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Case Report

# Deep Anterior Lamellar Keratoplasty in a patient with Mucopolysaccharidosis Type VII (Sly Disease)

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## Abstract

**Purpose:** To describe intraoperative anterior segment optical coherence tomography (ASOCT)-assisted deep anterior lamellar keratoplasty (DALK) in a teenage patient with corneal opacity due to mucopolysaccharidosis (MPS) type VII (Sly disease).

**Method:** Case report.

**Results:** A 15-year-old boy with known history of MPS type VII presented with bilateral worsening cornea opacity. Intraoperatively, ASOCT demonstrated near full thickness corneal opacity in the right eye. Once the anterior stromal opacity was manually dissected, the big-bubble DALK technique was successfully carried out under intraoperative guidance of ASOCT. The donor cornea was sutured in the recipient bed with intact Descemet's membrane. AS OCT-assisted DALK was carried out in the left eye six months later. The grafts remained clear at 18 month and 12-month post-operative visit, for the right and the left eyes, respectively.

**Conclusion:** This is the first reported DALK performed in a case of corneal opacity due to MPS type VII. Intraoperative anterior segment OCT provides useful information throughout crucial steps of the surgery in such cases with poor visualization. DALK is a viable surgical option for the patients with MPS type VII.

**Keywords:** Mucopolysaccharidosis type VII, Sly disease, Congenital corneal opacity, Deep anterior lamellar keratoplasty, Anterior segment optical coherence tomography

## Introduction

Mucopolysaccharidosis (MPS) VII, also known as Sly disease (OMIM 253220) is an autosomal recessive lysosomal storage disorder that results from a deficiency of β-D-glucuronidase (GUS) [1]. The enzyme is involved in the degradation of glycosaminoglycans (GAG) dermatan sulfate, heparan sulfate and chondroitin sulfate [2]. In the absence of functional GUS, the three types of GAG accumulate in the lysosomes of widespread tissues and lead to multiple organ dysfunction.

MPS VII shares clinical features similar to other mucopolysaccharidoses, such as MPS I (Hurler's, Hurler-Scheie, Scheie) and MPS II (Hunter) [3]. Most patients with MPS VII exhibit skeletal dysplasia (dystosis multiplex, loss of joint range of motion, restricted mobility, spine deformities), short stature, hepatosplenomegaly, coarse facies, decreased pulmonary function and cognitive impairment [3]. However, the phenotypes of MPS VII vary widely ranging from mild to severe, antenatal form [3-5].

The ocular manifestations of MPS VII include corneal clouding, heavy brows, visual impairment, optic nerve abnormalities, photosensitivity and refractive error [3,6]. Corneal opacification is the predominant ocular feature in MPS VII patients present in 50% of MPS VII patients [3]. Corneal clouding in MPS VII are typically moderate. This is distinct from severe corneal clouding seen in MPS I (Hurler's) and MPS VI (Maroteaux-Lamy) [6]. Glaucoma and retinopathy have not been described in MPS VII but the ERG changes has been documented in a 16 year-old male patient with moderate MPS VII [7].

In this report, we present a case of deep anterior lamellar keratoplasty (DALK) in a 15-year-old boy with MPS VII and corneal clouding, guided by intraoperative anterior segment optical coherence tomography (AS-OCT). This is the first reported case of DALK in MPS VII.

## Case Report

A 15-year-old boy with history of MPS VII was referred to the pediatric cornea at the Westchester Medical Center for the evaluation of bilateral corneal clouding. He manifested a constellation of medical problems related to MPS VII including kyphoscoliosis, chronic obstructive pulmonary disease and developmental delay. He had undergone multiple surgeries including gastrostomy, tracheostomy and cervical spine fusion. There was no history of enzyme replacement therapy or hematopoietic stem cell transplant. Corneal clouding has been noted to worsen progressively since birth.

