

## **Severe keratoconus: watch out for complications!**

### **ABSTRACT :**

Keratoconus is an evolving condition. The speed and severity of the course differs from patient to patient. We report the clinical observation of a 36-year-old patient with a history of severe atopy and who presents a neglected bilateral keratoconus. The clinical examination found sign of Munson Rizzuti, the corneal protrusion being more marked in the left eye. Biomicroscopic examination revealed corneal opacity in the central right eye with marked corneal protrusion and thinning. In the right eye, there was stromal corneal opacity with neovascularization, superficial and deep scar lines, epithelial microcystic edema and an intrastromal cyst. This finding correspond to anterior segment OCT Sandali stage 4 in both eyes. Penetrating keratoplasty was proposed to the patient for treatment. Subconjunctival injections of 2.5 mg bevacizumab were also undertaken at 1 month intervals. The advent of modern imaging techniques has enabled early diagnosis of keratoconus as well as its monitoring and screening for complications. New classifications aim to stage the pathology and to better codify the management. The most serious complication is the occurrence of corneal hydrops. Adequate management of the latter avoids complications including fibrosis and neovascularization, which improves the prognosis of a subsequent keratoplasty which remains the last resort in these patients.

**Keywords: Advanced Keratoconus; Hydrops; Neovascularization; Keratoplasty**

### **INTRODUCTION :**

Keratoconus is a progressive disease characterized by thinning and protrusion of the cornea. Involvement is irregular and asymmetrical in the majority of cases [1]. The evolution of Keratoconus remains unpredictable and variable. The evolution of topographic, tomographic and biomechanical corneal imaging techniques helps to better understand the pathology and to better codify management.

We report a clinical case of a 36-year-old woman with a history of severe atopy who presented with severe bilateral keratoconus.

We aim to report a serious case of spontaneous evolution of keratoconus towards neovascularization and fibrosis, and to show the seriousness of the patient's therapeutic non-compliance in these cases of progressive keratoconus. This manuscript aims is also to objectify the mandatory role of imaging (OCT of the cornea) to classify and objectify the severity of the pathology as well as to plan an adequate management.

### **CASE PRESENTATION :**

This is a 36-year-old patient with a history of severe atopy who has had a decline in visual acuity for 9 years, aggravated 3 years ago by photophobia and bilateral eye pain. Visual acuity was reduced to near counting fingers on the left and 1/6 on the right with normal IOP. The clinical examination found sign of Munson Rizzuti, the corneal protrusion being more marked in the left eye (Figure 1 a and b). Biomicroscopic examination revealed corneal opacity in the central right eye with marked corneal protrusion and thinning. In the right eye, there was stromal corneal opacity with neovascularization, superficial and deep scar lines, epithelial microcystic edema and an intrastromal cyst (Figure 2 a and b). Midstromal neovessels forming vascular trees with loops at their ends (Figure 3a and b). The patient was put on topical steroids.

We proposed an injection of anti-VEGF in the left eye and a corneal transplant. The patient was then lost to sight for 2 years. Examination found the same visual acuity with worsening stromal fibrosis and neovascularization of the left eye. Refraction is impossible in both eyes. The average keratometry of the right eye is at 79.5 D and that of the left eye at 103.5 D. The maximum keratometry is at 94.2 D at the level of the right eye and at 171 D at the level of the left eye. Central corneal pachymetry of the right eye is 178  $\mu$ m and not measurable at the level of the left eye. This correspond to a stage 4 keratoconus of the Amsler-Krumeich classification in both eyes (Figure 4). Corneal pentacam topography was uninterpretable given the corneal opacity. Anterior segment OCT objectified in the right eye a thickening of the epithelium with hyperreflectivity of Bowman's membrane and a stromal scar, corresponding to Sandali stage 4. The OCT of the left eye shows a significant modification of the corneal structure with scarring and panstromal fibrosis with a residual aspect of the rupture of Descemet's membrane, which corresponds to stage 5B of the Sandali classification (Figure 5). Penetrating keratoplasty was proposed to the patient for treatment. Subconjunctival injections of 2.5 mg bevacizumab were also undertaken at 1 month intervals.

