CASE REPORT

Hydrops as a Presenting Sign of Keratoconus in Down Syndrome: Case Report, Literature Review, and the Need for a Public Health Strategy

Adel Barbara[1], Cosimo Mazzotta[2], Mazen Sinjab[3], Ramez Barbara[4]

Received on: 24 January 2024; *Accepted on:* 26 July 2024; *Published on:* xx xxxx xxxx

Abstract

This case study highlights a 12-year-old male with Down syndrome (DS) presenting with hydrops as the initial sign of keratoconus in the left eye and concurrent keratoconus in the right eye. The discussion stresses the frequent occurrence of keratoconus among individuals with DS, emphasizing the significance of early diagnosis and treatment. Furthermore, the discussion proposes a plan for a comprehensive public health strategy to address the unique challenges associated with keratoconus in this population.

Keywords: Case report, Central corneal thickness, Cornea, Down syndrome, Genetics, Keratoconus.

International Journal of Keratoconus and Ectatic Corneal Diseases (2025): 10.5005/jp-journals-10025-1205

Case Description

A 12-year-old male diagnosed with Down syndrome (DS) visited Dr AB's clinic accompanied by his father, reporting tearing and a white spot in his left eye (LE) that had emerged 2 weeks prior. He had previously been referred to the hospital's emergency room, where he received treatment, including unspecified eye drops (likely antibiotics and steroids) for 4 days. Subsequently, these were replaced with NaCl 5% eye drops.

The patient, who is mentally challenged (with special demands), exhibited an inability to measure the visual acuity in the LE, while the right eye (RE) registered a three-meter finger count. Upon examination, the LE revealed an edematous cornea and a deep anterior chamber with limited details (Fig. 1). In contrast, the RE exhibited a clear cornea, and the remainder of the eye examination, including pupil dilation and fundus examination, showed normal findings.

Corneal ocular computerized tomography using CASIA 2 (Tomey, Japan) demonstrated increased corneal thickness and rupture of the Descemet membrane in the LE (Fig. 2) and keratoconus (KC) in the RE (Fig. 3). The possibility of performing collagen corneal crosslinking (CXL) to arrest the progression of KC was checked. Topical anesthesia drops were instilled, and a speculum was inserted in the RE under the microscope. The patient was cooperative, so immediate CXL in the RE was recommended. The patient had a follow-up appointment at the hospital the next day, where continuation of treatment for the LE was advised.

The risks associated with eye rubbing were explained to the patient's father. Immediate CXL was offered for his RE, and continuing the treatment of the LE at the public hospital.

The patient's father decided to continue the treatment at the public hospital and has given approval for the use of his son's data for this publication.

The young patient received ongoing eye care through the public system's ophthalmic clinic. Remarkably, at the age of 6 years, his father reported being informed that his son's eyes were normal, with no need for further follow-up.

[1]Department of Ophthalmology, IVISION Cornea and Refractive Surgery Center, Haifa, Israel

[2]Department of Medical, Surgical and Neurosciences, Ophthalmology Section, Siena University, Italy

[3]Consultant Ophthalmic Surgeon, Consultant Cornea, Anterior Segment, Refractive Surgery at Dr. Sulaiman Al Habib Hospital, DHCC, Dubai

[4]Department of Ophthalmology, Hillel Yaffe and Laniado Hospitals, Israel

Corresponding Author: Adel Barbara, Department of Ophthalmology, IVISION Cornea and Refractive Surgery Center, Haifa, Israel, Phone: +972 52-850-0061, e-mail: adelbarbara@yahoo.com

How to cite this article: Barbara A, Mazzotta C, Sinjab M, *et al*. Hydrops as a Presenting Sign of Keratoconus in Down Syndrome: Case Report, Literature Review, and the Need for a Public Health Strategy. Int J Kerat Ect Cor Dis 2025;xx(x):xx–xx.

Source of support: Nil

Conflict of interest: Dr Adel Barbara, Dr Cosimo Mazzotta, Dr Mazen Sinjab, and Dr Ramez Barbara are associated as the Editorial board members of this journal and this manuscript was subjected to this journal's standard review procedures, with this peer review handled independently of these Editorial board members and their research group.

