Bilateral *Pseudomonas aeruginosa* keratitis as presenting feature in an infant of cystic fibrosis

Meena Lakshmipathy, Manokamna Agarwal, Mamta Agarwal, Natraj Palanaiappan[1]

Key words: Bilateral keratitis, cystic fibrosis, infant, pediatric penetrating keratoplasty, *Pseudomonas keratitis*

Cystic fibrosis (CF) is caused by mutations in chromosome 7 that encodes the *CFTR* (cystic fibrosis trans membrane conductance regulator) gene, a chloride and bicarbonate ion transport channel responsible for maintaining osmotic balance across multiple epithelial surfaces in body.[1] This leads to multiple issues. First, xerophthalmia due to involvement of lacrimal gland. Second, vitamin A deficiency due to pancreatic insufficiency leading to keratomalacia. And third, increased susceptibility to *Pseudomonas aeruginosa* infection.

We report an infant with bilateral xerophthalmia, keratomalacia and pseudomonas keratitis as a presentation feature, which was later diagnosed as CF.

A two-month-old female infant, first born to second-degree consanguineous parents with uneventful neonatal period presented with right eye swelling and discharge for four days. No history of ocular trauma was noted. On torch light examination, right eye had perforated corneal ulcer with a pseudocornea and iris prolapse. Left eye was noted to be normal. An urgent therapeutic penetrating keratoplasty was planned for the right eye, but on systemic examination by pediatrician, baby appeared malnourished weighing 2.5 kg, was icteric, pale with firm hepatomegaly of 5 cm and had generalized hypotonia. She also had occasional white stools and high-colored urine for the past 10 days on retrospective history. Her labs revealed anemia (6.7 g/dl), conjugated hyper-bilirubinemia (6 mg/dl), mildly elevated transaminases with coagulopathy (INR > 6) and vitamin A deficiency (0.02 mg/dl). A normal abdominal ultrasonography (USG), urine succinyl-acetone, serum AFP, serum amino acid, and urine organic acid profile ruled out suspected metabolic liver disease, that is, tyrosinemia/hemochromatosis or TORCH infection. While the child was under systemic care, right eye underwent corneal scraping for smear and culture, cyanoacrylate glue application, and a bandage contact lens under topical anesthesia [Fig. 1a]. Patient underwent emergency therapeutic penetrating keratoplasty the next day [Fig. 1b]. *P. aeruginosa* was isolated on microbiology of corneal scraping and was sensitive to amikacin, gatifloxacin, ciprofloxacin, gentamycin, moxifloxacin, and ofloxacin. Postoperatively fortified amikacin (2.5%), 2% homatropine hydrobromide TID and both eyes 0.5% carboxymethylcellulose 6 times was started in view of dry lusterless appearance of the conjunctiva of both eyes. At one week, patient underwent examination under anesthesia. Right eye corneal graft was doing well, and left eye was showing a small area of infiltrate at nasal limbus and underwent corneal scraping [Fig. 2a and 2b]. Fortified amikacin was also initiated in left eye. Two weeks later, her condition deteriorated, and she presented with cough for past three days with respiratory distress. On evaluation, chest X-ray showed features of viral pneumonia, worsening LFTs with elevated lactate. CMV quantitative PCR showed 17,253 copies/ml[6] and patient was started on gancyclovir, oxygen, IV fluids, and liver protective measures. At this point, left eye was noted to have corneal ulcer that perforated

Access this article online

Quick Response Code:

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_2927_21

Department of Cornea & Refractive Surgery, Sankara Nethralaya, [1]Department of Pediatrics, Rainbow Children Hospital, Chennai, Tamil Nadu, India

Correspondence to: Dr Meena Lakshmipathy, Sankara Nethralaya, Medical Research Foundation, 18 College Road, Chennai - 600 006, Tamil Nadu, India. E-mail: drmly@snmail.org

Received: 20-Nov-2021 Revision: 01-Dec-2021
Accepted: 23-Mar-2022 Published: 30-Jun-2022

Cite this article as: Lakshmipathy M, Agarwal M, Agarwal M, Palanaiappan N. Bilateral *Pseudomonas aeruginosa* keratitis as presenting feature in an infant of cystic fibrosis. Indian J Ophthalmol 2022;70:2641-3.

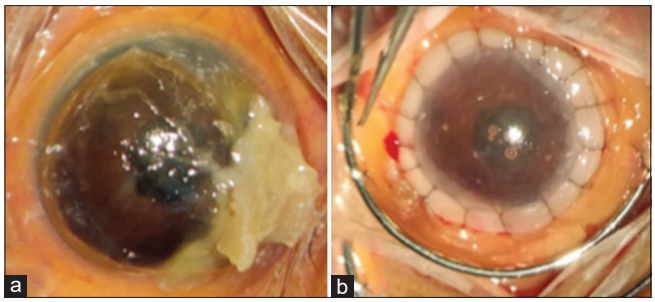

Figure 1: (a) Right eye photograph showing cyanoacrylate glue with total epithelial defect. (b) peri-operative photograph of right eye during penetrating keratoplasty