#### **DISCUSSION :**

“Keratoconus is a progressive, symmetrical, asymmetrical ectatic disease that causes progressive thinning and protrusion of the cornea resulting in irregular astigmatism and decreased visual acuity” [2]. “Keratoconus usually begins at puberty and tends to progress until the third or fourth decade of life. The progression of keratoconus varies between individuals and is more accelerated in younger patients. Spontaneous stabilization can be achieved approximately 20 years after the initial presentation” [3].

“Advanced or severe keratoconus may grade towards corneal hydrops following a rupture of Descemet's membrane. This rupture leads to stromal edema and potentially serious corneal scarring” [4]. “Detecting the disease in the early stages is essential to halt progression. Over the past decade, significant advances have been reported in the diagnosis and management of keratoconus” [5].

“Corneal topography and tomography (Scheimpflug imaging or anterior segment optical coherence tomography, OCT) allow (unlike older techniques) assesment of the anterior and posterior face of the cornea, can provide epithelial imaging and analysis of the anterior

segment” [6]. “Advances in technology have changed classification systems. The Amsler-Krumeich classification (Table 1), although still valid, does not combine topographic and tomographic indicators or maps and biomechanical parameters. The combination of topographic, tomographic and biomechanical information provides valuable information for the diagnosis and treatment of keratoconus such as Belin-Ambrosio Enhanced Ectasia” [7-8]. “The progression of keratoconus is defined by a modification of at least two of the following parameters (according to the Global Consensus on Keratoconus and ectatic Diseases): Increase in the curvature of the anterior corneal surface; The increase in curvature of the posterior corneal surface; Thinning and/or increased rate of change in corneal thickness” [9].

“Through the use of anterior segment OCT, Sandali and coauthors described a new classification based on the progressive corneal changes occurring in keratoconus throughout the course of the disease, classifying the severity of the disease”[10]. A recent study compared the Amsler-Krumeich classification and Sandali (Table 1). “The results of this comparative study were that the Amsler-Krumeich classification is more appropriate for identifying and longitudinally following patients with early stages of KC, while the Sandali classification for diagnosing and monitoring patients with later stages. advanced, especially when surgical planning must be chosen” [11].

Crosslinking is the treatment that aims to stop the progression of keratoconus, thus avoiding the need for a corneal transplant. “Conventional CXL is recommended in eyes with a corneal thickness of at least 400 microns after de-epithelialization to avoid endothelial toxicity. However, most keratoconic corneas requiring CXL may not meet this preoperative inclusion criterion. Moderate to advanced cases often present with pachymetry below this threshold. There are various modifications to the conventional method to circumvent this problem of thin corneas” [12].

Concerning keratoplasty in advanced cases of keratoconus, penetrating keratoplasty appeared until recently, the treatment of choice. However, technical improvements have increased the popularity of DALK given its advantages (lower risk of rejection, preservation of endothelial cells, avoidance of open surgery and shorter duration of postoperative treatment) [13]. The limits of this attractive technique remain corneal opacities, neovascularization and hydrops [14]. Studies comparing the two techniques report different results regarding the visual outcome of the two techniques. Some of these studies report more satisfactory results of KT, which can be explained by the depth of the DALK dissection [15-16].

The most threatening complication of these cases of advanced and potentially aggressive keratoconus is the occurrence of hydrops. Hydrops is the development of stromal edema due to descemetic breach manifested by acute loss of visual acuity, photophobia and pain [17]. This is a complication observed in 3% of cases of keratoconus [18]. Different risk factors for corneal hydrops include early onset age, eye rubbing, vernal keratoconjunctivitis, atopy, and Down syndrome [19]. It is a condition that usually resolves without intervention within 2 to 4 months, during which time the patient's vision and comfort are therefore compromised. The longer duration of edema is also more likely to lead to complications such as

neovascularization [20]. Treatment regimens for acute corneal hydrops can be divided into conservative, medical, and surgical options.