Discussion

Keratoconus stands out as the most prevalent corneal ectatic disorder, with an observed increase in prevalence and frequency over recent years. The historical frequency, previously cited as 1 per 2000, is now considered irrelevant, as it reports the prevalence of KC in a certain geographic area in the USA in 48 years starting from 1935 to 1983; at that time, corneal topography was not available.[1] Cornea topography is an essential tool for KC diagnosis. A recent epidemiological study in Holland revealed an estimated prevalence of KC in the general population at 1 in 375, marking a substantial

5-fold to 10-fold increase compared to previously documented prevalence and frequency in population studies.[2]

Noteworthy variations in prevalence are evident across different regions and ethnic groups. In Saudi Arabia, the highest reported frequency stands at 4.79%.[3] In Jerusalem, the prevalence of KC among all subjects was 2.34%, with rates of 2.2% among Jews and 3% among Arabs.[4] Similar patterns were observed among Arab students in Haifa, Israel.[5]

Geographic and ethnic factors play a significant role in influencing prevalence, with reported rates of 2.3% among Indians aged 30 years and above residing in the rural region of Central India,[6] in contrast to 86 patients per 1,00,000 in Denmark and 0.0004% in Russia.[7,8]

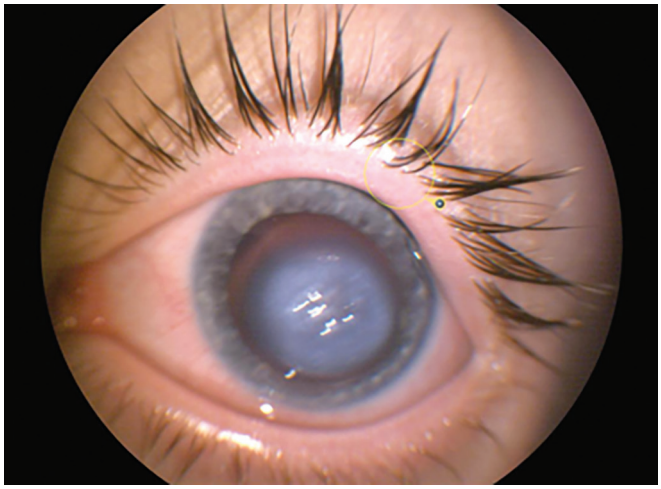

Fig. 1: Corneal edema LE

Fig. 2: CASIA 2 LE demonstrating the hydrops

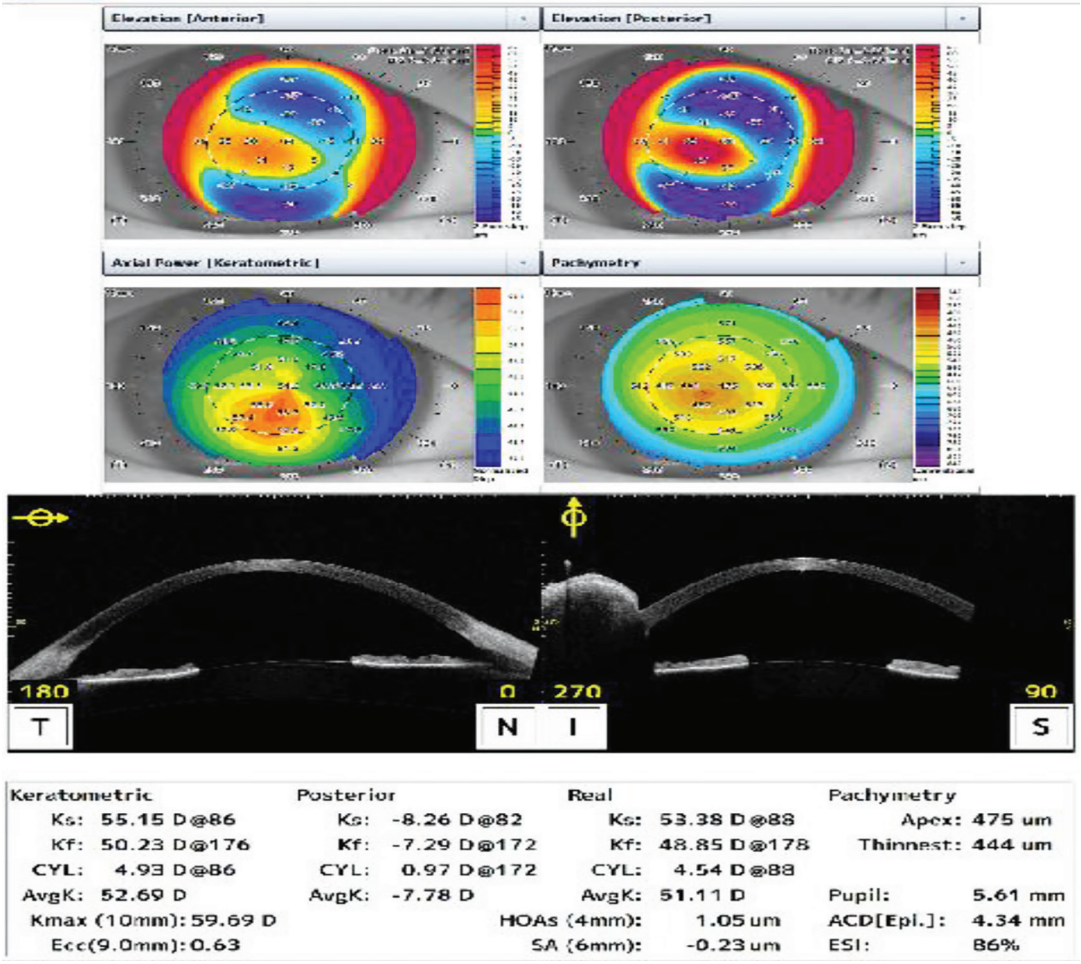

Fig. 3: Keratoconus (KC)

Hoffman was the first to describe acute K(hydrops) in Mongoloids, reporting two cases. Appelmanset et al. collected 52 cases from the literature. Notably, 17 cases were observed in mentally defective patients, with ten of these occurring in Mongoloids.[9]

The initial investigation into the occurrence of KC in individuals with DS was conducted by J. F. Cullen and H. G. Butler. They conducted a survey among visually impaired individuals at the Rosewood State Hospital in Maryland during 1961–1962, observing a notable prevalence of blindness or partial blindness among those with DS. Motivated by these findings, they conducted a dedicated survey, examining 143 patients with DS, and reported a 5.5% prevalence of KC in the examined group.[9]

The incidence of KC in DS ranges from 0 to 71%.[10]

In the existing literature, there is a lack of unanimous agreement on the accurate prevalence of KC among individuals with DS. Numerous studies appear to be constrained by small sample sizes, contributing to the absence of a definitive consensus. In addition, there is inconsistency in the study design, diagnostic criteria, participant age, sample size, methodologies employed, and diversity in ethnicity.

A national prevalence study of KC in persons with DS in Norway reported a prevalence of 5.5%. An 11-literature review identified studies that have reported KC in as many as 8%–36% of persons with DS.[11] Results from this literature review indicate a considerably higher proportion of KC in persons with DS compared with the general population.[11,12]

