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Case report

Recurrence of paraproteinemic keratopathy after penetrating keratoplasty and its assessment with confocal microscopy

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ABSTRACT

Purpose: To report on a case of recurrence of paraproteinemic keratopathy (PPK) associated with monoclonal gammopathy after bilateral penetrating keratoplasty.

Observations: Penetrating keratoplasty was performed on both eyes of a 45-year-old man due to bilateral progressive corneal stromal clouding. Recurrence of the corneal stromal opacities accompanied by a decrease in visual acuity was observed on slit-lamp examination already two years after penetrating keratoplasty. Confocal laser scanning microscopy (CLSM) of the corneal grafts performed three years after penetrating keratoplasty showed bilateral morphological changes identical to that found in the patient's corneas prior to penetrating keratoplasty. A hematological work-up revealed monoclonal gammopathy of type IgG kappa. The histochemical examination of the explanted corneas confirmed the diagnosis of PPK.

Conclusions and importance: Paraproteinemic keratopathy is an underdiagnosed ophthalmological condition, which may be associated with potentially life-threatening hematologic disorders. A hematological workup should be performed in patients with corneal opacities of uncertain etiology. Penetrating keratoplasty should be performed with caution in patients with monoclonal gammopathy due to the possibility of a very fast recurrence of PPK in the corneal graft. This is the first presentation of the recurrence of flake-like PPK after penetrating keratoplasty assessed with CLSM.

1. Introduction

Paraproteinemic keratopathy (PPK) or immunotactoid keratopathy is an umbrella term for a heterogenous group of corneal findings associated with monoclonal gammopathy. Monoclonal gammopathy is defined as a presence of abnormal protein (paraprotein), i.e. inoperable immunoglobulins or their parts (light or heavy chains), in the blood. Monoclonal gammopathies include disorders as: monoclonal gammopathy of undetermined significance (MGUS), smoldering multiple myeloma (SMM) or multiple myeloma (MM).

The incidence of MGUS is as high as 3.5% in people over 50 years of age and represents one of the most common premalignant disorders in Western countries.[1,2] MGUS may precede not only MM, but also other potentially life-threatening diseases such as B-cell non-Hodgkin lymphoma or chronic myeloid leukaemia.[3] According to hematological therapy guidelines, MGUS does not require any systemic therapy, but regular workup is needed in order to recognize its progression to MM or other immunoproliferative disorders.[4]

Early recognition of PPK by an ophthalmologist may help to diagnose some hematological disorders before a clinical progression occurs. The deposits of paraprotein in the cornea may reveal very distinct patterns and may involve all corneal layers. Crystalline and non-crystalline forms of PPK are known. Furthermore, PPK may imitate systemic and/or metabolic disorders; hereditary corneal dystrophies; inflammation or contact-lens related corneal damage. In addition to a detailed medical history, a general medicalexamination, check-up of family members and genetic analyses should be performed to exclude other reasons for corneal opacity. The new classification of PPK and detailed differential diagnoses have recently been reported by Lisch et al.[5]

In vivo confocal laser-scanning microscopy (CLSM) provides an insight into corneal morphology at the cellular level. Not only cells, but also extracellular deposits may be characterized.[6] The literature regarding CLSM findings in PPK is poor. So far it consists of only a few case reports regarding crystalline keratopathy associated with MM and SMM as well as one case of crystalline keratopathy in a patient suffering from MGUS.[7–10] Micali et al. presented a comparison between confocal a histopathological changes in a patient with MM[11]

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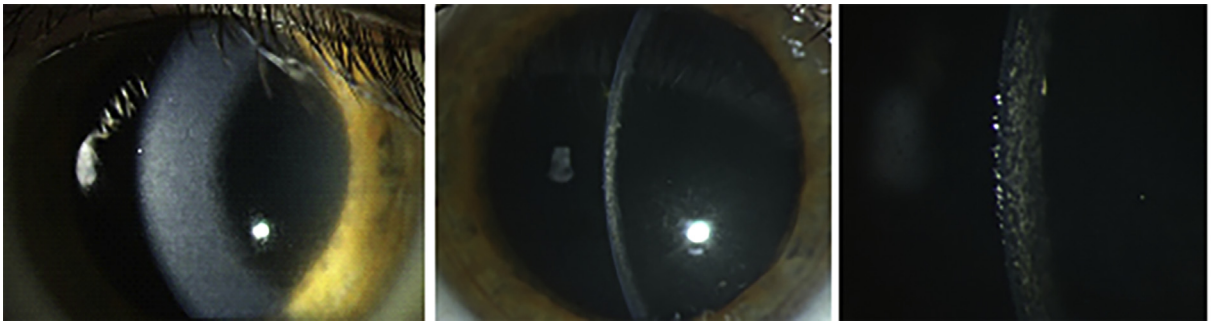

Fig. 1. Corneal clouding in diffuse illumination (a) and in optical section (b–c). Lisch et al. Trans Am Ophthalmol Soc 2016; 114:T7 (1–21).

This report presents a diagnostic chain, which was conducted in a patient with bilateral corneal clouding. To the best of our knowledge, this is the first description of a recurrence of a stromal flake-like PPK after bilateral penetrating keratoplasty assessed with CLSM.