Medical or conservative treatment is based on the proposed topical, hypertonic saline solution, cycloplegics, topical corticosteroids and positioning in the supine position allows endothelial redistribution on the ruptured descemet. The known time frame for full resolution can take 5 to 36 weeks. This delay depends on the extent of the descemetic tear. However, treatment with subconjunctival injections of anti-VEGF or eye drops can be promising [19].

Pneumodescemetopexy reduces the duration of corneal edema and the risk of complications such as corneal neovascularization, which can compromise subsequent keratoplasty [21]. For more severe cases, compression sutures can be added to intracameral gas injection to improve healing [22]. Thermokeratoplasty is a technique used in the treatment of hydrops, it induces contraction of the central cornea and flatten the prominent cone, accelerates closure of descemet membrane ruptures and prevents further influx of aqueous humor through the membrane of descemet in the intrastroma and leads to rapid absorption of corneal edema, closure of the descemet membrane and scarring of the corneal stroma. Healing of the descemetic breach (noted from the second week) reduces the risk of perforation during DALK [23]. Amniotic membrane transplantation and TKP can also be used in certain situations [24]. Although beneficial, none of these procedures improve final visual acuity and many patients will ultimately require corneal transplantation for visual rehabilitation. PKP, DALK, DSAEK and DMEK have all been used successfully in different contexts of acute hydrops.

### **CONCLUSION :**

Keratoconus is a progressive and asymmetrical condition. Advances in imaging have enabled early diagnosis and facilitated treatment. However, unscheduled cases continue to be seen in consultation. Advances in imaging, in particular OCT of the anterior segment, have enabled a new classification (the Sandali classification) to better codify management. Effective management of acute corneal hydrops in keratoconus relies on recognition and management of risk factors, prompt and effective treatment of the acute event to reduce the duration of edema and its complications, and ultimately a successful corneal transplantation with acceptable long-term survival rates. Finally, keratoplasty remains the last resort in these advanced stages of keratoconus. Screening and early treatment is the only way for us to prevent an evolution towards complications

### **Consent**

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

### **Ethical Approval:**

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

## **ABBREVIATIONS LIST :**

**DALK: Deep lamellar anterior keratoplasty**

**PKP: Penetrating keratoplasty**

**DSAEK: Descemet Stripping Automated Endothelial Keratoplasty**

**DMEK: Descemet Membrane Endothelial Keratoplasty**

**CXL: crosslinking**

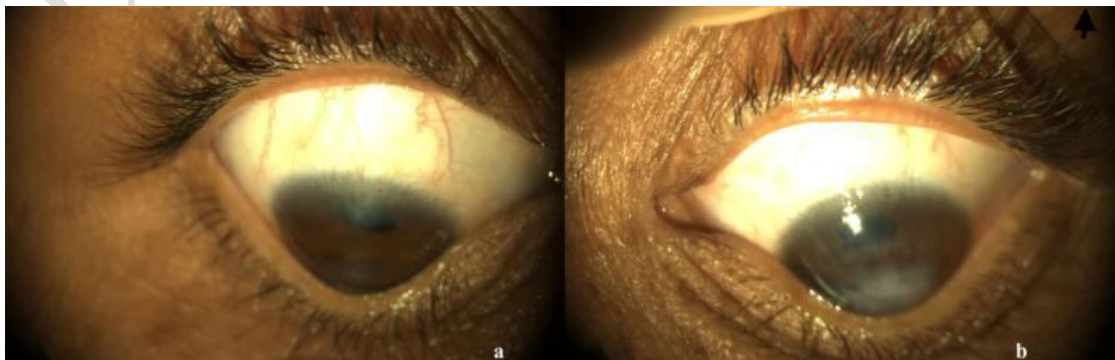
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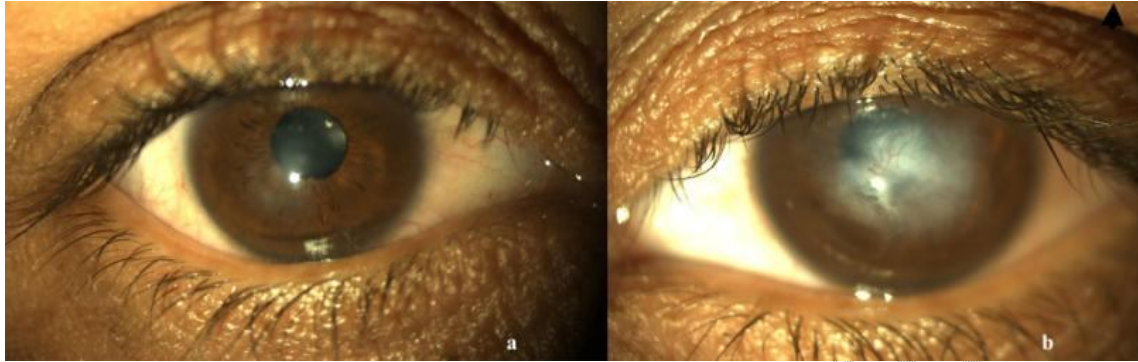
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**Table 1: Comparison of Amsler-Krumeich and Sandali classifications[11].**

