

# A Case of Bilateral Descemet's Membrane and Subepithelial Opacity: In vivo Laser Confocal Microscopic Study

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## Key Words

Descemet's membrane opacity · Subepithelial opacity · Confocal microscopy

## Abstract

**Purpose:** To report the in vivo laser confocal microscopy findings from a patient with Descemet's membrane and subepithelial opacity OU. **Case Report:** A healthy 41-year-old male with Descemet's membrane and subepithelial opacity OU was studied. Routine ophthalmic examination, standard slit-lamp biomicroscopy, and in vivo laser confocal microscopic analysis of the entire corneal layer were performed. Slit-lamp biomicroscopy revealed subepithelial opacity in the mid-peripheral to peripheral cornea and numerous opacities located at the level of Descemet's membrane. It was difficult to distinguish the precise histological location of the opacity. In vivo laser confocal microscopy showed numerous hyperreflective particles in the subepithelium to superficial stroma and hyperreflectivity of Descemet's membrane. No abnormalities could be detected in the epithelial cell layer, midstromal layer, deep stromal layer, or endothelial cell layer. **Conclusion:** Although the origin of the corneal opacities was unclear, in vivo laser confocal microscopy was useful for observing microstructural abnormalities in a case of Descemet's membrane and subepithelial opacity.

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## Introduction

At the level of the cornea which corresponds to the deep stroma and Descemet's membrane, abnormal materials can be deposited in many disorders, including Wilson's disease (copper), chalcosis (copper), chrysiasis (gold), argyrosis (silver), mottled cyan opacification, cornea farinata, pre-Descemet's membrane corneal dystrophy, fleck dystrophy, X-linked ichthyosis, and polymorphic amyloid degeneration [1, 2]. In these conditions, the detection of the precise histological deposit location is not always easy to obtain using slit-lamp biomicroscopy.

We report the in vivo laser confocal microscopy findings in a rare case of Descemet's membrane and subepithelial opacity OU, in which pre-Descemet's membrane corneal dystrophy and corneal argyrosis were excluded.

## Case Report

The present study was approved by the Ethical Committee of Kanazawa University Graduate School of Medical Science and followed the tenets of the Declaration of Helsinki. In January 2010, a corneal opacity OU was detected in a healthy 41-year-old male by his primary ophthalmologist when the patient was treated for hordeolum in the left eyelid. He was referred to Kanazawa University hospital for corneal opacity OU in May 2010. At the initial visit, his best-corrected visual acuity was 20/16 OD and 20/16 OS. Intraocular pressure was 17 mm Hg OD and 16 mm Hg OS. Central corneal thickness was 633  $\mu\text{m}$  OD and 648  $\mu\text{m}$  OS. Endothelial cell density was 2,336/ $\text{mm}^2$  OD and 2,352/ $\text{mm}^2$  OS. Slit-lamp biomicroscopy revealed a subepithelial opacity in the mid-peripheral to peripheral cornea OU and numerous opacities located at the level of Descemet's membrane OU; however, it was difficult to distinguish precisely the location of the opacity (i.e. deep stroma or Descemet's membrane) (fig. 1). No abnormal findings were noted upon fundus examination. In vivo laser confocal microscopy (Heidelberg Retina Tomograph 2 Rostock Cornea Module, Heidelberg Engineering GmbH, Dossenheim, Germany) showed numerous hyperreflective particles in the subepithelium to superficial stroma OU (fig. 2c, d) and hyperreflectivity of Descemet's membrane OU (fig. 2h). No abnormal findings were noted in the epithelial cell layer, midstroma, deep stroma, and endothelial cell layer (fig. 2a, b, e–g, i). The patient had been a soft contact lens user for 16 years. Although his used soft contact lens OU showed a brown discoloration, metal deposition was not detected with differential interference contrast microscope (fig. 3b). The patient had no skin disorders, no history of metal exposure, and no family history of corneal diseases. He had taken an alpha lipoic acid-containing dietary supplement for a 1-year period in 2005. No abnormal findings were noted on blood testing including serum copper, liver and renal function. Based on the clinical appearance and in vivo laser confocal microscopy findings, a differential diagnosis of pre-Descemet's membrane corneal dystrophy and corneal argyrosis was excluded, but the clinical diagnosis was unclear. Visual acuity, clinical symptoms, and degree of corneal opacity did not change in the 1-year follow-up period in this case of Descemet's membrane and subepithelial opacity OU with unknown origin.

