Case Series

Ocular manifestations in Kindler syndrome

Prafulla K Maharana, Pranita Sahay, Sohini Mandal, Ritu Nagpal, Namrata Sharma

We aimed describe the chronic ocular sequelae of Kindler syndrome. All cases of Kindler syndrome with ocular involvement that presented to a tertiary eye care center were included. Three cases of Kindler syndrome with ocular changes were reviewed. Case 1 (10 years, female) had recurrent epithelial breakdown with severe dry eye and corneal opacity secondary to keratitis. Case 2 (28 years, male) had symblepharon , ocular surface keratinization , and severe dry eye. Case 3 (16 years , female) had partial limbal stem cell deficiency with dry eye. All cases were treated with topical lubricants, short course of low-potency steroids and immuno-modulators. Attention must be paid to the eye in addition to the oro-an-genital mucosa to avoid longterm ocular sequelae.

Key words: Dry eye, kindler syndrome, limbal stem cell deficiency, Steven Johnson syndrome

Kindler syndrome is a rare autosomal recessive disease characterized by trauma-induced skin blistering, poikiloderma, skin atrophy, and photo-sensitivity.[1-4] The extra-cutaneous features include gingivitis, colitis, mucosal stenosis, syndactylyl, poor dentition, and nail dystrophy.[1-3,5-7] Ocular manifestations occur in the form of cicatricial ectropion, kerato-conjunctivitis, conjunctival scarring, blepharitis, recurrent corneal erosions, corneal opacity, corneal ectasia, symblepharon, pigment deposits over the lens capsule, and segmental chorioretinal atrophy.[3,5,8,9]

Herein, we present three such cases where the patient presented with features suggestive of a chronic ocular disease process that was poorly managed in the initial stage of the disease.

Access this article online

Quick Response Code:

Website: www.ijo.in

DOI: 10.4103/ijo.IJO_791_22

Case Reports

Case 1

A 10-year-old female presented with pain, redness, watering, and diminution of vision in the right eye for 20 days. There was a history of recurrence of similar episodes in the past. She had a visual acuity of hand movement and 6/6 in the right and left eyes, respectively. The right eye revealed a central corneal epithelial defect, 6 x 6 mm in size, with nebulo-macular corneal opacity in the surrounding cornea and 360-degree superficial vascularization [Fig. 1a and 1b]. The left eye had a normal anterior segment; however, the tear film height was <0.5 mm with punctate staining [Fig. 1c and 1d]. The tear film breakup time (TBUT) was instantaneous in the left eye, and Schirmer II test revealed values of 4 and 5 mm in the right and left eyes, respectively. Systemic examination revealed hypo- and hyper-pigmented patches (poikiloderma) with cutaneous atrophy of the dorsal surface of the arms, the hand, the foot and legs, pseudoainhum of the fourth and fifth digits of the toe, facial skin atrophy, and hyper- and hypo-pigmentation patches with scaling. The patient was started on topical antibiotics, lubricants, and low-potency steroids in the right eye. Lubricants and cyclosporine 0.05% were started in the left eye. Because there was no improvement, amniotic membrane transplantation was performed to aid epithelial healing [Fig. 2a], and complete healing was noted at 3 weeks follow-up [Fig. 2b and 2c].

Case 2

A 28-year-old male presented with a loss of vision in both the eyes for the past 10 years. A history of recurrent episodes of pain, redness, and watering was present, for which he was treated with topical antibiotics and lubricants by the primary physician. At presentation, the visual acuity was perception of light in both the eyes. Slit lamp examination of the right eye showed nebulo-macular corneal opacity, ectasia, and 360-degree superficial vascularization [Fig. 3a]. Superior symblepharon, upper lid entropion, and trichiasis were noted in both the eyes [Fig. 3b]. The left eye showed a keratinized ocular surface with the presence of corneal pannus [Fig. 3c]. TBUT was instantaneous in both the eyes with Schirmer II being 2 mm and 0 mm in the right and left eyes, respectively. Systemic examination revealed similar features to the previous case [Fig. 4a-e]. Nail dystrophy was noted in the great toe of both the feet with pseudoainhum of the third, fourth, and fifth digits of the foot [Fig. 4e]. The patient was started on topical lubricants and cyclosporine and was advised ocular surface stabilization surgery followed by keratoprosthesis for visual rehabilitation.