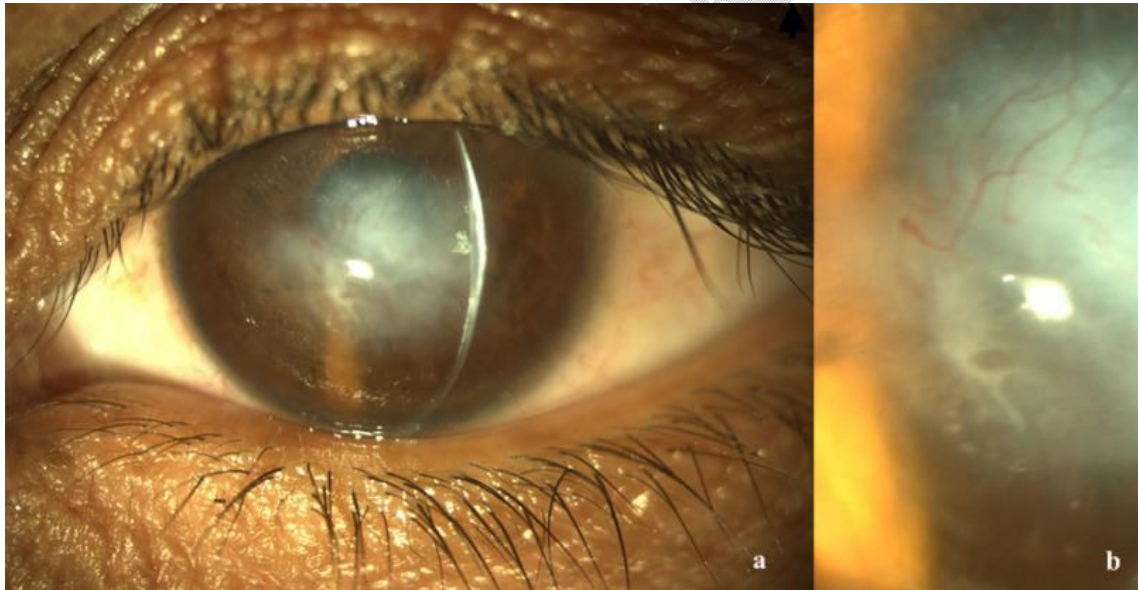
Amsler-Krumeich Classification	Sandali Classification
<b>STAGE 1</b> <b>Myopia/astigmatism with eccentric curvature &lt; 5.00 D</b> <b>Mean keratometry value &lt; 48.0 D</b>	<b>STAGE 1</b> <b>Thinning of the epithelial and stromal layers at the level of the cone</b> <b>Normal-appearing corneal layers</b>
<b>STAGE 2</b> Myopia/astigmatism > 5.00 D but < 8.00 D Mean keratometric value < 53.0 D Absence of scars Minimum apical corneal thickness > 400 m	<b>STAGE 2A:</b> <b>Bowman's layer hyperreflectivities with epithelial thickening</b> <b>STAGE 2B:</b> <b>Hyperreflectivities at Bowman's layer with epithelial thickening and stromal opacities</b>
<b>STAGE 3</b> Myopia/astigmatism > 8.00 D but < 10.00 D Mean keratometric value > 53.0 D Absence of scars Minimum apical corneal thickness < 400 m but > 300 m	<b>STAGE 3A:</b> <b>Posterior displacement of hyperreflective structures at Bowman's layer with increased epithelial thickening</b> <b>Stroma thinning</b> <b>STAGE 3B:</b> <b>Posterior displacement of hyperreflective structures at Bowman's layer with increased epithelial thickening</b> <b>Stromal thinning and presence of stromal opacities</b>
<b>STAGE 4:</b> <b>Refraction not possible</b> <b>Mean keratometric value &gt; 55.0 D</b> <b>Central corneal scar</b> <b>Minimum apical corneal thickness &lt; 300 m</b>	<b>STAGE 4:</b> <b>Panstromal scar</b> <b>STAGE 5A:</b> <b>Acute onset with rupture of Descemet's membrane and tearing of collagen lamellae, large fluid-filled intrastromal cysts and formation of epithelial edema</b> <b>STAGE 5B:</b> <b>Healing stage of 5A with panstromal healing with residual appearance of Descemet's membrane rupture.</b>



