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CASE REPORT

Confocal microscopy in a case of crystalline keratopathy in a patient with smouldering multiple myeloma

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Abstract We report the clinical and confocal microscopic findings of the cornea in a patient with smouldering multiple myeloma (SMM) using in vivo scanning laser confocal microscopy. A 72-year-old female underwent a complete ophthalmological examination including slit-lamp biomicroscopy with digital photography, HRT II laser scanning in vivo confocal microscopy and haematological laboratory assessment. Corneal biomicroscopy revealed the presence of bilateral diffuse microgranular tiny grey opacities. In vivo confocal microscopy showed randomly oriented hyper-reflective needle-shaped crystals throughout all levels of the stroma, sparing epithelium and endothelium. In vivo confocal microscopy was very helpful in the differential diagnosis by allowing the nature of the corneal deposits to be established, revealing the typical aspect of the crystals, and excluding granular dystrophy, leading to a suspected diagnosis of SMM. Crystalline corneal deposits may easily be confused as crumb-like opacities typical of granular dystrophy on slit-lamp examination even by experienced ophthalmologists.

Keywords Confocal microscopy · Corneal crystals · Smouldering myeloma · Corneal dystrophies

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Introduction

Plasma cell diseases represent a group of haematological tumours derived from clonal proliferation of B lymphocytes leading to abnormal synthesis of immunoglobulins (Igs) or their fragments (heavy and light chains) [1]. Smoudering multiple myeloma (SMM) is defined as an asymptomatic variant characterised by the presence of IgG or IgA M-protein levels >3 g/dL in serum or >10 % plasma cells in bone marrow in the absence of anaemia, renal insufficiency, hypercalcaemia or skeletal lesions that can be attributed to the underlying disorder [2].

An involvement of ocular structures is reported in the literature [3]. In particular, the whole cornea may be affected by crystalline deposits. In vivo confocal microscopy represents a low-invasive high-resolution diagnostic technique to explore corneal microstructures. To the best of our knowledge, confocal microscopic features of corneal crystals in SMM have not been previously described. Moreover, identification of the corneal deposits in this report allowed a diagnosis of SMM.

Case report

A 72-year-old Caucasian female was referred to our clinic with a suspected diagnosis of corneal dystrophy. She reported bilateral symptoms of photophobia and visual fluctuation. She underwent a complete

ophthalmological examination, including slit-lamp biomicroscopy, anterior segment digital photography (C.S.O., Florence, Italy), in vivo HRT II scanning laser confocal microscopy (Heidelberg, Germany) and haematological laboratory assessment. Best-spectacle corrected visual acuity was 0.8 Snellen lines (SL) in the right eye and 0.9 SL in the left eye. Slit-lamp examination of the cornea revealed the presence of diffuse bilateral microgranular tiny grey opacities with a full-thickness spread, sparing epithelium and endothelium (Fig. 1).

Ocular fundus examination was within normal limits. Medical and pharmacological anamnesis was otherwise unremarkable, and there was no family history of corneal dystrophies. The patient underwent in vivo confocal microscopic examination by Heidelberg Engineering HRT II confocal microscope (Rostock Cornea Module). Several confocal scans were taken of the central and peripheral part of the cornea. In vivo confocal microscopy showed randomly oriented needle-shaped crystals variably spreading at all corneal levels, except in the epithelium, Bowman's layer and endothelium (Fig. 2).

Discussion

Clinical evidence of diffuse opacities, also in the perilimbal area, was different from the typical appearance of granular dystrophy with mainly central crumb-like deposits. Moreover, the confocal finding of needle-shape deposits indicated a diagnosis of a deposition keratopathy, specifically of crystalline origin. This led us to take into consideration a series of differential diagnosis among various diseases that fall under this aspect [4].

Schnyder's corneal dystrophy was excluded because is an autosomal dominant disease and there was no family history of this disease in our patient. Lecithin cholesterol acyltransferase deficiency was also excluded because of the lack of family history for this type of disease and because of the characteristic changes in the lipid profile (increase in levels of unesterified cholesterol, very-low-density lipoprotein and triglycerides, esterified cholesterol and high-density lipoprotein are reduced by up to 90 %). Cystinosis, obviously the adult form, also known as ocular non-nephropathic cystinosis, was the only one that was taken into account given the age of the patient and the absence of other diseases in her history; however, it was considered less likely because it is an inherited autosomal recessive disease and the patient is the penultimate of ten siblings, seven men and three women.

Bietti's crystalline dystrophy was excluded because there was no family history of this disease and because of the characteristic retinal involvement with glistening yellowish white crystalline deposits scattered throughout the posterior pole and mid-peripheral retina, retina pigmented epithelium and choriocapillaris atrophy, pigment clumping and retinal scarring [5].

Gout was excluded due to the lack of typical symptoms and signs in joints, kidneys and soft tissue that could suggest this disease. Infectious crystalline keratopathy was excluded because it is caused by indolent and fastidious organisms which become implanted in the corneal stroma in a setting of immunosuppression such as from corticosteroid use, contact lens wear or infected corneal grafts. In addition, the pharmacological history of our patient was negative for drugs such as chloroquine, chlorpromazine, clofazimine, gold and rifabutin which have

