Congenital corneal anesthesia: A case series

Aruna P Jayarajan, Ashok Sharma[1], Rajan Sharma[1], Verinder S Nirankari[2], Shivananda Narayana, Josephine S Christy

Congenital corneal anesthesia (CCA) is an extremely rare condition where the cornea is affected in isolation or as a part of congenital syndrome, or can be associated with systemic anomalies. This case series of 12 eyes provides an overview of various clinical presentations and their final treatment outcomes. The average age of presentation was 3.2 years with a female preponderance (75%). Fifty percent of the patients had bilateral involvement and 50% had corneal ulcers at presentation. Two eyes required therapeutic keratoplasty for corneal perforation. All patients had isolated CCA except for one who had an associated hereditary and sensory autonomic neuropathy.

Key words: Congenital corneal anesthesia, hereditary and sensory autonomic neuropathy, absent corneal sensation

Congenital corneal anesthesia (CCA) is an extremely rare disorder that either has an isolated corneal involvement or can be associated with somatic malformations or neurological disorders.[1] The common manifestation of CCA is neurotrophic keratopathy that presents as dry geographic spots on the cornea, recurrent epithelial defects, or frank stromal lysis with perforation and secondary infections.[2] Therefore, accurate diagnosis and recognition of risk factors is important for avoiding long-term sequelae of this condition.

Case Reports

We present a case series of 8 patients (12 eyes) of CCA to spotlight the spectrum of presentation, associated systemic features and the role of symptomatic treatment. The age of presentation ranged from 2 months to 7 years with female preponderance (6 patients) and 4 patients had bilateral involvement [Table 1]. Though all patients had a history of recurrent epithelial defect, 4 patients presented with various stages of sterile corneal ulcer [Fig. 1a and 1b] including perforation during their course of treatment. None had a positive family history and all patients had normal developmental milestones with no associated skeletal anomalies. Only one patient had associated systemic features like dry skin and drooping of saliva with tongue ulceration [Fig. 1c]. She was diagnosed as a case of hereditary sensory and autonomic neuropathy type VIII after detailed neurological examination. Diagnosis of corneal anesthesia was established in all patients after the confirmation of absent corneal sensation in cotton wick test [Fig. 2]. A meticulous and detailed examination was done in all cases to rule out nutritional deficiency and other secondary causes of corneal anesthesia like herpes simplex infection and cerebellopontine angle tumors. Ocular examination revealed lusterless cornea and reduced tear film height in the affected eye of all patients. Microbiologic workup (smear, culture and PCR) was negative in all eyes with corneal infiltrate. All patients were treated with broad spectrum topical antibiotics, topical lubricants and ointments till epithelial defect healed, and maintained on 0.5% carboxymethyl cellulose eye drops TDS. One eye required tarsorraphy [Fig. 3] to facilitate wound healing, and two more eyes underwent therapeutic keratoplasty (TPK) with tarsorrhaphy for perforated ulcer. Average treatment duration ranged from 4 weeks to 4 months.

Discussion

Congenital corneal anesthesia (CCA) is a rare condition that is frequently misdiagnosed as nutritional keratopathy, herpetic viral keratitis, or dry eye which are secondary causes of corneal anesthesia. Primary CCA occurs due to developmental brainstem anomaly or a conduction defect of the trigeminal nerve, or may occur because of a local neurologic defect.[3] Though most cases are sporadic, familial pattern of inheritance has also been described. Rosenberg[4] classified congenital trigeminal anesthesia into three groups such as group I with isolated trigeminal anesthesia, which is usually bilateral and typically involves the first division of fifth nerve; group II with trigeminal anesthesia with associated congenital mesenchymal anomalies such as Möbius or oculo-auriculo-vertebral dysplasia; and group III with trigeminal anesthesia with associated brainstem signs. Although isolated CCA (group 1) is usually bilateral, we had four patients with isolated unilateral involvement which is a rare occurrence. Also, we had one patient with an unusual association of hereditary sensory and autonomic neuropathy type VIII (HSAN-VIII) presenting as CCA. HSAN-VIII is characterized by five main features such as insensitivity to pain and thermal stimuli, self-mutilation behaviour, altered sweat and tear formation,