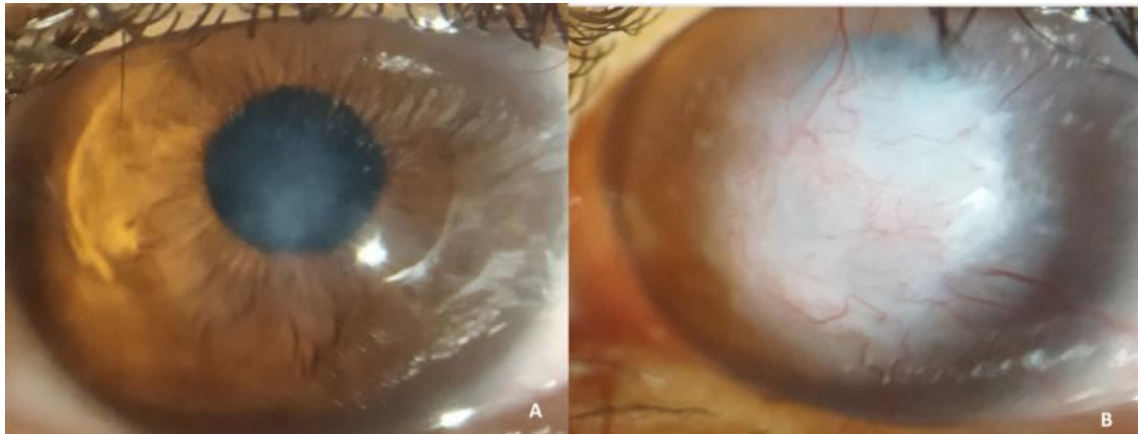
**Figure 1: Munson Rizzuti's sign: Corneal protrusion causes angulation of the lower eyelid when the patient looks down. Corneal protrusion in round cone or nipple. a: Right eye; b: Left eye.**