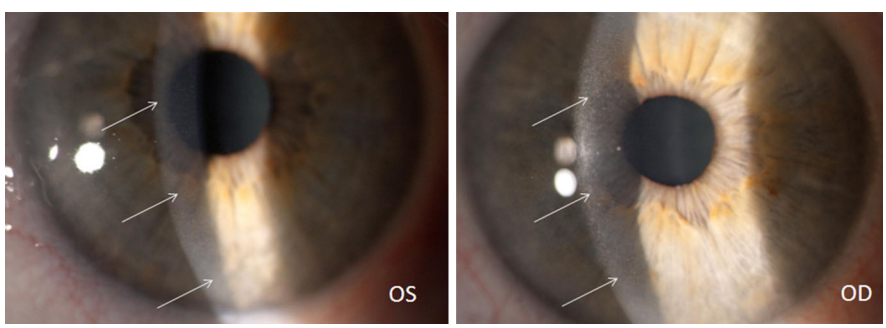

Fig. 1 Corneal biomicroscopy (×20 magnification). Slit-lamp examination showed diffuse bilateral microgranular tiny grey opacities of the cornea in both eyes (*white arrows*) from the limbus to the central part of the cornea

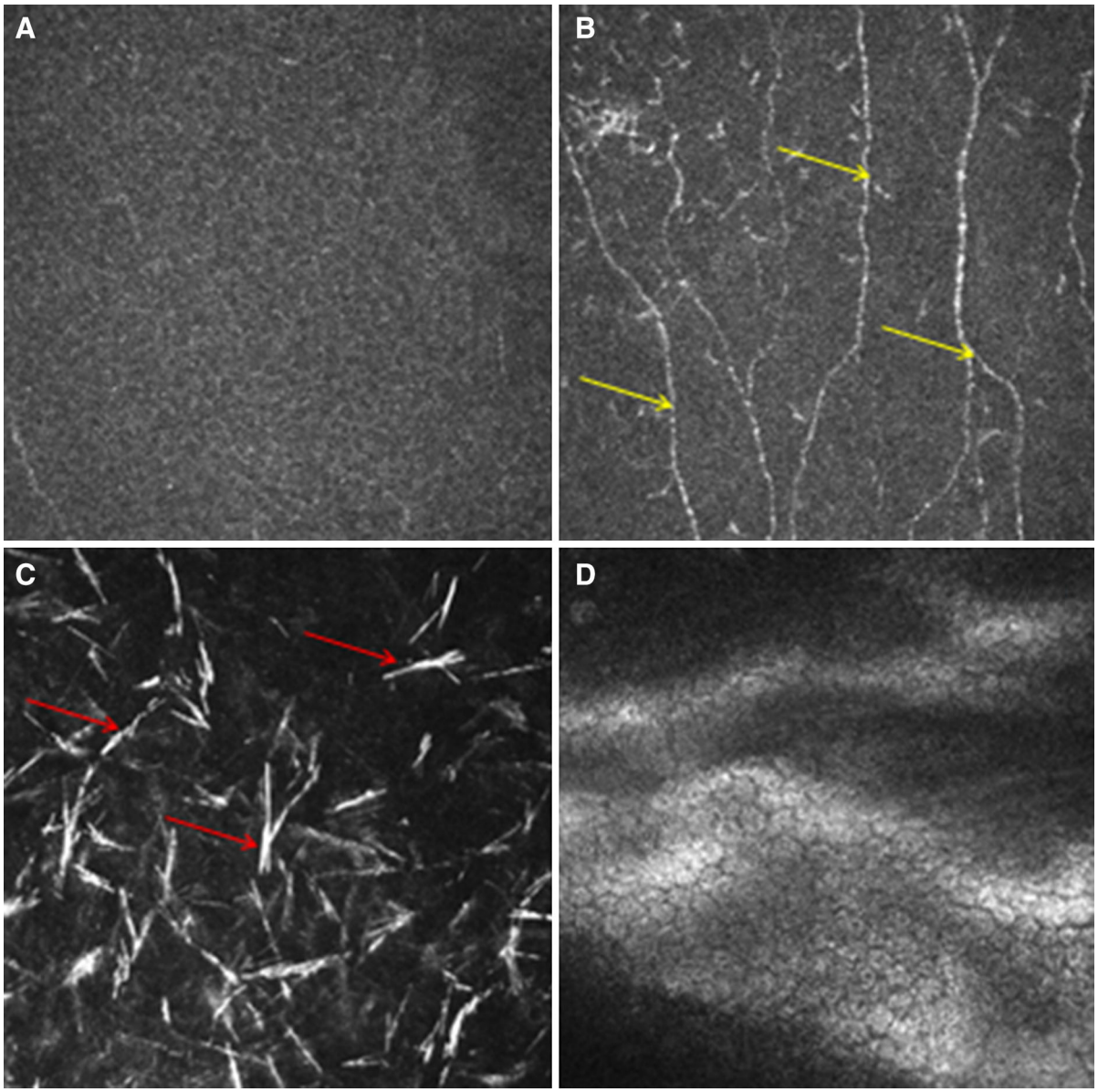

Fig. 2 In vivo HRT II scanning laser confocal microscopy. **a** Basal epithelial cells unaffected by crystals deposits. **b** Subepithelial plexus nerve fibres (*yellow arrows*) without crystal deposition at the level of Bowman's membrane. **c** Randomly oriented needle-shaped hyper-reflective crystals (*red arrows*), variably spreading in the whole stroma starting under Bowman's lamina until pre-Descemet's level. **d** Endothelial cells unaffected by deposits, with pleomorphic aspect

the ability to cause corneal deposits as previously described in the literature [4, 6]. A possible diagnostic option of paraproteinemia or related disorders like multiple myeloma was investigated and the patient was referred to the Department of Haematology and Oncology of our University Hospital where, by means of laboratory tests, she was diagnosed with SMM. In vivo confocal microscopy played an important role by allowing precise qualitative and topographic identification of the corneal deposits, leading to a correct differential diagnosis among corneal deposition pathologies, and excluding the presence of corneal dystrophy.

Conflict of interest Authors declare no financial interest. Nothing to disclose.

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