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Case Report

Pierre Robin sequence and keratoconus, a rare association

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ABSTRACT

Pierre Robin sequence (PRS) is an inherited disorder that affects one in between 8,500 and 14,000 people and is characterized by a triad of clinical signs. These include micrognathia, glossoptosis and obstruction of the upper airway, typically associated with palatal cleft. PRS has also been associated with various ocular complications, including high congenital myopia, congenital glaucoma, and retinal detachment.

Because of the clinical importance of PRS, it is critical to illustrate the features of the Robin sequence to clearly define its primary and secondary clinical signs. We describe a patient with PRS who developed keratoconus as a rare manifestation of the disease and its management.

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Síndrome de Pierre Robin y quearotocono, una rara asociación

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RESUMEN

La secuencia de Pierre Robin (PRS) es una patología hereditaria que afecta a una de entre 8.500 y 14.000 personas y está caracterizada por una triada de signos. Estos incluyen micrognatia, glosptosis y obstrucción de vías aéreas altas, típicamente asociados a labio leporino.

PRS ha sido también relacionado con afectación oftalmológica, incluyendo miopía congénita, glaucoma congénito o desprendimiento de retina.

Debida a la importancia clínica de la PRS, es fundamental describir las distintas características de la secuencia Pierre Robin, para así definir los signos principales y secundarios de la patología. Describimos el caso de una paciente con PRS que desarrolló queratocono como una extraña manifestación de la enfermedad.

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1. INTRODUCTION

Pierre Robin Sequence (PRS) is a disorder affecting fundamentally the head and face, defined by micrognathia, glossoptosis and ultimately, airway restriction. Typically, a wide U-shaped cleft palate has been described associated with this syndrome [1, 2].

The Pierre Robin condition is illustrated as a sequence because of the progression of its features. The underdevelopment of the mandible is thought to be secondary to an impairment in intrauterine growth. This micrognathia leads to downward displacement or retraction of the tongue (glossoptosis), which eventually results in airway obstruction and feeding difficulties [3].

Some patients have the features of PRS as part of a syndrome that affects other organs and tissues in the body, such as Stickler syndrome (most frequent) or campomelic dysplasia. When Pierre Robin sequence occurs by itself, it is described as nonsyndromic or isolated [3].

Isolated PRS is typically sporadic but familiar heritance with autosomal dominant heritance has also been described. Various chromosomal anomalies have been associated with PRS, including regions 2q24.1–33.3, 4q32-qter, 17q21–24.3, and 11q21–23.1 [4].

Other associations include gene SOX9, known to be the most common cause of isolated Pierre Robin sequence. Such gene plays a major role in the formation of different tissues during the embryonic development, through the regulation of other genes, mainly those involved in the formation of the mandible. Alterations in the SOX9 gene derive in phenotype changes from cartilage defects during early facial growth [5–7].

Santoro et al recently studied the prevalence of the disease, analyzing the cases of PRS collected by the population-based congenital anomaly registries of EUROCAT and found that the overall prevalence was 12.0 per 100 000 births, being higher in the most recent 10-year period (2008–2017) [8].

PRS is frequently associated with systemic affections, but also to ophthalmologic clinic such as high myopia, congenital glaucoma or retinal detachment but the cases described that associate this disease with keratoconus are very few in the scientific literature. We describe the case, follow up and management of a patient diagnosed of PRS at birth who developed keratoconus.

2. CASE REPORT

A 28-year-old female was admitted to our Hospital for the evaluation of presumed visual defect. Although the patient only referred mild photophobia, her parents assured she had been suffering from vision loss. She had a general history of Pierre Robin sequence associated with intellectual disability. No prior visual examinations had been performed until the day of the first visit. Parents denied any history of atopy, eye rubbing or other systemic conditions.

Upon examination, best corrected visual acuity (BCVA) using the Snellen Chart was 20/200 (sph-2,5 cyl-3,25 axis 30) on the right eye (OD), and 20/200 (sph-4 cyl -2,5, axis 125) on the left eye (OS). Slit-lamp examination of OD showed Vogt's striae, and OS showed Vogt's striae as well as apex fibrosis. Corneal topography (Oculus Pentacam) was performed (Figure 1), showing maximum keratometry values of 72.6D and 75.3D on OD and OS respectively.