## Discussion

In this study, we reported a rare case of corneal opacity OU in a healthy 41-year-old male without visual disturbance. As a result, a differential diagnosis of pre-Descemet's membrane corneal dystrophy and corneal argyrosis was excluded; however, the clinical diagnosis was unclear (table 1).

Pre-Descemet's membrane corneal dystrophy, corneal farinata, and fleck dystrophy can present as tiny opacities of deep stroma usually without concomitant visual disturbance [2–10]. Pre-Descemet's membrane corneal dystrophy on slit-lamp examination shows larger and more polymorphous opacities than those of cornea farinata, which is more often considered an age-related degeneration [3, 4]. Fleck dystrophy is a rare autosomal dominant stromal dystrophy having stromal opacity throughout by slit-lamp biomicroscopy [5, 10]. In our patient, numerous opacities were observed at the level of Descemet's membrane under magnification of slit-lamp biomicroscopy; however, it was difficult to distinguish the precise histological location of the opacities.

There are several reports on pre-Descemet's membrane corneal dystrophy using white light confocal microscopy [5–7]. Grupcheva et al. [5] reported 2 cases of pre-Descemet's membrane corneal dystrophy. One case showed highly reflective irregular particles only in pre-Descemet's stroma. The other case showed highly reflective irregular intracellular particles throughout the cornea with a predilection for the deep stroma. Holopainen et al. [6] showed multiple intra- and extracellular hyperreflective particles in the posterior stroma. In Holopainen et al.'s [6] case, the corneal thickness was increased, similar to that observed in our patient. Ye et al. [7] reported the pleomorphic structures (suspected enlarged keratocytes) containing dense hyperreflective inclusions in the posterior stroma. Recently, Yeh et al. [8] reported on combined pre-Descemet's membrane corneal dystrophy and Fuchs' endothelial dystrophy using in vivo laser confocal microscopy; hyperreflective inclusions in the cytoplasm of keratocytes, and guttae in the endothelial layer were observed. Histopathological examination of one case of pre-Descemet's membrane corneal dystrophy demonstrated that the pathological findings were limited to the keratocytes of the posterior stroma [4]. Within the keratocytes there were cytoplasmic vacuoles that contained lipid-like material (lipofuscin). Hyperreflective particles observed in pre-Descemet's membrane corneal dystrophy might represent lipofuscin. In our patient, hyperreflective small particles in the posterior stroma, as in pre-Descemet's membrane corneal dystrophy, were not observed. Conversely, a hyperreflective Descemet's membrane was observed. Therefore, a differential diagnosis of pre-Descemet's membrane corneal dystrophy was excluded.

Corneal argyrosis manifests as scattered gray opacities in the stroma and at the level of Descemet's membrane. This condition occurs as the result of occupational exposure, systemic absorption and topical exposure to silver, including photographic materials, electrical conductors, dental alloys, jewelry, mirror-making products, colloidal silver eye drops, and eyelash tints. Almost all cases of corneal deposition are associated with a grayish discoloration of the conjunctiva [11]. The silver deposit rarely interferes with vision. Sánchez-Pulgarín et al. [12] reported a jeweler with corneal argyrosis, demonstrating in vivo laser confocal microscopy findings. Hau and Tuft [13] also reported on in vivo laser confocal microscopic observations in presumed corneal argyrosis associated with silver nitrate-coated cosmetic soft contact lens wear. They showed hyperreflective keratocytes across the entire stromal surface and 2 hyperreflective plaques coinciding with areas of metal deposition, one at Descemet's membrane and the other at Bowman's layer [12, 13]. In vivo laser confocal findings in our patient, such as numerous hyperreflective particles in the

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subepithelium to superficial stroma and a hyperreflective Descemet's membrane, resembled previous reports of corneal argyrosis; however, our patient had no history of silver exposure and no discoloration of the conjunctiva or skin. Therefore, it was difficult to make a diagnosis of silver deposition in this patient. Additionally, other metal depositions, including copper (chalcosis) and gold (chrysiasis), were excluded by slit-lamp findings and the absence of metal exposure history.

Hyperreflective stromal 'microdot deposits' (1–2  $\mu\text{m}$  diameter) are observed with a confocal microscopy throughout the corneal stroma in higher numbers in contact lens wearers [14, 15]. The higher grade assigned to microdots in contact lens wearers indicates that lens wear exacerbates otherwise normal corneal morphological features or processes [15]. The brown discoloration of used soft contact lens might have affected subepithelial opacity formation in our patient; however, the origin of the subepithelial opacity was still unclear.