On ophthalmologic exam, the uncorrected visual acuity was hand motions in each eye. The intraocular ocular pressure was 26 mmHg and 18 mmHg in the right and left eye, respectively. The pachymetry was 758 μm in the right and 769 μm in the left eye. The external exam revealed telecanthus and epicanthus inversus. The slit-lamp examination showed bilateral diffuse corneal clouding with no visible iris stranding. The anterior chamber was deep and quiet in each eye. The dilated fundus exam was limited due to corneal opacity. The right eye had normal red reflex; the left eye had blunted red reflex.

DALK of the right eye with intraoperative AS-OCT assistance was planned. The standard anterior segment protocol of intraoperative AS-OCT (Rescan, Carl Zeiss Meditec, Jena, Germany) was used. The corneal opacity on AS OCT was identified to be approximately 90% of thickness but was denser in the anterior 50% of the stroma (Figure 1A). The cornea was partially trephined with a 7mm recipient blade, and the manual dissection was performed until the stromal opacity was largely removed. Then, a Fogla cannula was introduced into the stroma. The intraoperative AS-OCT was used to guide the depth of the cannula. Once the pre-Descemet's level of depth was confirmed on AS-OCT, air was injected successfully creating a big bubble. AS-OCT confirmed the separation of the stroma from the Descemet's membrane (Figure 1B). All stroma anterior to the bubble was excised using Wescott scissors (Figure 1C). Then, the donor cornea, after removal of the corneal endothelium, was trephined to 7.50 mm and placed on top of the patient's cornea and sutured to the recipient bed with 10-0 nylon sutures. The intraoperative AS-OCT was used to confirm all layers of the cornea were intact at the end of the case (Figure 1D).

The surgical pathology reported Alcian blue staining of the excised cornea more vibrant in the anterior stroma. The sutures were