Access this article online

Quick Response Code:

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_3001_21

Cornea and Refractive Services, Aravind Eye Hospital, Pondicherry, [1]Department of Ophthalmology, Dr.Ashok Sharma's Cornea Centre, Chandigarh, India, [2]Department of Ophthalmology, University of Maryland, USA

Correspondence to: Dr. Josephine S Christy, Aravind Eye Hospital, Cuddalore Road, Thavalakuppam, Pondicherry - 605 007, India. E-mail: josyfred@gmail.com

Received: 03-Dec-2021 Revision: 16-Jan-2022
Accepted: 12-Apr-2022 Published: 30-Jun-2022

Cite this article as: Jayarajan AP, Sharma A, Sharma R, Nirankari VS, Narayana S, Christy JS. Congenital corneal anesthesia: A case series. Indian J Ophthalmol 2022;70:2588-91.

Table 1: Summary of clinical presentation and treatment outcome

Age at onset/Sex	Eye	Systemic associations	Clinical signs at presentation	Medical treatment	Surgical treatment	Clinical outcome	Visual outcome
04 months/F	OS	HSAN type VIII	Sterile corneal ulcer with hypoyon	Gatifloxacin 0.3%, Carboxymethyl cellulose 0.5%	Nil	Corneal opacity	Able to pick up cake decoration
04 months/F	OD	HSAN type VIII	Sterile corneal ulcer	Gatifloxacin 0.3%, Carboxymethyl cellulose 0.5%	Nil	Corneal opacity	Able to pick up cake decoration
03 months/M	OD	Nil	Recurrent epithelial defect	Tobramycin 0.3%, Carboxymethyl cellulose 0.5%	Nil	Recurrent SPK	Able to pick up cake decoration
02 months/F	OS	Nil	Recurrent epithelial defect	Tobramycin 0.3%, Carboxymethyl cellulose 0.5%	Nil	Corneal opacity, amblyopia	6/36
3.5 years/F	OD	Nil	Sterile corneal ulcer	Topical Tobramycin (1.4%) and Cefazolin (5%)	Nil	Corneal opacity	2/60
3.5 years/F	OS	Nil	Sterile corneal ulcer	Topical Tobramycin (1.4%) and Cefazolin (5%)	Tarsorrhaphy	Corneal opacity	4/60
4.5 years/F	OD	Nil	Recurrent epithelial defects	Moxifloxacin 0.5%, Carboxymethyl cellulose 0.5%	Nil	Recurrent SPK	6/12
4.5 years/F	OS	Nil	Recurrent epithelial defects	Moxifloxacin 0.5%, Carboxymethyl cellulose 0.5%	Nil	Recurrent SPK	6/12
7 years/F	OD	Nil	Recurrent epithelial defects	Moxifloxacin 0.5%, Carboxymethyl cellulose 0.5%	Nil	Recurrent SPK	6/9
7 years/F	OS	Nil	Recurrent epithelial defects	Moxifloxacin 0.5%, Carboxymethyl cellulose 0.5%	Nil	Recurrent SPK	6/9
5 years/F	OS	Nil	Perforated corneal ulcer	Moxifloxacin 0.5%, Carboxymethyl cellulose 0.5%	Therapeutic keratoplasty + Tarsorrhaphy	Opaque graft	HM
2.5 years/M	OD	Nil	Perforated corneal ulcer	Topical Tobramycin (1.4%) and Cefazolin (5%)	Therapeutic keratoplasty + Tarsorrhaphy	Opaque graft	HM

OD – Oculus dextrus, OS – Oculus sinister, SPK – Superficial punctate keratitis, HSAN – Hereditary sensory and autonomic neuropathy

absent corneal reflexes and presence of repeated infections of the skin and bone. Absence of corneal reflexes in these patients can lead to frequent corneal ulcers and progressive corneal scarring.[5] Lack of corneal sensation that is seen in CCA can result in devastating complications if not treated promptly. The aberrant reduction in the lacrimation reflex and blinking triggers a detrimental loop of corneal damage. Corneal nerves and epithelial cells support each other, mutually maintaining symbiosis through the release of trophic factors that promote epithelial cell proliferation, migration, and differentiation, as well as nerve development and survival.[6] This complex reciprocal relationship between the epithelial cells and nerves is crucial for the physiologic renewal of corneal epithelium and wound healing. Absence of either mechanism, leads to expedited damage to epithelial cells along with a parallel deficiency in spontaneous repair of epithelium.

