Commentary: Genetic testing in cases of pediatric cataract

Pediatric cataract is a common cause of childhood blindness. In developing countries like India, it is 10 times more prevalent than in developed countries, where the prevalence is 2.03–2.49 per 10,000 children.[1,2] Early diagnosis and timely intervention in pediatric cataract cases improve the visual outcomes significantly.[3,4] Identifying the etiology of cataracts in children is also very important for counseling and preventive public programs. The most common etiology for congenital cataracts in India is Toxoplasma gondii, other agents, rubella, cytomegalovirus (CMV), and herpes simplex virus (HSV) (TORCH) infections (33.4%), followed by familial causes (18.3%) and developmental anomalies (10.1%).[5-7] Congenital cataract has a lot of phenotypic heterogeneity also, with various genetic and environmental causes to consider. Genetic causes are also responsible for one-fifth of cases of unilateral cataracts and majority of bilateral cataracts in children. Autosomal dominant inheritance is the most common pattern of inheritance, followed by autosomal recessive mode in such cases. The morphology of

a cataract can often guide us toward the etiology of the cataract. Apart from detailed history, appropriate investigations should be done in all congenital cataract cases, including complete blood examination, serum calcium and phosphorus, blood sugar levels, urine for reducing sugars, and TORCH titers. If all these investigations are inconclusive of etiology, genetic testing becomes essential. Some mutations may be associated with some peculiar morphologies. The case published in this issue[8] highlights how morphology can sometimes be misleading and how crucial genetic testing is in such cases of pediatric cataracts. The authors report two cases of membranous cataracts in siblings with homozygous missense mutation in exon 3 of glucosaminyl (*N*-acetyl) transferase (*GCNT2*) gene.

In particular, a membranous cataract is a congenital disorder in which the lens is absorbed and flattened with no or little fibers. A membranous cataract is usually diagnosed during late childhood, but can also be seen in early childhood. Patients with a familial nature of cataract associated with Hallermann–Streiff–Francois syndrome, Lowe's syndrome, and few inheritable mutations reported like *LIM2* (autosomal dominant)[9] and *GCNT2* (autosomal recessive) mutation,[10,11] as well as patients with intrauterine TORCH infections can have membranous cataracts.

Mutations in the genes encoding lens proteins can directly cause cataracts. Although most of these are inherited as autosomal dominant, five loci have been linked to autosomal recessive inheritance. A recent addition to this literature is the *GCNT2* gene that highlights the association between autosomal recessive congenital cataract and the rare adult i blood group phenotype. Further, three different transcript forms, designated as GCNT2A, -B, and -C, have been described of the *GCNT2* gene. Mutations in exon 1 of *GCNT2B* selectively inactivate the transcript expressed in the lens, resulting in congenital cataracts without the i blood phenotype. The case reported here has mutations in exon 3, and hence both reticulocytes and lens epithelial cells are likely to be affected. Altered protein glycosylation is a common feature of cancers, and hence, *GCNT2* could be a marker of systemic cancers.[12]

Accurate pediatric cataract diagnosis is crucial for patients and their families as it facilitates genetic counseling. There is a lot of variability in the investigative pathways of pediatric cataract patients. Hereditary cases in our country might be underestimated because of inconsistent testing. Hence, an attempt should be made to investigate the etiology of congenital cataracts thoroughly with the efficient use of supportive genetic tests. Not only does it establish the etiology of cataract, but also it guides us to approach other associated and undiagnosed systemic conditions.

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References

1. Yi J, Yun J, Li ZK, Xu CT, Pan BR. Epidemiology and molecular genetics of congenital cataracts. Int J Ophthalmol 2011;4:422-32.
2. Haargaard B, Wohlfahrt J, Fledelius HC, Rosenberg T, Melbye M. A nationwide Danish study of 1027 cases of congenital/infantile cataracts: Etiological and clinical classifications. Ophthalmology 2004;111:2292-8.
3. Yangzes S, Kaur S, Gupta PC, Sharma M, Jinagal J, Singh J, *et al*. Intraocular lens implantation in children with unilateral congenital cataract in the first 4 years of life. Eur J Ophthalmol 2019;29:304-8.
4. Sukhija J, Kaur S, Ram J. Outcome of primary intraocular lens implantation in infants: Complications and rates of additional surgery. J Cataract Refract Surg 2016;42:1060-5.
5. Eckstein M, Vijayalakshmi P, Killedar M, Gilbert C, Foster A. Aetiology of childhood cataract in south India. Br J Ophthalmol 1996;80:628-32.
6. Jain I, Pillay P, Gangwar D, Kaul V. Congenital cataract: Etiology and morphology. J Pediatr Ophthalmol Strabismus 1983;20:238-42.
7. 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.
8. 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.
9. Pei R, Liang PF, Ye W, Li J, Ma JY, Zhou J. A novel mutation of LIM2 causes autosomal dominant membranous cataract in a Chinese family. Int J Ophthalmol 2020;13:1512-20.
10. Happ H, Weh E, Costakos D, Reis LM, Semina EV. Case report of homozygous deletion involving the first coding exons of GCNT2 isoforms A and B and part of the upstream region of TFAP2A in congenital cataract. BMC Med Genet 2016;17:64.
11. Pras E, Raz J, Yahalom V, Frydman M, Garzozi 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.
12. Sweeney JG, Liang J, Antonopoulos A, Giovannone N, Kang S, Mondala TS, *et al*. Loss of GCNT2/I-branched glycans enhances melanoma growth and survival. Nat Commun 2018;9:3368.

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