Dr. Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi, India

Correspondence to: Dr. Prafulla K Maharana, Associate Professor of Ophthalmology, Cornea, Cataract and Refractive Surgery Services, Dr Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, Ansari Nagar, New Delhi - 110 029, India. E-mail: drpraful13@gmail.com

Received: 29-Mar-2022 Revision: 05-Apr-2022
Accepted: 19-Apr-2022 Published: 30-Jun-2022

Cite this article as: Maharana PK, Sahay P, Mandal S, Nagpal R, Sharma N. Ocular manifestations in Kindler syndrome. Indian J Ophthalmol 2022;70:2585-7

Case 3

A 16-year-old female presented with complaints of foreign body sensation and irritation in both the eyes since childhood. The visual acuity in both the eyes was 6/6 with Schirmer II of 4 and 5 mm in the right and left eyes, respectively, and TBUT of 5 and 6 seconds. Slit lamp examination revealed a reduced tear film height with partial limbal stem cell deficiency. Systemic features were similar to the findings noted in the above two cases. The patient was started on a short course of topical steroids, cyclosporine, and lubricants.

The family history was negative in all the cases.

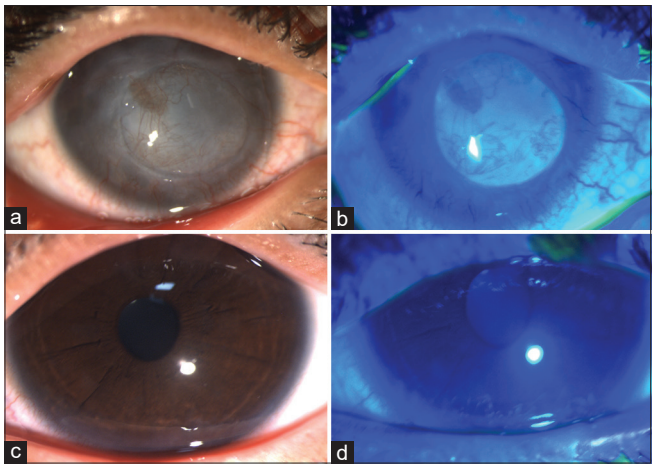

Figure 1: Slit lamp photograph of case 1: (a) right eye under diffuse illumination showing a central, epithelial defect of 6 x 6 mm with a punched-out border and surrounding corneal opacity with vascularization; (b) right eye under a cobalt blue filter with fluorescein stain; (c) left eye under diffuse illumination showing a normal anterior segment; (d) left eye under a cobalt blue filter with fluorescein stain showing a decreased tear film height and punctate staining of the inferior cornea

Discussion

Kindler syndrome, a variant of epidermolysis bullosa, is a skin-blistering disorder that usually presents at birth.[10] It is caused by FERMT1 gene mutation that encodes kindlin-1 protein.[10,11] This protein is responsible for cell–cell adhesion, cell signaling, differentiation, morphogenesis, and migration. Hence, abnormality of kindlin-1 protein results in skin blisters because of cleavage at multiple skin planes.[10] Photo-sensitivity, progressive poikiloderma, and cutaneous atrophy are the striking features of this disorder, which helps to distinguish it from other skin-blistering disorders.[5] The extra-cutaneous features include gingivitis, colitis, mucosal stenosis, syndactylyl, poor dentition, and nail dystrophy.[2,7]

Ocular manifestations may result from both the primary kindling-related loss of corneal epithelial integrity and exposure keratopathy because of eyelid malposition. The reported clinical features include cicatricial ectropion, kerato-conjunctivitis, conjunctival scarring, blepharitis, recurrent corneal erosions, corneal opacity, corneal ectasia, symblepharon, pigment deposits over the lens capsule, and segmental chorioretinal atrophy.[3,5,8,9]