All patients in our case series were treated via conventional methods like hourly antibiotics until the underlying cause of corneal hypo/anesthesia was detected, thus resulting in a prolonged recovery time. Although these patients when treated promptly can have quick healing, if done otherwise, they can even result in serious complications like corneal perforation. Management of CCA in children is usually challenging due to various factors. One of the prime reasons is a delayed diagnosis due to difficulties in evaluating children. Consequently, there is ocular toxicity induced by prolonged use of drugs with preservatives during the initial stages of misdiagnosis in addition to the inherent poor wound healing mechanism because of corneal denervation.

Despite the modern medicine reaching heights, there is no curative treatment for CCA at present. Hence a timely diagnosis and management is crucial to minimize the risk of amblyopia due to corneal ulcers and scars. Lack of pain and photophobia, quiet/comfortable kid despite keratitis, recurrent corneal erosions and retractable corneal ulcers in infancy should always prompt a diagnosis of CCA [Fig. 4]. Other

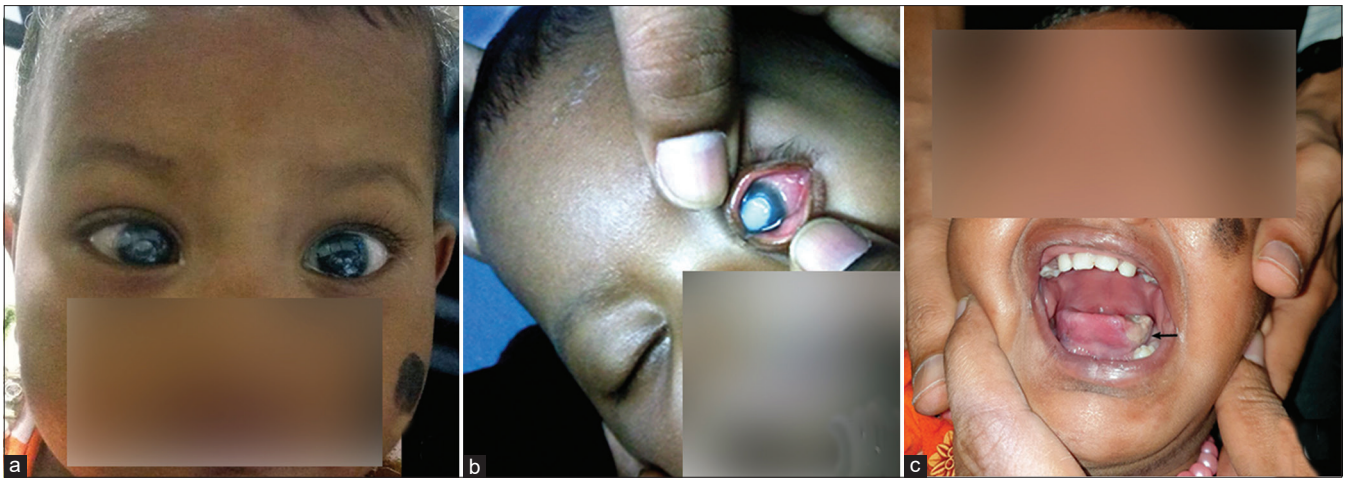

Figure 1: (a) (Case 1) Right eye showing 4 mm epithelial defect with 2 × 3 mm corneal infiltrate and normal left eye. (b) (Case 1) Left eye showing central 7 × 5 mm corneal infiltrate (presented after 4 months of RE involvement). (c) Tongue ulceration in the lateral margin due to chronic biting

