

# Corneal cross-linking in a child with osteogenesis imperfecta syndrome and keratoconus

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## CASE STUDY

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## ABSTRACT

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Cross-linking (CXL) is a well-established procedure in children with keratoconus (KC), but cases of CXL and osteogenesis imperfecta (OI) have not been published in the literature, despite the association between physiopathology of these diseases. This is the first case, to the best of our knowledge, of a young girl with both OI and KC that underwent a CXL treatment. In this case, CXL was performed at 6-years-old prior to an expected progression, without complications and probably stopped further keratoconus progression.

### Key Words

Osteogenesis imperfecta, keratoconus, corneal cross-linking, collagen disorders

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### Implications for Practice:

#### 1. What is known about this subject?

Cross-linking (CXL) is a well-established procedure in children with keratoconus. Cases of CXL and osteogenesis imperfecta have not been published in the literature.

#### 2. What new information is offered in this case study?

A case report of CXL and osteogenesis imperfecta (OI).

#### 3. What are the implications for research, policy, or practice?

Open the discussion about the safety of CXL in OI patients, the choice of CXL, timing to treat and risk of induced visual loss.

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### Background

Keratoconus is an ectatic degenerative eye disease. Characterized by biomechanical instability and stromal corneal thinning, KC lead to progressive irregular astigmatism, high order aberrations, progressive keratometric steepening, or even corneal scarring.<sup>1</sup>

The biomechanical instability seems to be caused by less, or weak collagen cross linking between the corneal collagen fibrils. The severity is inversely correlated with age, leading to more advanced and aggressive cases in child and adolescence.<sup>2</sup>

Around 10 per cent of the keratoconus patients have family history of keratoconus. The disease may be correlated with ocular and/or systemic disorders such as vernal keratoconjunctivite, Down Syndrome, retinitis pigmentosa, and collagen disorders such as Ehlers-Danlos and imperfect osteogenesis syndromes.<sup>2,3</sup>

Osteogenesis imperfecta (OI) disease is a connective tissue disorder genetically determined and classified by different mutations.<sup>4</sup> It is characterized by bone fractures and deformities, due to deficits in type I collagen. The diagnosis is made from clinical, genetic and radiographic features. Occurs every 1:60.000 births.<sup>5</sup>

Despite the association of ectatic corneal diseases and connective tissue disorders, keratoconus is an unusual report case. Blue sclera is a recognized characteristic find in OI patients.<sup>6-8</sup>

Although the initial concerns about safety and induced vision loss in pediatric patients, CXL is the most promising and established treatment for corneal ectasias.<sup>9-12</sup>

We report the first case, to the best of our knowledge, of a pediatric case of OI and KC treated with traditional CXL.

### Case details

A 6-years-old girl with OI was diagnosed with bilateral KC at her first appointment for progressive visual impairment with no other complaints. OI diagnosis was made by history of multiple fractures, deformities and typical radiological findings.

Best-spectacle corrected visual acuity (BSCVA) was 20/30 in both eyes with a cycloplegic refraction of -1,50 -0,75 @ 170° in the right eye (OD) and -1,75 -0,50 @ 20° in the left eye (OS). Slit lamp examination and retinal exam were normal. Corneal Scheimpflug tomography (Bausch and Lomb Topographer Orbscan II) revealed OD: SimK 47.8x49.6 D, Kmax 49.83D and thinnest point of 445µm; OS: SimK 47.0x47.8 D, Kmax 48.48 D, thinnest point of 420µm.

Color-coded maps of Orbscan demonstrated high keratometric values and bow-tie asymmetric astigmatism that correlated with the anterior and posterior high elevation and thinnest points in both eyes (Figure 1). Considering the patient's age, OI diagnosis and complementary exams, KC diagnosis with presumed high risk of progression was established and the initial treatment with anti-allergic eye drops as well as CXL were indicated after family consent.

Traditional CXL protocol was performed first in OS, and a month later in OD, with an Opto XLink – Corneal Crosslinking System (Opto industries, São Paulo, Brazil). Written informed consent was obtained from the parents. The patient was examined at 3, 6, 12, 22, 39 and 51 months post-operatively, with topographies revealing corneal aplannation and relatively stable paquimetry (Figure 2).

Corneal paquimetry had no statistically significant variation along the follow up period, except between the pre-op and the 22 month visit, which may be due to inter tomography variance from Orbscan to Pentacam (Figure 3). In the last visit (month 51) Pentacam paquimetry was 447µm in right eye and 456µm in the left eye.

At the last follow-up visit, 51 months after the first CXL, KC remained stable, with BSCVA of 20/25 OD and 20/30 OS. Refraction had a myopic deviation during the follow-up period, with a cycloplegic refraction of -3.00 -2.00 @ 180°OD and -3.00 -1.50 @ 180° in the last follow-up visit.

