

Recurrent Haemophilus Influenzae Conjunctivitis and Corneal Scarring in a Boy with X-Linked Agammaglobulinemia

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Background

- X-linked agammaglobulinemia (XLA) is a rare immunodeficiency caused by mutations in the BTK gene, leading to absent B cells and near-zero antibody production ¹.
- XLA affects 1–9 per million, primarily in males, and predisposes to recurrent bacterial infections like conjunctivitis ^{2,3}.
- Corneal scarring as an ocular complication from conjunctivitis is rarely reported. Only three cases and one retrospective review exist in the literature ⁴⁻⁷.

Patient Presentation

Ophthalmic History

- Age 2: Referred for intermittent exotropia and a compensatory head posture
- No ocular signs of XLA; underwent strabismus surgery
- Age 5: Discharged with improved binocularity and head posture

Medical History of XLA

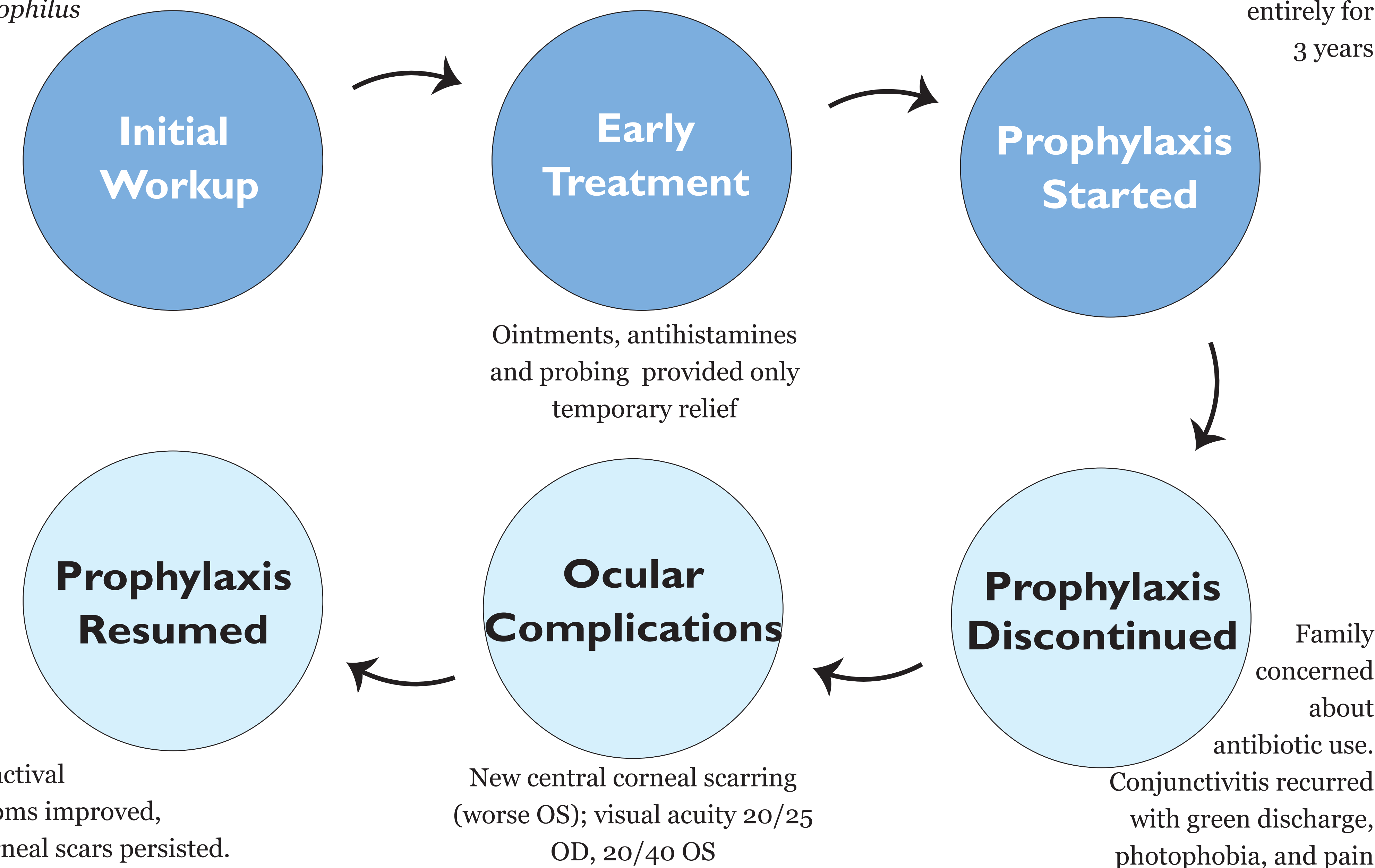
- Early childhood diagnosis based on absent B cells ($<0.01 \times 10^9/L$) and reduced immunoglobulin levels (IgG 1.34 g/L; undetectable IgA and IgM; IgE 1.1 kU/L)
- Reduced BTK expression, confirmed BTK mutation (c.974+1del) and a positive family history
- Started on monthly IVIG with target IgG >9 g/L.