Figure 2: Absent corneal sensation on cotton wick test

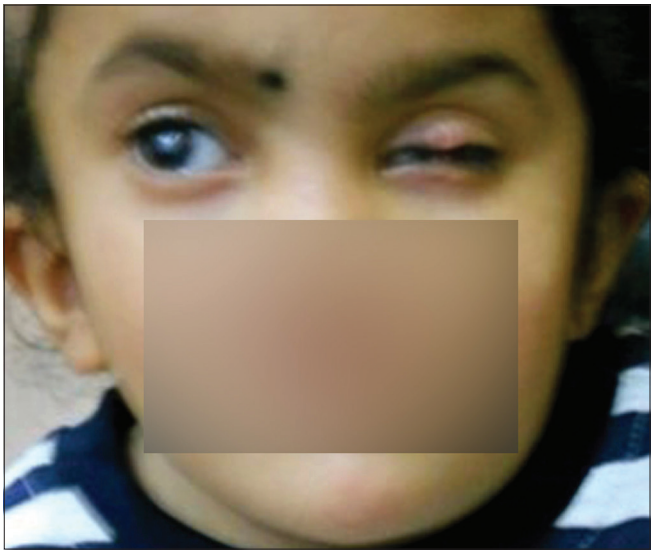

Figure 3: Left eye showing central temporary tarsorrhaphy

minor clues are inadequate response to eye drop instillation and decreased reflex tearing/blink rates. Corneal sensation can be checked by a simple cotton wick test or esthesiometer. *In vivo* confocal microscopy can also be a useful tool to assess the sub-basal nerve density in cases of CCA.[7] Once the diagnosis is made, a multidisciplinary approach is needed for detection of associated systemic features and further management. Family pedigree construction is essential to diagnose others at risk factors, and genetic counselling is offered to those at inheritance risk.

Treatment is primarily aimed at preventing epithelial breakdown and this can be achieved by routine use of preservative-free artificial tears and ointments. Permanent tarsorrhaphy is an effective way to limit corneal exposure and help in maintaining a good ocular surface. Corneal transplantation in these patients poses a very high risk, owing to poor wound healing and eventual vascularization that makes them liable for allograft rejection.[8]

The limitation of our study was an objective measurement of corneal sensation and lack of confocal microscopy to document sub-basal nerve density. Also acquiring anterior segment pictures were difficult since this involved a pediatric population.

Conclusion

CCA should be considered as an important differential diagnosis in all children with recurrent/intractable corneal ulcers. Prompt diagnosis can result in early recovery and better visual outcome.

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.