In conclusion, although the origin of corneal opacities was unclear, in vivo laser confocal microscopy was useful for observing microstructural abnormalities in a case of Descemet's membrane and subepithelial opacity.

### Disclosure Statement

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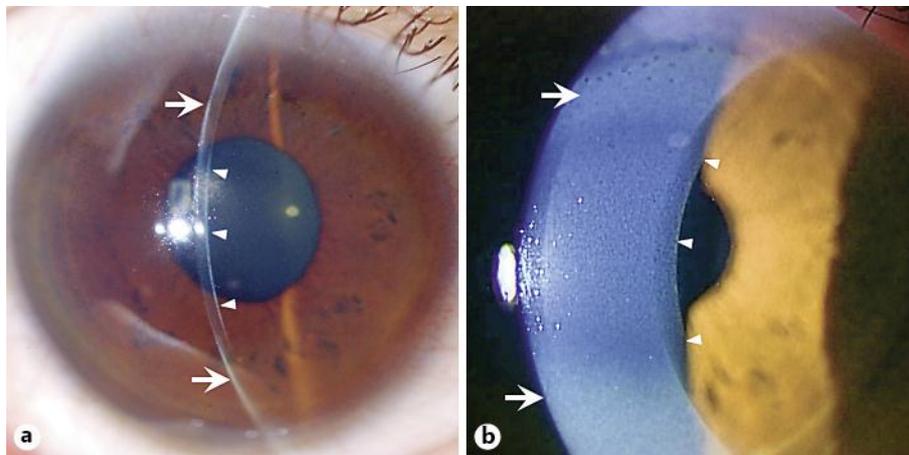
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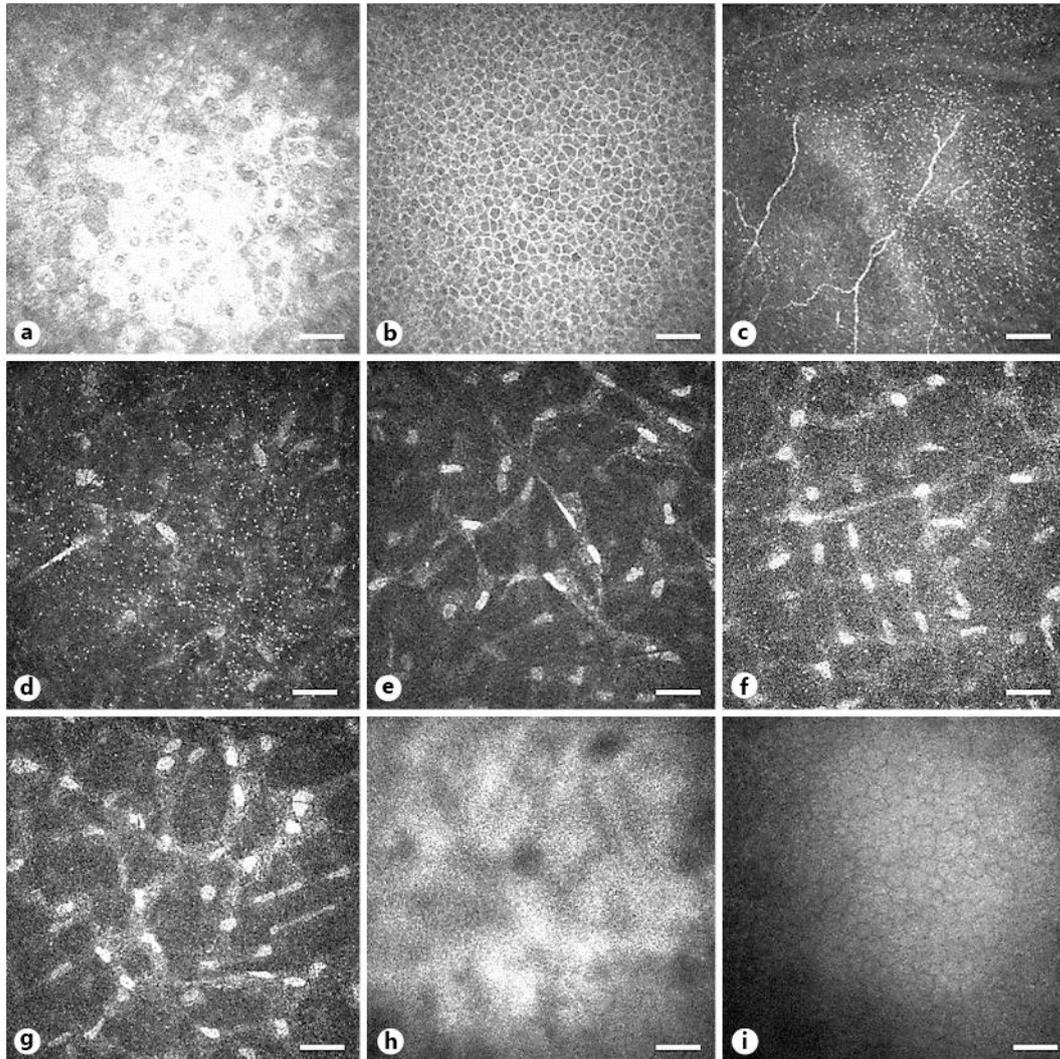
**Table 1.** Clinical features and in vivo confocal microscopy findings of the differential diagnosis