Onset of Ocular Symptoms

- Age 6: Presented with a 9-month history of recurrent conjunctival redness and mucopurulent discharge
- First documented ocular manifestation of XLA
- Initial visual acuity: 20/30 OD, 20/25 OS

Clinical Course

At age 6, Conjunctival swabs positive twice for *Haemophilus*



Discussion

IVIG alone did not prevent conjunctivitis in our patient, a finding consistent with previous reports ^{3,8}.

Three cases link conjunctivitis in XLA to corneal scarring: two untreated *H. influenzae* cases, one *C. trachomatis* case unresponsive to treatment, and one adult with progressive keratoconjunctivitis ⁴⁻⁶.

Early reports linked recurrent conjunctivitis in XLA to absent secretory IgA, which is not replaced by IVIG ^{2,4}.

A study reports 41% of XLA patients had recurrent conjunctivitis, with scarring in four cases, versus none in an IgA-deficient control group, **suggesting a vulnerability unique to XLA ⁷.**

We suspect nasopharyngeal *Haemophilus influenzae* **ascended the nasolacrimal duct to cause conjunctivitis ^{5,9}.**

Symptoms improved with amoxicillin. **After it was stopped, conjunctivitis returned and corneal scarring followed, suggesting a link between recurrence and damage.**

Conjunctivitis in XLA may appear mild due to muted immune responses ¹⁰.

Early antibiotic treatment, culture-guided therapy, prophylaxis for recurrent cases, and annual ophthalmology follow-up are essential to prevent vision-threatening complications.

References

1. Lackey AE, Ahmad F. X-Linked Agammaglobulinemia. In: StatPearls. StatPearls Publishing; 2024. Accessed January 5, 2025. <http://www.ncbi.nlm.nih.gov/books/NBK549865/>
2. Vosoughimotlagh A, Rasouli SE, Rafiemanesh H, et al. Clinical manifestation for immunoglobulin A deficiency: a systematic review and meta-analysis. *Allergy Asthma Clin Immunol Off J Can Soc Allergy Clin Immunol.* 2023;19:75. doi:10.1186/s13223-023-00826-y
3. Williams KW. X-linked Agammaglobulinemia: Infection Frequency and Infection-Related Mortality in the USIDNET Registry. *Pediatrics.* 2022;150(Supplement 3):S56-S57. doi:10.1542/peds.2022-059346III
4. Hansel TT, O'Neill DP, Yee ML, Gibson JM, Thompson RA. Infective conjunctivitis and corneal scarring in three brothers with sex linked hypogammaglobulinaemia (Bruton's disease). *Br J Ophthalmol.* 1990;74(2):118-120.
5. al GHONAUM A, Ziegler J, Tridgell D. Bilateral chronic conjunctivitis and corneal scarring in a boy with X-linked hypogammaglobulinaemia. *J Paediatr Child Health.* 1996;32(5):463-465. doi:10.1111/j.1440-1754.1996.tb00950.x
6. Mielke S, Grundel B, Schmidt SM, Tost F. Keratoconjunctivitis as a Single Entity in X-linked Agammaglobulinemia? *Ocul Immunol Inflamm.* 2023;31(3):665-670. doi:10.1080/09273948.2022.2042824
7. Redenbaugh V, Sloan A, Sui J, Edgar JD, Coulter T. XLA and Recurrent Conjunctivitis: a Unique Association? *J Clin Immunol.* 2023;43(3):548-549. doi:10.1007/s10875-022-01424-0
8. Abolhassani H, Hirbod-Mobarakeh A, Shahinpour S, et al. Mortality and morbidity in patients with X-linked agammaglobulinaemia. *Allergol Immunopathol (Madr).* 2015;43(1):62-66. doi:10.1016/j.aller.2013.09.013
9. Ulanova M, Tsang RS, Goldfarb DM, et al. Prevalence of *Haemophilus influenzae* in the nasopharynx of children from regions with varying incidence of invasive *H. influenzae* serotype a disease: Canadian Immunization Research Network (CIRN) study. *Int J Circumpolar Health.* 83(1):2371111. doi:10.1080/22423982.2024.2371111
10. Fortingo N, Melnyk S, Sutton SH, Watsky MA, Bollag WB. Innate Immune System Activation, Inflammation and Corneal Wound Healing. *Int J Mol Sci.* 2022;23(23):14933. doi:10.3390/ijms232314933