In a multicenter study conducted by Alio et al., a comparison of corneal topographies between patients with DS and a control group revealed distinctive characteristics. Individuals with DS exhibited steeper and thinner corneas, accompanied by topographical alterations. Moreover, corneal morphology consistent with the diagnosis of KC was frequently observed in DS patients thinner corneas were reported in DS patients.[13,14]

It appears justified to presume that there might be a considerable number of undetected KC, especially among individuals with DS. This is because identifying this eye condition relies on effective symptom communication, prompt referral, positive collaboration during eye examinations, and public education for early awareness of the disease. Detecting early-stage KC using only the slit lamp can be difficult, and obtaining cooperation for corneal tomography is often a hurdle for individuals with DS. The use of retinoscopy may prove beneficial in identifying abnormal motions of the retinoscopy reflex. Using the retinoscopy to detect the scissoring reflex was useful, especially in rural areas where advanced technology might not be available. However, the scissoring reflex is not specific to keratoconus; it is found with irregular astigmatism, subtle corneal opacities, and early cataract.[15]

Down syndrome ranks among the prevalent chromosomal conditions globally, impacting approximately 1 in 400 to 1 in 500 births. This multisystem genetic disorder exhibits a diverse array of ophthalmic manifestations, such as strabismus, amblyopia, accommodation defects, refractive error, eyelid abnormalities, nasolacrimal duct obstruction, nystagmus, keratoconus, cataracts, retinal abnormalities, optic nerve abnormalities, and glaucoma. Notably, these ophthalmic conditions are more frequently observed in children with DS compared to the broader pediatric population.[16]

Numerous genetic studies have suggested associations between KC and DS.[17]

Several studies have suggested vigorous eye rubbing as a potential risk factor for KC.[18,19] Eye rubbing behavior is also common in DS and may further contribute to the development and progression of the disease.[10]

The findings from this case report and the literature review highlight a significantly elevated prevalence of KC among individuals with DS in comparison to the general population. This noteworthy observation underscores the importance of considering screening measures for this specific group, particularly given the potential challenges faced by many of these patients in effectively communicating their symptoms. When evaluating the necessity for such screenings, it is essential to incorporate health economic considerations.

Cross-linking has demonstrated effectiveness in arresting the progression of KC. Long-term follow-up studies have reported stability over time.[20–24] Early detection through screening is crucial for implementing timely interventions, and CXL has emerged as a promising treatment option.