	Pre-Descemet's membrane corneal dystrophy	Corneal argyrosis	Our case
Pathogenesis	The inheritance is not determined The gene is unknown	Systemic or topical exposure to silver	Unknown
Deposits	Lipofuscin in the keratocytes	Silver	Unknown
Eye	Bilateral	Bilateral (or unilateral)	Bilateral
Visual disturbance	No	No	No
Slit-lamp biomicroscopy findings	Tiny opacities of deep stroma	Gray opacities in the stroma and Descemet's membrane. Grayish discoloration of the conjunctiva	Opacities located in the subepithelium and Descemet's membrane
In vivo confocal microscopy findings			
Epithelium	Normal	Normal	Normal
Bowman's layer	Normal	Hyperreflective particles	Hyperreflective particles
Superficial stroma	Normal	Hyperreflective particles	Hyperreflective particles
Midstroma	Normal	Hyperreflective particles	Normal
Deep stroma	Hyperreflective particles in the keratocytes	Hyperreflective particles	Normal
Descemet's membrane	Normal	Hyperreflectivity	Hyperreflectivity
Endothelium	Normal	Normal	Normal



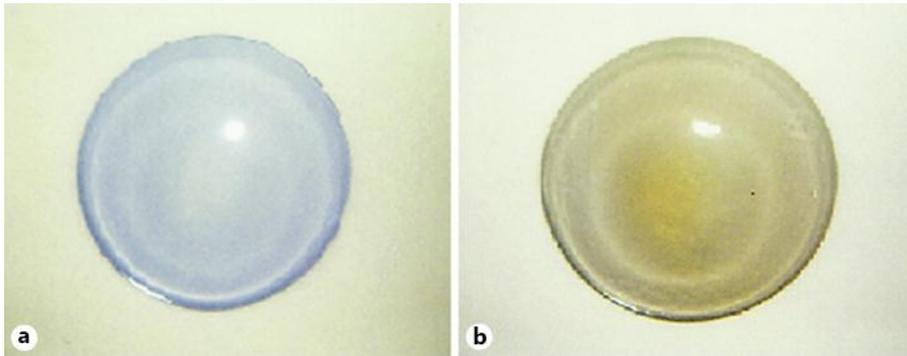
**Fig. 1.** Subepithelial opacity (arrows) in the mid-peripheral to peripheral cornea and numerous opacities located near Descemet's membrane (arrow heads) from a 41-year-old male; similar findings were observed in both eyes. **a** Photograph with narrow slit illumination. **b** Photograph with wide slit illumination.

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**Fig. 2.** In vivo laser confocal microscopic image by Heidelberg Retina Tomograph 2 Rostock Cornea Module (Heidelberg Engineering GmbH, Dossenheim, Germany). Similar findings were observed in both eyes. No differences were detected between the central and peripheral regions (scale bar = 50  $\mu$ m). **a** The superficial epithelial cell layer was normal. **b** The basal epithelial cell layer was normal. **c** In the subepithelium to Bowman's layer, numerous hyperreflective particles were observed. **d** In the superficial stroma, numerous hyperreflective particles were observed. **e** The midstroma was normal. **f, g** The deep stroma was normal. Hyperreflective inclusions as in pre-Descemet's membrane corneal dystrophy were not observed. **h** Descemet's membrane itself had high reflectivity. **i** The endothelial cell layer was normal.

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**Fig. 3.** **a** The unused soft contact lens (Aime super-soft, Aime, Yokohama, Japan) had a light blue color. The hydroxyethyl methacrylate-based contact lens was categorized as FDA group I (low water content, nonionic). **b** One-year used soft contact lens showed a brownish discoloration. Similar discoloration was noted in both of the patient's contact lenses. Metal deposition was not detected with differential interference contrast microscope.