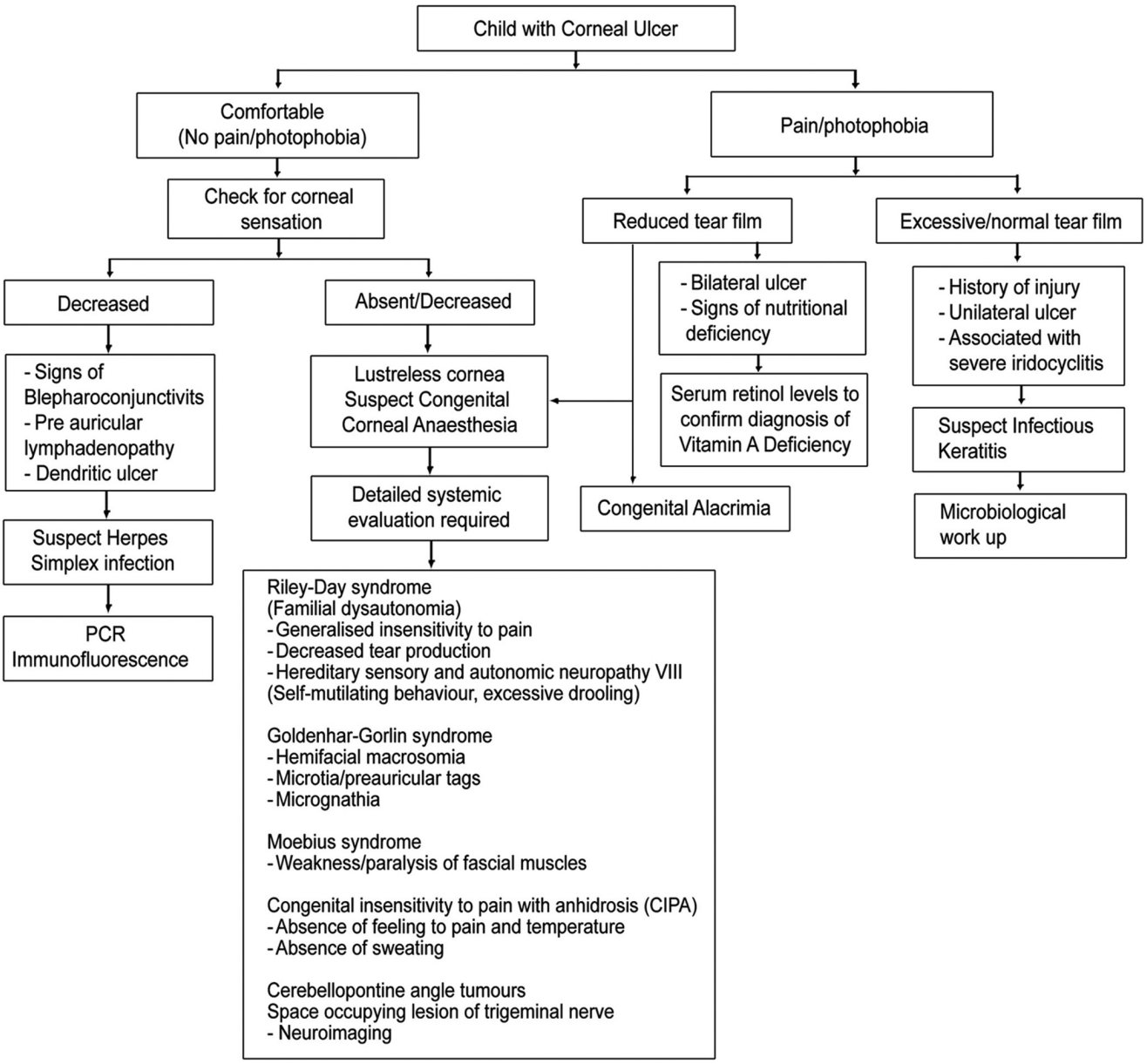

Figure 4: Diagnostic algorithm for a child presenting with corneal ulcer

References

1. Ramaesh K, Stokes J, Henry E, Dutton GN, Dhillon B. Congenital corneal anesthesia. Surv Ophthalmol 2007;52:50-60.
2. Kaur M, Nair S, Titiyal JS. Commentary: Congenital corneal anesthesia. Indian J Ophthalmol 2021;69:266-7.
3. Mathen MM, Vishnu S, Prajna NV, Vijayalakshmi P, Srinivasan M. Congenital corneal anesthesia: A series of four case reports. Cornea 2001;20:194-6.
4. Rosenberg ML. Congenital trigeminal anaesthesia. A review and classification. Brain 1984;107:1073-82.
5. Elhennawy K, Reda S, Finke C, Graul-Neumann L, Jost-Brinkmann PG, Bartzela T. Oral manifestations, dental management, and a rare homozygous mutation of the PRDM12 gene in a boy with hereditary sensory and autonomic neuropathy type VIII: A case report and review of the literature. J Med Case Rep 2017;11:233.
6. Versura P, Giannaccare G, Pellegrini M, Sebastiani S, Campos EC. Neurotrophic keratitis: Current challenges and future prospects. Eye Brain 2018;10:37-45.
7. Gopal M, Ramappa M, Mohamed A, Dhakal R, Chaurasia S. Quantitative corneal neural imaging using *in vivo* confocal microscopy in cases of congenital corneal anesthesia: A prospective analysis and clinical correlation. Indian J Ophthalmol 2021;69:262-6.
8. Ramappa M, Chaurasia S, Chakrabarti S, Kaur I. Congenital corneal anesthesia. J AAPOS 2014;18:427-32.