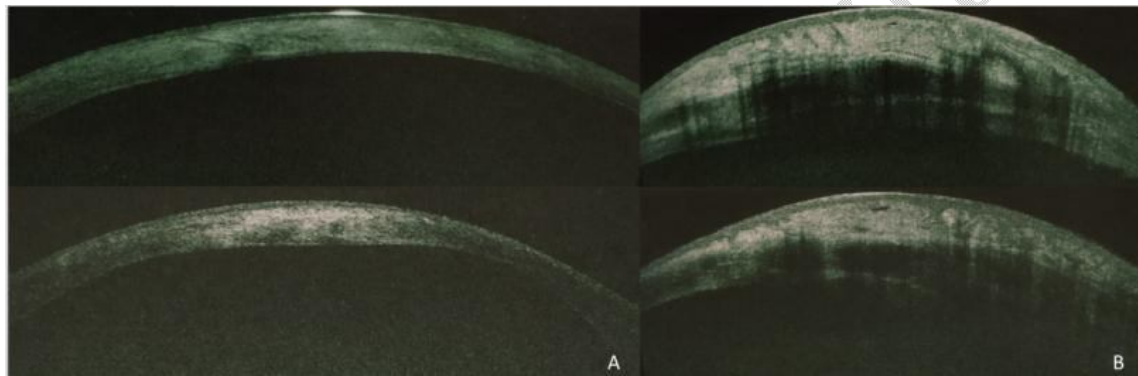
**Figure 2: Stage 4 bilateral Keratoconus with sequelae of hydrops in the left eye: significant corneal opacity with neovascularization. a: Right eye; b: Left eye.**



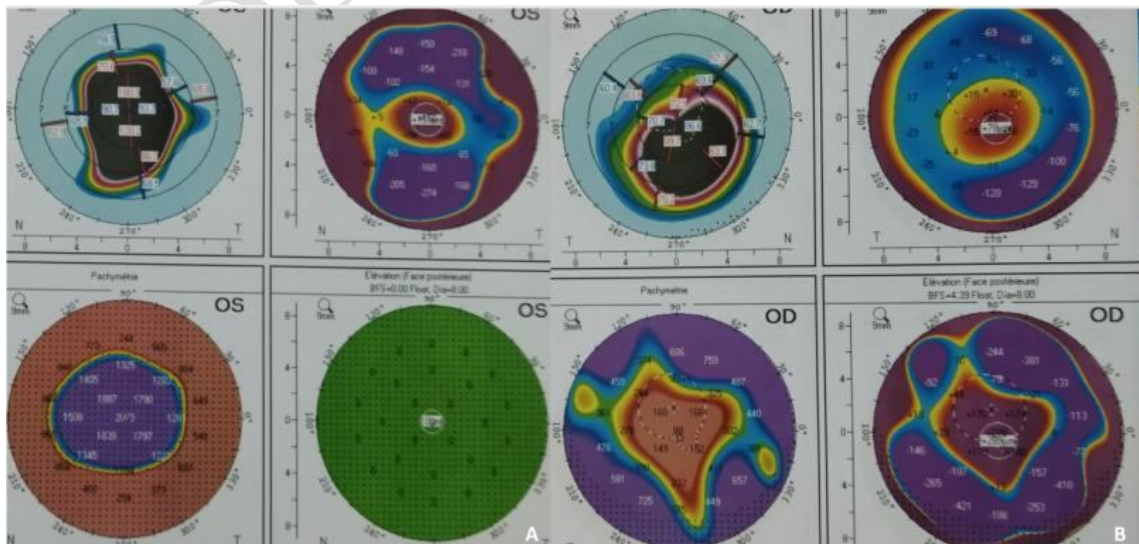
**Figure 3: Midstromal neovascularization forming vascular trees with loops at their ends, epithelial microcystic edema and intrastromal cyst.**  
a: Left eye; b: At high magnification.



**Figure 4: Worsening left eye corneal neovascularization and stromal fibrosis. A: Right eye; B: Left eye.**



**Figure 5: OCT of cornea: A: right eye: Thickening of the epithelium with hyperreflectivity of Bowman's membrane and a stromal scar, corresponding to Sandali stage 4. B: Left eye: significant modification of the corneal structure with scarring and panstromal fibrosis with residual aspect of the rupture of Descemet's membrane, which corresponds to stage 5B of the Sandali classification.**



**Figure 6: Topography (Pentacam) rendered uninterpretable by corneal opacities. A: Right eye; B: Left eye.**

UNDER PEER REVIEW