2. Case report

2.1. Findings prior to penetrating keratoplasty

A 43-year-old man was examined for the first time at the Department of Ophthalmology of the University Medical Center in Mainz in 2009 due to bilateral worsening of visual acuity and photophobia. The patient's medical history was uneventful. He had never suffered from systemic or metabolic diseases. He had never used any systemic medication, eye drops or contact lenses. He had no history of any ocular or refractive surgery. The family history regarding ocular diseases was negative. At presentation, the BCVA was 0.63 in both eyes. Slit-lamp examination revealed bilateral diffuse yellowish corneal deposits localized in the corneal stroma (Fig. 1). Central corneal thickness was 543 μm in the right and 542 μm in the left eye. The intraocular pressure (IOP) was 15 mm Hg and the examination of the retina revealed normal findings. Bilateral progression of corneal clouding was accompanied by a decrease in visual acuity to 0.25 in the right and 0.16 in the left eye during the following three years. A genetic evaluation was performed as we suspected a congenital stromal corneal dystrophy (CSCD). However, it did not reveal any mutation in the transforming growth factor β-induced (TGFBI) and decorin (DCN) genes. The CLSM performed using the Heidelberg Retina Tomograph (HRT II) in conjunction with the Rostock Cornea Module (RCM) [Heidelberg Engineering GmbH, Heidelberg, Germany][12] revealed rarefied keratocytes and decreased transparency of the extracellular matrix in the anterior stroma (Fig. 2a); loss of keratocytes and “coral” – like hyperreflective structures in the mid stroma (Fig. 2b and c); more homogenous hyperreflection and obscured details in the posterior stroma (Fig. 2d). Increased reflectivity of the stroma prevented visualization of the corneal endothelium. The findings were similar in both eyes.

Non-HLA-matched penetrating keratoplasty was performed on the left eye in March 2012. HLA-matched penetrating keratoplasty was performed on the right eye in November 2012. The HLA-matching of the second PKP was due to participation in the FANCY study.[13] Both keratoplasties were uneventful and fixed with double running sutures, which were removed one year after surgery. The postoperative course was also uneventful.

2.2. Findings after penetrating keratoplasty

A follow-up examination conducted two years after penetrating keratoplasty revealed recurrence of the fine corneal stromal deposits. At this time point BCVA was 0.63 in the right and 0.8 in the left eye. The progressive corneal clouding caused decline of BCVA to 0.32 in the right and to 0.5 in the left eye three years postoperatively. At that time the slit lamp appearance of the corneal deposits was almost identical to the preoperative findings (Fig. 3). The anterior segment spectral domain - OCT revealed homogenous hyperreflectivity of the cornea consistent with the clinical features. IOP measurement and fundoscopy revealed normal findings. At the time of the manuscript submission BCVA declined further to 0.16 in the right and 0.32 in the left eye.

CLSM performed three years postoperatively revealed rarefied keratocytes and decreased transparency of the anterior stroma (Fig. 4 a); loss of keratocytes and “coral” – like hyperreflective structures in the middle stroma (Fig. 4b and c) with increasing homogenous hyperreflection in the posterior stroma (Fig. 4d) almost identical to the preoperative findings. The findings were again similar in both eyes.

2.3. Hematological workup

The patient had not presented B symptoms. The first hematological laboratory diagnostics performed as soon as stromal opacities recurred revealed IgG, IgM and IgA within the normal range; increased free kappa light chains by 19.7 mg/l (normal values 3.3–19.4 mg/l); increased kappa-lambda quotient 4.7 (normal values 1.3–2.6). No free light chains in the urine. The immunfixation of urine was normal. The plasma immunfixation confirmed the diagnosis of monoclonal gammopathy of type IgG kappa of intermediate-high risk.

Bone marrow biopsy presented no relevant proliferation of plasma cells. The whole-body low-dose computer tomography did not reveal

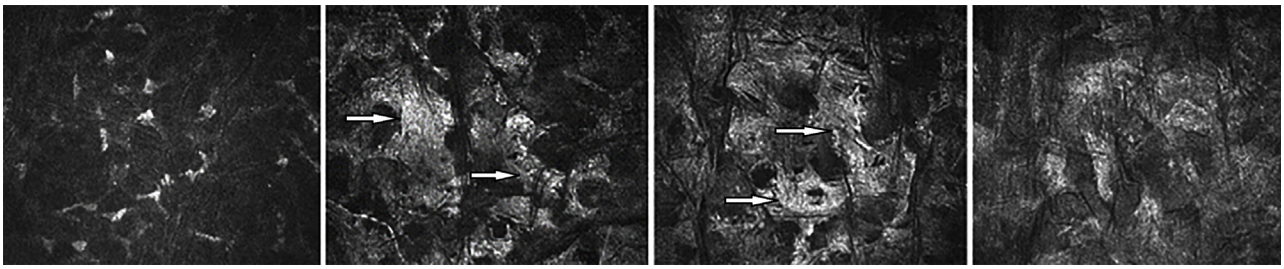

Fig. 2. In vivo confocal laser-scanning microscopy of the clouded cornea of the right eye before penetrating keratopasty at the depth of a) 125 μm, b) 201 μm, c) 276 μm, d) 380 μm. Arrows indicate the “coral” – like hyperreflective structures in the middle stroma.