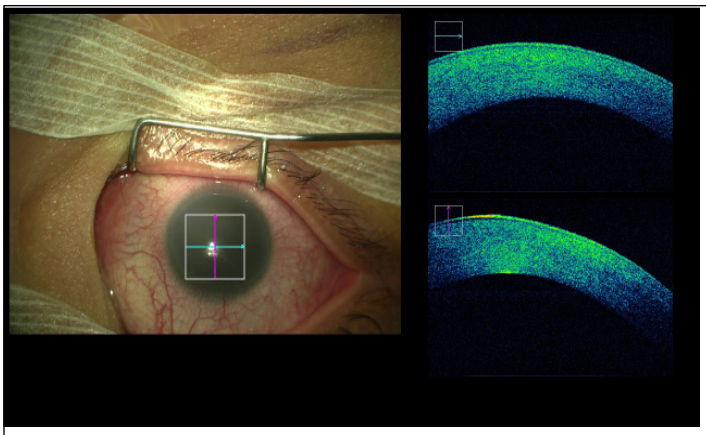

**Figure: 1-A**

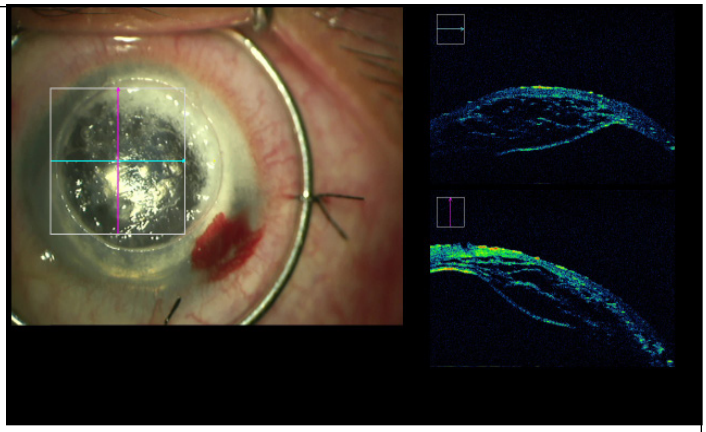

**Figure: 1-B**

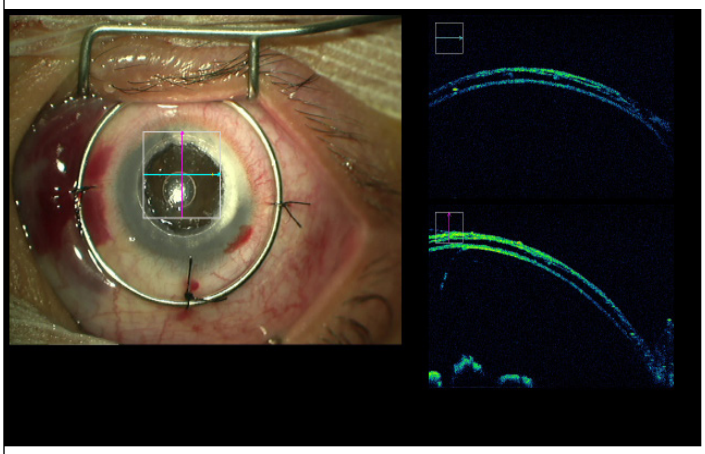

**Figure: 1-C**

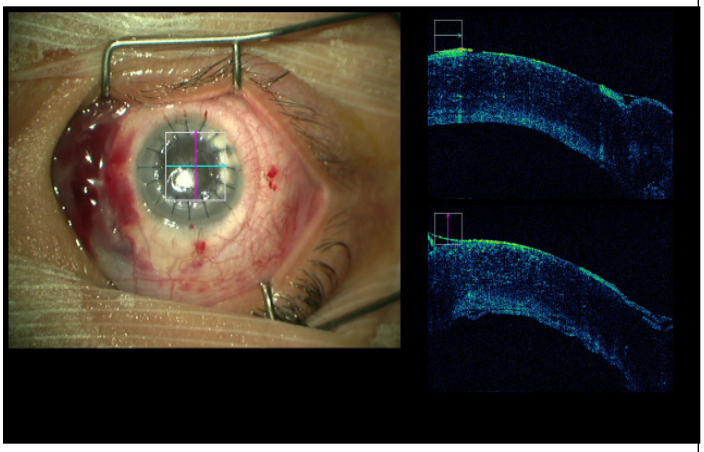

**Figure: 1-D**

**Figure 1: Intraoperative images obtained during deep anterior lamellar keratoplasty (DALK) of patient with mucopolysaccharidosis type VII.**
**A. Photograph and anterior segment optical coherence tomography (AS-OCT) show corneal opacity dense in the anterior stroma prior to keratoplasty.**
**B and C. Intraoperative photograph and AS-OCT confirm the separation of Descemet membrane following air injection and removal of corneal stroma.**
**D. Intraoperative photograph and AS-OCT demonstrate all layers of cornea after completion of DALK.**

removed seven months post-operatively. At the 18-month postoperative visit, patient had clear graft with no sign of rejection in the right eye (Figure 2A). The left eye also underwent AS OCT-assisted DALK with clear graft at one-year post-operative visit (Figure 2B).

## Discussion

MPS VII is one of the rarest MPS diseases with only 144 reported cases since its first description in 1973 [2,8]. The estimated incidence is between 1 in 200,000 births and 1 in 350,000 births [3]. Because of its rarity, its epidemiologic data are sparse, and its clinical characterization has been limited.