For optimal results, it is important to perform CXL early in the course of KC when the condition is still in its initial stages. This proactive approach can help maintain good visual acuity and prevent further deterioration of vision. However, the success of CXL may be influenced by the level of patient's cooperation. Some patients may be unable to comply with the standard treatment protocol.

To address the challenges posed by patients with limited cooperation, modifications to the CXL technique may be necessary. This can involve considering accelerated versions of the treatment or even exploring the option of performing CXL with an epithelial-on approach.

The flexibility to adapt the CXL technique to accommodate patients with limited cooperation further emphasizes the need for personalized approaches in managing KC in this specific group of patients.

This proactive approach not only aims to prevent the progression of the condition but also seeks to circumvent the development of advanced stages, where corneal transplantation becomes a potential intervention. It is crucial to note that corneal transplantation, with its inherently intricate nature, poses particular challenges for individuals with DS, making early detection and intervention even more imperative.

Moreover, considering that a substantial proportion of individuals with DS already experience visual impairment, advanced-stage KC likely contributes significantly to this issue.

Therefore, addressing KC in this population becomes not only a matter of preserving visual acuity but also a crucial aspect of managing overall visual health and potentially mitigating the broader challenges associated with visual impairment in individuals with DS.

Here is a proposal for a comprehensive plan:

1. Screening program:
   - Develop a comprehensive screening program for DS individuals.
   - Collaborate with healthcare providers and organizations to raise KC awareness.
2. Education:
   - Provide educational materials about KC to caregivers, parents, and individuals with DS.
   - Conduct workshops to enhance awareness of early detection.

3. Regular eye examinations:
   - Encourage routine eye exams for DS individuals, starting early in life.
   - Include specific KC screening protocols in routine eye exams.
4. Advanced diagnostic tools:
   - Equip eye care professionals with advanced diagnostic tools.
   - Ensure practitioners are trained to recognize early KC signs.
5. Collaboration between clinics:
   - Facilitate collaboration between DS clinics and ophthalmology departments.
   - Establish communication channels for information transfer.
6. Research and guidelines:
   - Support KC research in DS individuals.
   - Contribute to the development of early detection and management guidelines.
7. Early intervention:
   - Highlight the benefits of early intervention in preventing KC progression.
   - Collaborate with healthcare professionals for tailored intervention plans.
8. Monitoring visual health:
   - Establish a systematic approach to monitor visual health.
   - Conduct regular follow-up assessments to track visual acuity changes.
9. Raise awareness:
   - Engage in public awareness campaigns about DS and KC.
   - Advocate for early detection to address broader visual impairment challenges.
10. Collaboration with support organizations:
    - Work with DS support organizations for holistic visual health care.
    - Utilize support networks to disseminate information and provide resources.

The objective of this plan is to detect KC in DS individuals early, allowing for timely intervention and preserving visual acuity and overall visual health.

In conclusion, this case report highlights the critical need for early detection and intervention in managing KC in individuals with DS. The elevated prevalence of KC in this population, coupled with the challenges of effective symptom communication and cooperation during eye examinations, underscores the necessity for a tailored public health strategy.

Early screening programs, educational initiatives, and the integration of advanced diagnostic tools can significantly improve outcomes for individuals with DS. Moreover, promoting awareness and collaboration among healthcare providers, caregivers, and support organizations is vital for addressing the broader visual health challenges faced by individuals with DS. Timely interventions, such as corneal cross-linking, can prevent disease progression and preserve visual acuity, highlighting the importance of proactive management.

This case emphasizes the need for continued research and the development of guidelines to ensure that all individuals with DS receive the appropriate eye care, ultimately improving their quality of life and visual health.