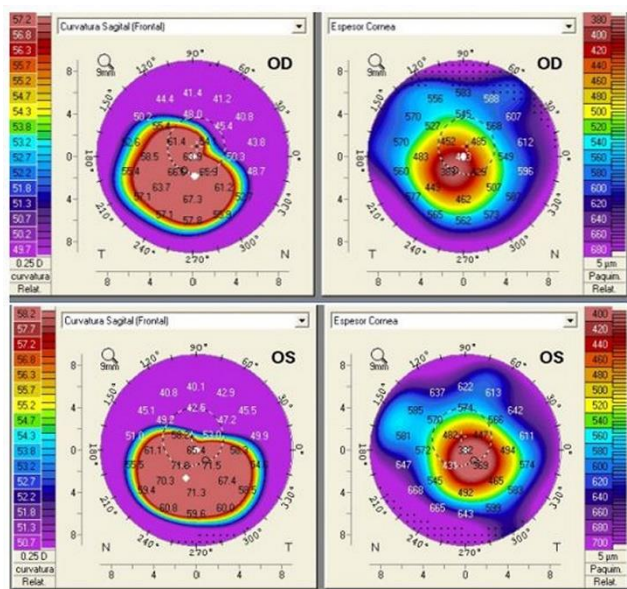


Figure 1: Corneal topography of the patient, upon first consultation at our hospital, showing a maximum keratometry value of 72.6D on OD (a), and minimal corneal thickness of 378 µm (b). On OS, maximum keratometry value of 75.3D (c), and minimal corneal thickness of 359 µm (d).

In regards to OS, her initial treatment, although complicated due to her intellectual disability and difficulty for topical anesthesia, consisted of left eye penetrating keratoplasty (PK). This was performed one year after the initial diagnosis. Visual acuity (VA) 1 month after surgery had improved on OS from 20/200 to 20/50. Follow-up was made through corneal topography, showing significant improvement, with a maximum keratometry value of 61.5D, and minimal corneal thickness of 564 µm at year 3 after the surgery (Figure 2). Current topographic values (Figure 3) show maximum keratometry value of 61.3D, and minimal corneal thickness of 550 µm, in this case 7 years after the surgery. Postoperative treatment consisted in topical ciprofloxacin 1 drop/4h, topical dexamethasone/3h, oral ciprofloxacin 500mg/12h and Prednisone 30mg/24h. An anterior pole image was successfully achieved at month 3 after the surgery, showing corneal transparency, no tyndall, no keratic precipitates, and no new vessel formation.

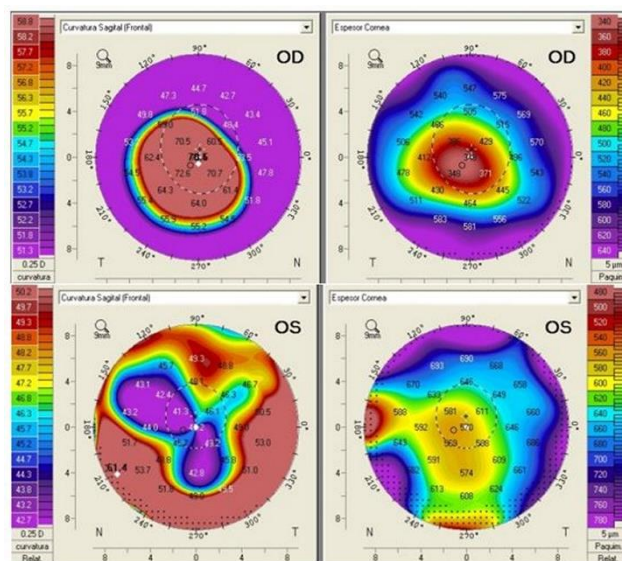


Figure 2: Corneal topography on first follow-up, year 4 after the diagnosis, showing progression of keratoconus on OD, with maximum keratometry value of 78.5D (a) and minimal corneal thickness of 335 µm (b). OS shows a maximum keratometry value of 61.5D (c) and minimal corneal thickness of 564 µm (d).

In regards to OD, a progression of the keratoconus was detected on routine follow-up (Figure 2), precisely 4 years after the initial diagnosis, with her keratometry maximum value increasing to 78.5D and minimal corneal thickness decreasing 335 µm (image 2). A deep anterior lamellar keratoplasty (DALK) was performed on OD. VA after the surgery went from 20/200 to 20/63 four months after the operation. Follow-up was also made through corneal topography, with keratometry values at the present time (showing maximum keratometry of 64.6D and minimal corneal thickness of 444 µm at year 2 after the OD surgery (Figure 3). Postoperative treatment consisted in a topical combination of Tobramicine + Dexamethasone applied topically every 4 hours, and Prednisone 45mg/24h orally. Subsequent to the topical corticosteroid treatment used throughout the surgery and on post-operative treatment, our patient seemed to develop two complications on OD. First, a steroid-induced glaucoma, which was clinically diagnosed on follow-up through a Goldmann Applanation Tonometer, with pressures oscillating between 42-44mmHg, and later confirmed on Heidelberg Eye Explorer optical coherence tomography, through a nerve fiber loss most acute on the superior and inferior quadrants. Treatment was successfully achieved with a combination of bimatoprost/timolol and brimonidine and brinzolamide. And secondly, a posterior subcapsular cataract. In this case, using the biometric formula SRK/T (T for theoretical), a phacoemulsification was performed, with the implant of an intraocular lens (IOL) Tecnis®+16D.