Recently, an international survey of 56 patients presented valuable information on its wide phenotypic spectrum [3]. This study demonstrated that the most severe form of MPS VII present with non-immune hydrops fetalis, often in the antenatal period These

**Figure: 2-A**

**Figure: 2-B**

**Figure 2: A. An external photograph shows clear graft of the right eye 18 months after deep anterior lamellar keratoplasty (DALK). B. An external photograph demonstrates clear graft of the left eye 12 months after DALK.**

severe cases commonly result in a stillborn or death shortly after birth due to heart, kidney or respiratory failures [2,3]. A moderate phenotype is typically diagnosed in early childhood with or without history of non-immune hydrops fetalis. Patients have varying combinations and severity of coarse facial features, corneal clouding, frequent respiratory infection, short stature, skeletal dysplasia, macrocephaly, hepatomegaly, hernia and mental retardation. The survey also showed that the high proportion of hydrops fetalis is the important clinical feature that distinguishes MPS VII from other types of MPS. It, however, also does not predict the severity of the disease: 13 out of 23 with prenatal onset disease survived into the late teens with a mild to intermediate course [3]. While most patients with MPS VII have shortened lifespan, patients with mild MPS VII have been reported to survive into the middle age [3].

Corneal clouding is one of the early signs of MPS VII and develop in MPS VII patients of all severities. Chondroitin sulfate and dermatan sulfate hybrids are the main GAG between collagen fibrils forming cornea lamellae [9]. It has postulated that the over-abundance of these two GAG play a role in corneal clouding in MPS VII [10]. While the exact mechanism of the corneal opacity is to be elucidated, electron microscopy and electron tomography findings (poorly-defined Bowman's layer, diffuse epithelial basal lamina, stromal keratocyte enlargement, extracellular accumulation of GAG, non-uniform collagen fibril diameters, elongated proteoglycan) suggested the GUS deficiency alters interfibrillar and fibrillary extracellular organization, leading to corneal opacity [10].

The wide range of phenotypes and progressive nature of MPS VII drive the evaluation and management of corneal clouding individualized to each patient's need. Basic ocular evaluation includes the assessment of best-corrected visual acuity, binocular function, color vision, visual field, intraocular pressure, slit lamp exam and fundus evaluation. The worsening corneal opacity can also be monitored using the Iris camera corneal opacity measure (COM) score as shown in patients with MPS I or VI [11].

There is only one report of surgical intervention for corneal clouding in patients with MPS VII beside this study. Bergwerk et al. [12] described a 15 year-old male who underwent penetrating keratoplasty. The graft remained clear for two years, until the time of publication [12]. Penetrating keratoplasty in many MPS types has

been reported to be successful [13]. Recently, however, DALK has gained a favor over PK for MPS patients [13,14]. DALK preserves the endothelium avoiding the possibility of endothelial rejection associated with penetrating keratoplasty [15]. The reported cases of DALK, thus far, have shown a varying degree of successful "big-bubble" in the cases of MPS [13,14,16]. The additional technical difficulty is thought to be related to the rigidity of MPS corneas. The intraoperative use of AS OCT, as shown in this case, provides a distinct advantage in executing DALK by allowing the assessment of the depth of lamellar dissection and the status of the Descemet's membrane throughout the procedure [17].

In addition to supportive measures, hematopoietic stem cell transplant (HSCT) and enzyme replacement therapy (ERT) are now the mainstay of therapy in many MPS diseases [18]. Both HSCT and ERT have been administered in MPS VII patients [5,19]. The efficacy of HSCT has not been conclusive due to scarcity of data. Recombinant human β-glucuronidase was approved by the Food and Drug Administration in November of 2017 for adult and pediatric patients with MPS VII [5]. The early studies with ERT with Rh GUS have shown to decrease urine GAG levels with the administration of Rh GUS and also improve pulmonary function and also quality of life in general [19]. It is unknown whether corneal clouding is changed with ERT in MPS VII patients. The effects of HSCT and ERT in corneal clouding in other MPS types have been variable [5,9,11].

## Conclusion

In summary, we present a rare case of corneal clouding due to MPS VII successfully treated with DALK assisted by intraoperative AS OCT. As the early diagnosis and therapy improve for MPS VII patients, decreased vision from corneal clouding will become an important aspect to manage the quality of life. While there is not enough number to make a conclusion, we believe that DALK is an excellent option for patients with MPS VII.

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