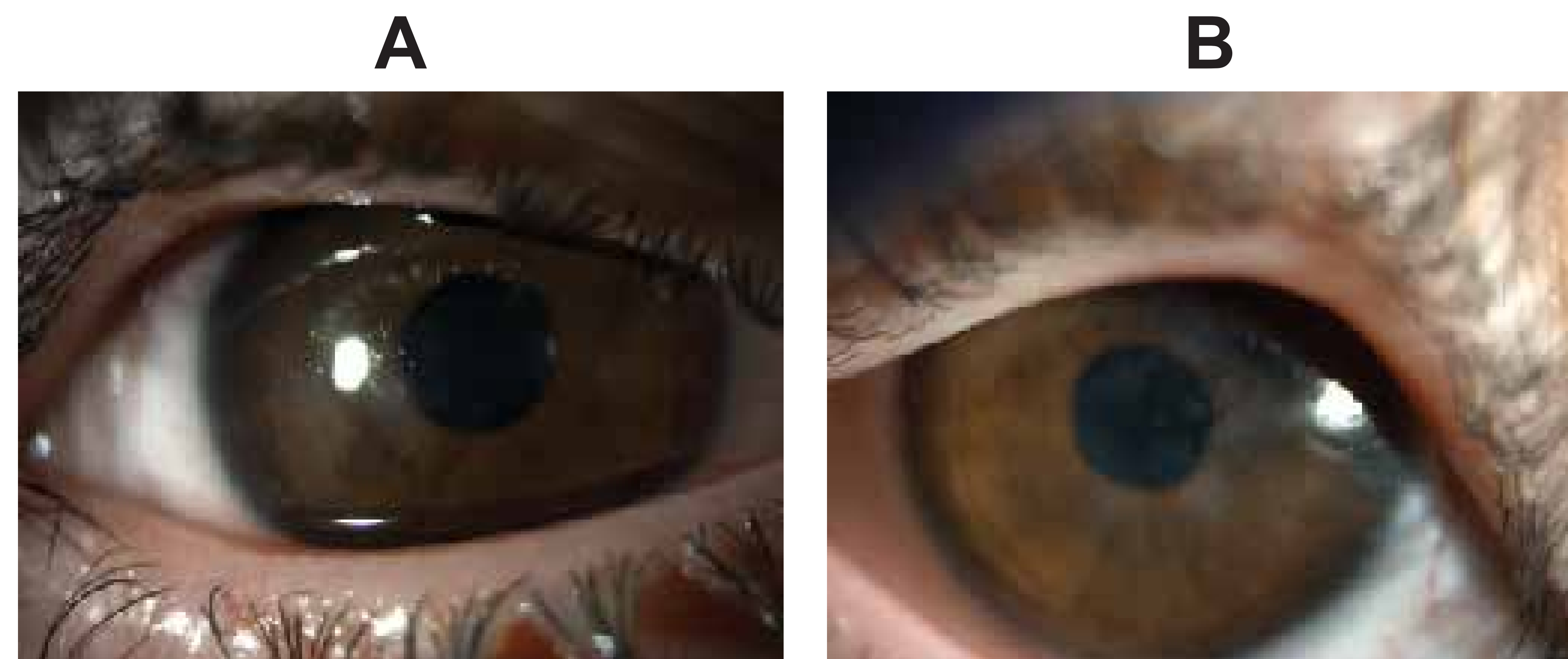


Figure 1. Slit lamp photographs of the right (A) and left (B) eyes. Both images were taken following recurrence of severe conjunctivitis after discontinuation of systemic amoxicillin prophylaxis. The right eye (A) demonstrates mild central corneal haze with preserved visual axis. The left eye (B) shows more pronounced central corneal scarring with increased stromal opacity, correlating with greater visual acuity reduction (20/25 OD vs. 20/40 OS) .