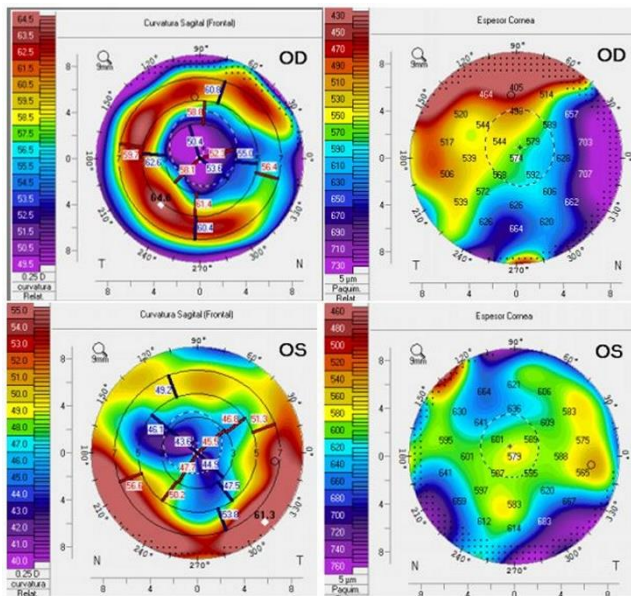


Figure 3: Corneal topography on our last follow-up, year 8 after the diagnosis, showing maximum keratometry value on OD of 64.6D (a), and minimal corneal thickness of 444µm (b). On OS maximum keratometry value is 61.3D (c) and minimal corneal thickness of 550µm.

At the present time, our patient is able to see OD sph-3,25 cyl-3 axis 90=20/32 and OS sph 1,25 cyl-2,5 axis 135=20/25, using the Snellen Chart, and maintenance treatment consists of dorzolamide every 12h and fluorometholone once daily, on oculus uterque (OU). The patient's last keratometric values can be seen on Figure 3.

3. DISCUSSION

Many ophthalmic manifestations have been described in association with PRS. These include high congenital myopia, strabismus, Möbius syndrome, congenital glaucoma and retinal detachment. In our case report, we describe a patient diagnosed with Pierre Robin syndrome, who also presented keratoconus [1, 9].

Keratoconus is a condition relatively common in general population. Prevalence of keratoconus have been estimated to be between 0.2 and 4,790 per 100,000 persons, with the highest incidence rates typically occurring in 20 to 30 year old. The prevalence varies greatly according to the different geographical areas, being much higher in Asia and Middle East and lower in Nordic countries [10].

The etiology of keratoconus remains unknown. It is usually acquired sporadically, although a few cases have been described of either autosomal dominant or recessive inheritance. Other factors that predispose to keratoconus include rubbing of the eyes or atopic dermatitis, as well as

allergies [11].

Management and treatment of the disease is different depending on the severity. Mild cases can be treated with spectacles, although the patient often does not report good visual acuity due to irregular astigmatism. Rigid contact lenses are the preferred option in moderate keratoconus, including the piggyback systems and corneoscleral rigid lenses. In our case, the disease was too advanced to consider the previous options and surgical intervention was necessary. Corneal transplantation is the most frequent treatment for severe keratoconus, mostly penetrating keratoplasty or DALK. In addition, a close monitoring of the disease must be done, to avoid arriving to severe stages. When progression cannot be stopped with conservative options, corneal cross-linking may be performed.

Keratoconus is present in many ophthalmic as well as systemic manifestations, but to date, the cases reported of keratoconus and Pierre Robin sequence are very limited [12]. Our case description demonstrates that ocular manifestations are important but understudied contributors to disease burden in this patient population.

To conclude, patients diagnosed of Pierre Robin sequence complaining of poor vision should be examined through corneal topography for keratoconus, as well as more frequent ophthalmic manifestations. Early diagnosis is of special interest, since it could prevent both deterioration of visual acuity, and future needs of surgery and general anesthesia, avoiding intubation in subjects where micrognathia and glossoptosis impair airway management.

4. CONFLICT OF INTERESTS

The authors have no conflict of interest to declare. The authors declared that this study has received no financial support.

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