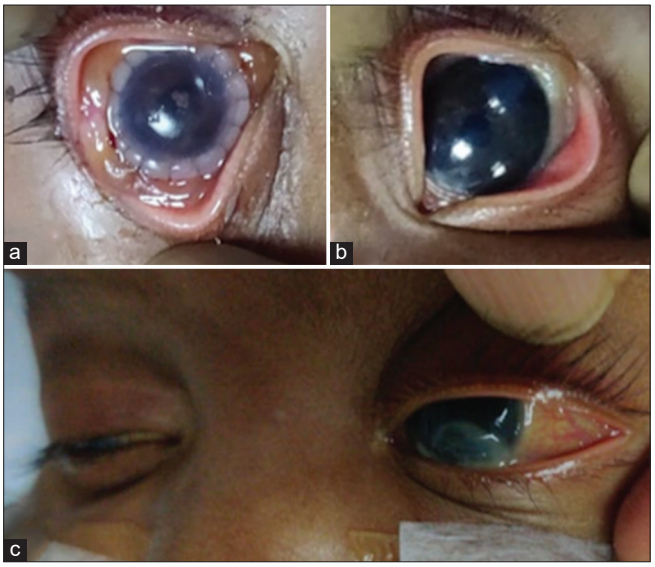

Figure 2: (a) Right eye photograph during examination under anaesthesia showing clear corneal graft with intact sutures (b) Left eye photograph during examination under anaesthesia showing area of corneal infiltrate in the nasal limbus (c) Photograph showing left eye perforated corneal ulcer

within 24 hours of admission [Fig. 2c]. Left eye underwent cyanoacrylate glue application with bandage contact lens and a subsequent therapeutic keratoplasty was planned once the infant was stable. In view of failure to thrive, fat globules in stool, and keratomalacia with heavy pseudomonas growth, CF was suspected. Genetic evaluation revealed CF homozygous mutation in c. 2619 + 1G >A (splice variant) of Intron 15 of *CFTR* gene, pathogenic variant in the index patient and both parents were asymptomatic heterozygous carriers. Because of CMV pneumonitis, the patient succumbed to severe lung involvement. Parents were encouraged to seek genetic counselling.

Discussion

CF is a genetic disorder leading to abnormal transport of chloride/sodium and water across the epithelial surfaces in various organs.[2] As a result, the pancreatic ducts are blocked with mucus leading to pancreatic insufficiency in almost 90% of patients.

Pancreatic insufficiency causes deficiency of fat-soluble vitamins (A, D, E and K) as these are co-absorbed with fat. This leads to keratomalacia.[3] CF also leads to damage of lacrimal glands and causes aqueous deficient dry eye as a result of abnormal basal tear production. Advanced xerophthalmia has been reported as an initial sign of CF.[4] In our case, the infant presented with perforated corneal ulcer secondary to severe keratomalacia as a result of vitamin A deficiency due to CF. Subsequently, there was superadded bacterial keratitis. Wamsley *et al*.[5] have described a similar case of a five-month-old girl who presented with bilateral ulcerative keratitis and failure to thrive. In addition to penetrating keratoplasty, she was given 50,000 IU of vitamin A prior to surgery, as was done in our case.

As a result of thickened pulmonary secretions as well as other mucosal secretions, clearing of mucous is hampered leading to increased susceptibility to harbor organisms like *P. aeruginosa.* This is being attributed to secretion of CFTR inhibitory factor (Cif) by this gram-negative organism. The Cif is epoxide hydrolase virulence factor that decreases the level of CFTR and facilitate biofilm formation and infection.[6] In healthy individuals, CFTR protein also provides immunity towards *P. aeruginosa* by ingestion of pathogen and its phagocytosis. In CF, the deficiency in CFTR protein and secretion of Cif by the Pseudomonas further increases the chances of infection.[7] This susceptibility of *P. aeruginosa* to cause ocular infections in CF has been previously reported in literature.[8–10]

Ocular surface health needs optimum vitamin A and deficiency leads to spectrum from mild xerophthalmia to keratomalacia. Pseudomonas keratitis is a potentially devastating condition leading to early perforation. Without history of prior ocular trauma and bilateral presentation, a suspicion of CF should be clinically made in such patients and the pediatrician should carry out a thorough systemic evaluation for the same. As in our case, the infant was apparently normal prior to the ocular condition, but developed subsequent systemic complications leading to unfavorable outcomes.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Riordan JR, Rommens JM, Kerem BS, Alon N, Rozmahel R, Grzelczak Z, *et al*. Identification of the cystic fibrosis gene: Cloning and characterization of complementary DNA. Science 1989;245:1066-73.
2. Nebbioso M, Quattrucci S, Leggieri E, Spadea L, Vingolo EM. Cystic fibrosis and new trends by ophthalmological evaluation: A pilot study. Biomed Res Int 2014;2014:580373.
3. Dodge JA, Turck D. Cystic fibrosis: Nutritional consequences and management. Best Pract Res Clin Gastroenterol 2006;20:531-46.

4. Lindenmuth KA, Del Monte M, Marino L. Advanced xerophthalmia as a presenting sign in cystic fibrosis. Ann Ophthalmol 1989;21:189-91.
5. Wamsley S, Patel SM, Wood MG, Villalobos R, Albert DM, Mootha VV. Advanced keratomalacia with descemetocele in an infant with cystic fibrosis. Arch Ophthalmol 2005;123:1012-6.
6. Vallières E, Elborn JS. Cystic fibrosis gene mutations: Evaluation and assessment of disease severity. Adv Genomics Genet 2014;4:161-72.
7. Grassmé H, Kirschnek S, Riethmueller J, Riehle A, von Kürthy G, Lang F, *et al*. CD95/CD95 ligand interactions on epithelial cells in host defense to Pseudomonas aeruginosa. Science 2000;290:527-30.
8. Motley WW 3rd, Augsburger JJ, Hutchins RK, Schneider S, Boat TF. Pseudomonas aeruginosa endogenous endophthalmitis with choroidal abscess in a patient with cystic fibrosis. Retina 2005;25:202-7.
9. Reedy JS, Wood KE. Endogenous pseudomonas aeruginosa endophthalmitis: A case report and literature review. Intensive Care Med 2000;26:1386-9.
10. Hall DS, Goyal S. Cystic fibrosis presenting with corneal perforation and crystalline lens extrusion. J Royal Soc Med 2010;103:30-3.