997;23(Suppl 1):601-4.
2. Singh VM, Badakere A, Patil-Chhablani P, Kekunnaya R. Profile of congenital cataract in the first year of life from a tertiary care center in South India-A modern series. *Indian J Ophthalmol* 2021;69:932-6.
3. Pasyanthi B, Mendonca T, Sachdeva V, Kekunnaya R. Ophthalmologic manifestations of Hallermann-Streiff-Francois syndrome: Report of four cases. *Eye (Lond)* 2016;30:1268-71.
4. Pras E, Raz J, Yahalom V, Frydman M, Garzozzi HJ, Pras E, *et al.* A nonsense mutation in the glucosaminyl (N-acetyl) transferase 2 gene (GCNT2): Association with autosomal recessive congenital cataracts. *Invest Ophthalmol Vis Sci* 2004;45:1940-5.
5. Li J, Leng Y, Han S, Yan L, Lu C, Luo Y, *et al.* Clinical and genetic characteristics of Chinese patients with familial or sporadic pediatric cataract. *Orphanet J Rare Dis* 2018;13:94.
6. Irum B, Khan SY, Ali M, Daud M, Kabir F, Rauf B, *et al.* Deletion at the GCNT2 locus causes autosomal recessive congenital cataracts. *PLoS One* 2016;11:e0167562.
7. Yu LC, Twu YC, Chou ML, Reid ME, Gray AR, Moulds JM, *et al.* The molecular genetics of the human *I* locus and molecular background explain the partial association of the adult *i* phenotype with congenital cataracts. *Blood* 2003;101:2081-8.
8. Yamaguchi H, Okubo Y, Tanaka M. A note on possible close linkage between the *Ii* blood locus and a congenital cataract locus. *Proc Jpn Acad* 1972;48:625-8.
9. Cooling L. An update on the *I* blood group system. *Immunohematology* 2019;35:85-90.