References

1. Kennedy RH, Bourne WM, Dyer JA. A 48-year clinical and epidemiologic study of keratoconus. Am J Ophthalmol 1986;101:267–273. DOI: 10.1016/0002-9394(86)90817-2.
2. Godefrooij DA, de Wit GA, Uiterwaal CS, et al. Age-specific incidence and prevalence of keratoconus: A nationwide registration study. Am J Ophthalmol 2017;175:169–172. DOI: 10.1016/j.ajo.2016.12.015.
3. Torres Netto EA, Al-Qtaidi WM, Hafezi NL, et al. Prevalence of keratoconus in paediatric patients in Riyadh, Saudi Arabia. Br J Ophthalmol 2018;102:1436–1441. DOI: 10.1136/bjophthalmol-2017-311391.
4. Millodot M, Shneor E, Albou S, et al. Prevalence and associated factors of keratoconus in Jerusalem: A cross-sectional study. Ophthalmic Epidemiol. 2011;18:91–97.
5. Shneor E, Millodot M, Gordon-Shaag A, et al. Prevalence of keratoconus among young arab students in Israe. Int. J. Keratoconus Ectatic Corneal Dis 2014;3:9–14. DOI: 10.5005/jp-journals-10025-1070.
6. Jonas JB, Nangia V, Matin A, et al. Prevalence and associations of keratoconus in rural Maharashtra in Central India: The Central India eye and medical study. Am J Ophthalmol 2009;148:760–765.
7. Nielsen K, Hjortdal J, Nohr EA, et al. Incidence and prevalence of keratoconus in Denmark. Acta Ophthalmol Scand 2007;85:890–892.
8. Gorskova EN, Sevost'ianov EN. Epidemiology of keratoconus in the Urals. Vestn Oftalmol 1998;114:38–40.
9. Cullen JF, Butler HG. Mongolism (down's syndrome) and keratoconus. Br J Ophthalmol 1963;47:321–330. DOI: 10.1136/bjo.47.6.321.
10. Akoto T, Li JJ, Estes AJ, et al. The underlying relationship between keratoconus and down syndrome. Int J Mol Sci 2022;23:10796. DOI: 10.3390/ijms231810796.
11. Kristianslund O, Drolsum L. Prevalence of keratoconus in persons with Down syndrome: A review. BMJ Open Ophthalmol 2021;6:754. DOI: 10.1136/bmjophth-2021-000754.
12. Kristianslund O, Drolsum L. Prevalence of keratoconus in persons with down syndrome in a national registry in Norway. JAMA Netw Open 2021;4(3):e210814. DOI: 10.1001/jamanetworkopen.2021.0814.
13. Alio JL, Vega-Estrada A, Sanz P, et al. Corneal morphologic characteristics in patients with down syndrome. JAMA Ophthalmol 2018;136:971. DOI: 10.1001/jamaophthalmol.2018.2373.
14. Aslan L, Aslankurt M, Yüksel E, et al. Corneal thickness measured by Scheimpflug imaging in children with Down syndrome. J AAPOS Off Publ Am Assoc Pediatr Ophthalmol Strabismus 2013;17:149–152. DOI: 10.1016/j.jaapos.2012.10.020.
15. Al-Mahrouqi, Haitham, Saif Bani Oraba, et al. Retinoscopy as a screening tool for keratoconus. Cornea 2019;38(4):442–445. DOI: 10.1097/ICO.0000000000001843.
16. Sun E, Kraus CL. The ophthalmic manifestations of down syndrome. Children 2023;10:341.
17. Kristianslund O, Drolsum L. Prevalence of keratoconus in persons with Down syndrome: A review. BMJ Open Ophthalmol 2021;6:e000754. DOI: 10.1136/bmjophth-2021-000754.
18. Hawkes E, Nanavaty MA. Eye rubbing and keratoconus: A literature review. Cor Dis 2014;3:118–121. DOI: 10.5005/jp-journals-10025-1090.
19. Gatinel D. Eye rubbing, a Sine Qua Non for keratoconus? Int J Keratoconus Ectatic Corneal Dis 2016;5(1):6–12. DOI: 10.5005/jp-journals-10025-1114.
20. Wollensak G, Spörl E, Seiler T. Treatment of keratoconus by collagen cross linking. Ophthalmologe 2023;100:44–49. DOI: 10.1007/s00347-002-0700-3.
21. Caporossi A, Mazzotta C, Baiocchi S, et al. Long-term results of riboflavin ultraviolet a corneal collagen cross-linking for keratoconus in Italy: The Siena eye cross study. Am J Ophthalmol 2010;149:585–593. DOI: 10.1016/j.ajo.2009.10.021.
22. Raiskup F, Herber R, Lenk J, et al. Corneal crosslinking with riboflavin and UVA light in progressive keratoconus: Fifteen-year results. Am J Ophthalmol 2023;250:95–102. DOI: 10.1016/j.ajo.2023.01.022.
23. Raiskup F, Hillen M. Corneal cross-linking can halt the progression of keratoconus, but what is the best approach. Int J. Keratoconus Ectatic Corneal Dis 2015;4(2):47–51. DOI: 10.5005/jp-journals-10025-1097.
24. Barbara R, Pikkel J, Garzozi H, et al. Collagen cross-linking and keratoconus in pediatric patients. Int J Keratoconus Ectatic Corneal Dis 2012;11:57–60. DOI: 10.5005/jp-journals-10025-1010.