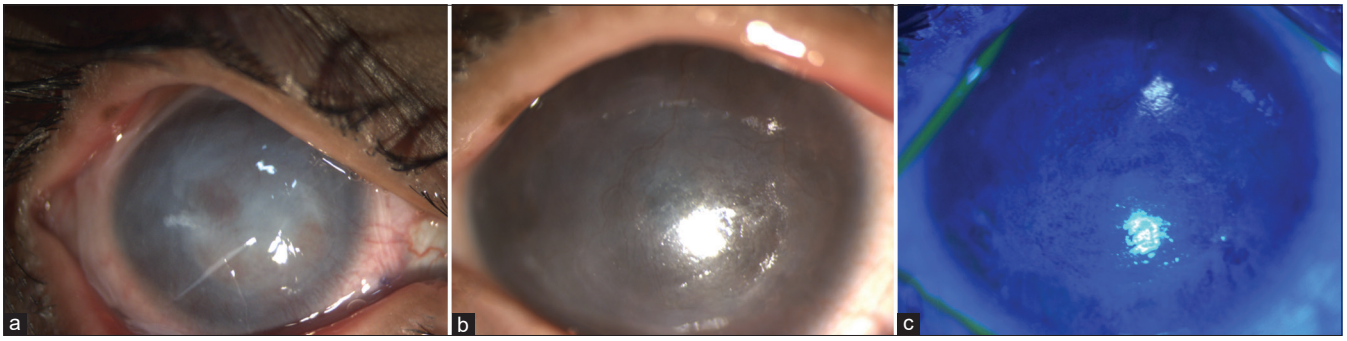

Figure 2: Slit lamp photograph of the right eye: (a) on post-operative day 1 following amniotic membrane transplantation (AMT); (b) in diffuse illumination on day 21 post AMT with complete epithelial healing; (c) in a cobalt blue filter with fluorescein staining showing no epithelial defect

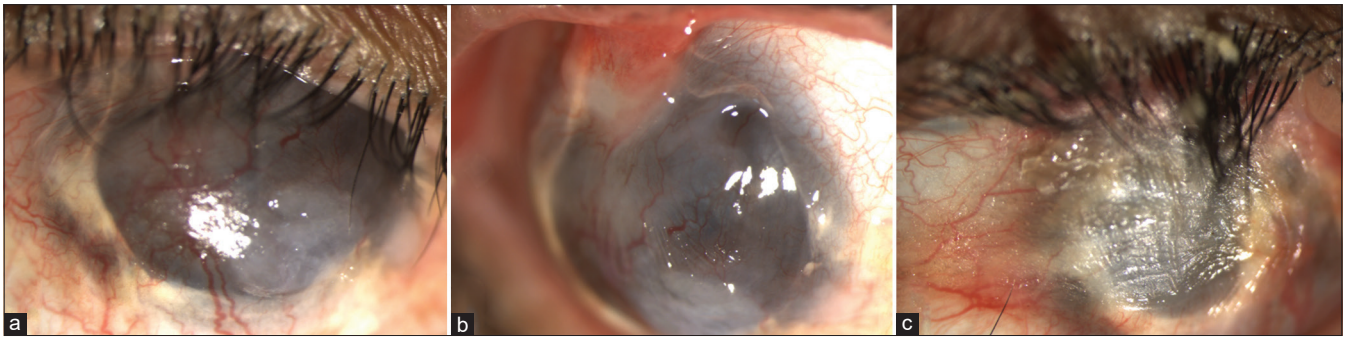

Figure 3: Slit lamp photograph of case 2 (a) right eye showing upper lid entropion, trichiasis, nebulo-macular corneal opacity involving the entire cornea, and corneal thinning with 360-degree superficial vascularization; (b) right eye showing superior symblepharon; (c) left eye showing entropion and a keratinized ocular surface with a severe dry eye