### Discussion

Osteogenesis imperfecta has various forms of severity. It is not a surprise that a connective tissue disorder that affects collagen formation can manifest in almost all organs. Bones, meninges, dermis and the eye, are common sites of collagen disorders associated with OI.<sup>4,6</sup>

The pathophysiology of corneal ectasia in OI is still unclear, but we expect to find a biomechanical weakening caused by defective corneal collagen, and maybe the absence of Bowman's membrane. Although the absence of Bowman's membrane can frequently occur without clinical corneal disease. Blue sclera is considered as a typical find of OI. Although KC is not considered a typical find of OI, it seems to have an association between physiopathology of these diseases, reinforced by reports of multiple families with very high incidence of blue sclera and corneal ectasia.<sup>13,14</sup>

Since 1998, when Dresden Technical University first described CLX, the technique has been established as a gold standard for progressive KC treatment and development of new protocols. The traditional Dresden protocol is still a reference point as it established parameters to total irradiancy, safety, and effectiveness. However, newer protocols with oxygen delivery control, higher UVA energy levels, faster treatments, or even pulsed UVA irradiation seems to be the future.<sup>15</sup>

Corneal experts had recently published the Global Consensus on Keratoconus and Ectatic Diseases, which helps to guide ophthalmologists to answer most questions about KC management.<sup>12</sup> According to this consensual paper, the initial protocol of excluding patients under the age of eighteen is no longer recommended. CXL is now discouraged in patients over forty, with no progression. Documented progression remains as an inclusion criteria at all ages, but is not a mandatory criteria in high-risk patients under eighteen when rapid treatment should be considered. The risk of corneal haze and consequent visual impairment is still a concern, and there is no consensus yet on visual acuity to indicate or contra-indicate CXL. Fortunately, earlier diagnosis and treatment is seen with the use of Scheimpflug based technologies and corneal biomechanical studies.<sup>12</sup>

### Conclusion

Despite of well-established studies of pediatric CXL, we describe an important case to open the discussion about the safety of CXL in OI patients, the choice of CXL, timing to treat, risk of CXL induced visual loss, and new perspectives for CXL. Finally, our case report favors CXL in children with

OI, which seems to be safe and effective after a 4-year period of follow-up. Further studies are needed to better understanding the CXL in OI patients.

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The authors declare that they have no competing interests.

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## PATIENT CONSENT

The authors, *Kwitko S, Pretto J*, declare that:

1. They have obtained written, informed consent for the publication of the details relating to the patient(s) in this report.
2. All possible steps have been taken to safeguard the identity of the patient(s).
3. This submission is compliant with the requirements of local research ethics committees.

Figure 1: Pre-CXL Orbscan, 08/29/2011

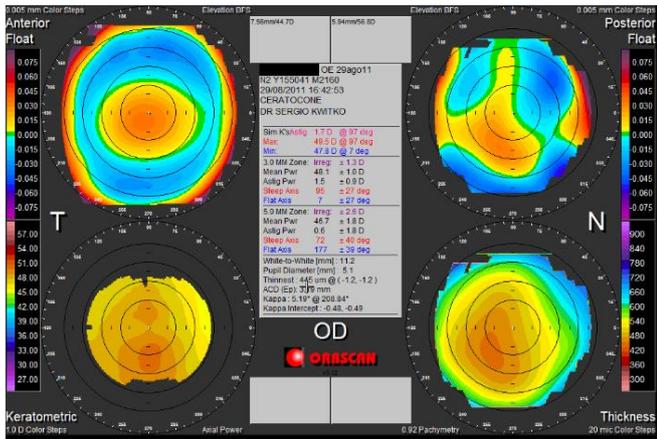


Figure 3: Corneal thickness (thinnest point)

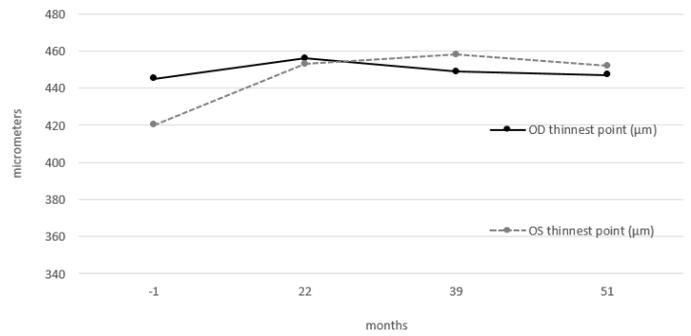


Figure 2: Anterior corneal curvature (Kmax, AveK, FlatK and StepK)