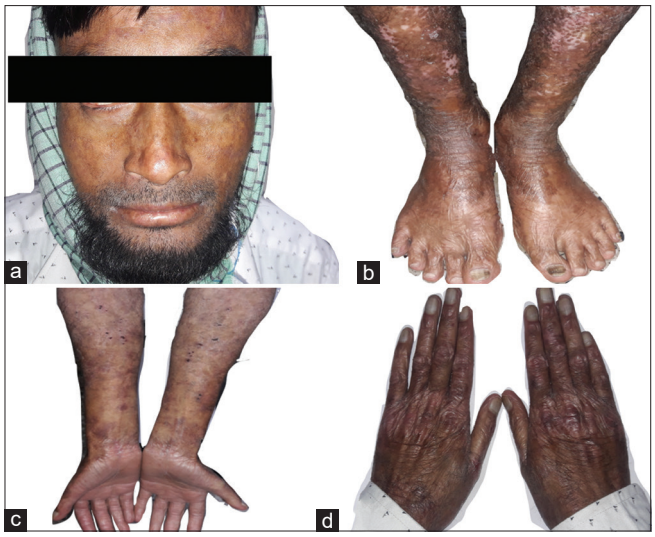

Figure 4: Clinical photograph of case 2: (a) face showing hyper- and hypo-pigmentation; (b) feet and leg showing poikiloderma, nail dystrophy, and pseudoainhum of the third, fourth, and fifth toes (c) forearm showing poikiloderma with scab formation on both the plantar and dorsal surfaces (d) dorsum of the hand showing cutaneous atrophy and hyper- and hypo-pigmentation (poikiloderma)

In our case series, we observed kindler syndrome with ocular involvement of varying severity. Kerato-conjunctivitis sicca and limbal stem cell deficiency were common to all. In addition, case 1 had corneal opacity as a result of recurrent epithelial breakdown, and case 2 had a keratinized ocular surface with symblepharon, entropion, and trichiasis. It is important to note that none of the patients were referred to an ophthalmologist for screening of ocular involvement on confirmation of the diagnosis of Kindler syndrome. We suspect that a timely screening of these cases and initiation of appropriate therapy could have salvaged vision in these young patients. This was missed in all our cases by the primary treating physician.

Conclusion

To conclude, Kindler syndrome can have ocular involvement of variable severity early in their life. Hence, a timely referral at the confirmation of diagnosis to an ophthalmologist for screening is a must.

Meeting presentation

Poster presentation at KERACON 2019.

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. Anwar MI, Rashid A, Ghafoor R, Tahir M, Rao SU, Mir F. Kindler's syndrome: A report of five cases in a family. J Coll Physicians Surg Pak 2014;24:763-5.
2. Ashton GHS. Kindler syndrome. Clin Exp Dermatol 2004;29:116-21.
3. Satter EK. A presumptive case of Kindler syndrome with a new clinical finding. Pediatr Dermatol 2008;25:646-8.
4. Diociaiuti A, Zambruno G, Giancristoforo S, Proto V, Boldrini R, Castiglia D, *et al*. Acral skin atrophy in an infant: An early clue to Kindler syndrome diagnosis. J Eur Acad Dermatol Venereol 2016;30:1046-9.
5. Jen M, Nallasamy S. Ocular manifestations of genetic skin disorders. Clin Dermatol 2016;34:242-75.
6. Almeida HL de, Heckler GT, Fong K, Lai-Cheong J, McGrath J. Sporadic Kindler syndrome with a novel mutation. An Bras Dermatol 2013;88 (6 Suppl 1):212-5.
7. Barbosa NM, Visioli F, Martins MD, Martins MAT, Munerato MC. Oral manifestations in Kindler syndrome: Case report and discussion of literature findings. Spec Care Dentist 2016;36:223-30.
8. Signes-Soler I, Rodriguez-Prats JL, Carbonell S, Tañá-Rivero P. Corneal erosion and Kindler syndrome. Optom Vis Sci 2013;90:e9-10.
9. Chéour M, Mazlout H, Ben Jalel W, Brour J, Baroudi B, Kraiem A. [Corneal lesions in Kindler syndrome: A case report]. J Fr Ophtalmol 2012;35:46.e1-5.
10. Gonzalez ME. Evaluation and treatment of the newborn with epidermolysis bullosa. Semin Perinatol 2013;37:32-9.
11. Wada M, Masuda K, Tsuruta D, Tamai K, Lai-Cheong JE, McGrath JA, *et al*. Case of Kindler syndrome resulting from mutation in the FERMT1 gene. J Dermatol 2012;39:1057-8.