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ORIGINAL PAPER

Clinical diversity in macular corneal dystrophy: an optical coherence tomography study

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Abstract
Purpose To characterise the corneal deposits of macular corneal dystrophy and correlate with high-resolution optical coherence tomography (OCT).
Methods A total of 23 eyes of 15 patients were evaluated for clinical features on slit lamp biomicroscopy, and high-resolution OCT was performed to correlate the clinical findings. The deposits were characterised based upon their location and level in the corneal layers.
Results Mean age was 31.5 (Range 20–67) years. The stromal deposits were restricted to central 8 mm in 9 eyes; in the rest of the 14 eyes, the deposits were seen in both central and peripheral cornea. In one patient, no such distinction could be made due to diffuse nature of the deposits throughout the cornea with sparing of 1–2 mm of the cornea internal to the limbus. The central deposits were in the anterior stromal layers, while the peripheral deposits were in the deep stromal corneal layers and non-contiguous with the anterior stromal deposits. In one patient aged 67 years, the peripheral deposits in deep corneal layers were more prominent than the central anterior stromal deposits and were associated with a significant thickening of Descemet membrane.
Conclusions MCD exhibits a clinically diverse presentation as revealed on the clinical and optical coherence tomography study. Immunophenotype and genotype–phenotype correlation may further help in understanding various clinical presentations of MCD.

Keywords Macular corneal dystrophy · Corneal dystrophy · Optical coherence tomography

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Introduction

Macular corneal dystrophy (MCD) is a category 1 corneal stromal dystrophy as per the International Committee for Classification of Corneal Dystrophies (IC3D) classification [1]. There is a deposition of glycosaminoglycans in the Bowman's layer, keratocytes, extracellular matrix and the endothelium [2]. Typically, the deposits of MCD are seen to arise as superficial grey–white deposits in the central cornea that coalesce later to progressively involve the entire corneal stroma limbus to limbus [3, 4]. The posterior membrane abnormalities in MCD have been studied on ultrasound bio microscopy and optical coherence tomography [5].

Although majority patients with MCD in the early stage present with stromal deposits in the anterior

stroma in the central cornea, we observed that in some patients who were evaluated in the early age with central deposits also had discrete peripheral deposits which were distinctly located to deeper layers of cornea. Further, in one patient aged 67 years, there was a relative paucity of anterior stromal deposits with more conspicuous peripheral deep stromal opacities and extensive thickening of Descemet membrane [6].

Hence, the purpose of this study was to characterise the clinical spectrum of macular corneal dystrophy and correlate with high-resolution optical coherence tomography findings.

Materials and methods

The study group comprised of 23 eyes of 15 patients with MCD. The 15 patients belonged to different families and were not related. All procedures performed were in accordance with ethical standards of institutional research and adhered to the tenets of Helsinki declaration. The slit lamp photograph documentation, high-resolution optical coherence tomography (RTVue XR Avanti, Optovue Inc., USA) and IOL master 700 (Carl Zeiss Meditec AG, Jena) were performed in all eyes. In seven patients, only one eye was available for optical coherence tomography as the other eye had previously had keratoplasty. The demographics, age of onset of complaints, pachymetry, visual acuity and clinical features were documented in all eyes. The diagnosis of macular dystrophy was made based on the clinical and family history and the characteristic corneal deposits on slit lamp examination. In seven patients who had a prior keratoplasty, the histology of the corneal buttons showed typical characteristic alcian blue positive deposits of MCD.

The distribution of deposits was categorised with respect to the location within the central 8 mm versus peripheral cornea. The deposits evaluated on slit lamp examination were correlated with the OCT findings. The central pachymetry was assessed with both the IOL master and OCT calliper tool.

Results

Mean age was 31.5 (Range 20–67) years, with an equal number of males and females. In eight patients where both eyes were included, the clinical picture was identical in the two eyes. The mean visual acuity was 20/160 (20/50–20/630). Mean pachymetry was 457 ± 41.5 (range 390–553) microns with the IOL master and 458 ± 41.7 (393–556) microns using the OCT callipers tool. There was no significant difference in the pachymetry assessment with the two devices ($p = 0.76$).

The stromal deposits were restricted to central 8 mm in 9 eyes; in the rest of the 14 eyes, deposits were seen in both central and peripheral cornea. In one patient, no such distinction could be made due to diffuse nature of the deposits throughout the cornea with sparing of 1–2 mm of the cornea internal to the limbus. Table 1 illustrates the demographics, clinical characterisation of the deposits on slit lamp examination and OCT. Figures 1, 2, 3, 4, 5 and 6 show the representative slit lamp and OCT images of some patients.

The characteristic central corneal deposits that are essential to the diagnosis of MCD in early stage were present in all eyes. In addition to central deposits, distinct peripheral deposits were observed in 13 eyes. The peripheral deposits were noted in the deeper layers of the cornea. In one eye of a patient aged 67 years, diffuse haze was noticed throughout the cornea with sparing of 1–2 mm of the peripheral cornea from the limbus. In the same eye, spheroidal degeneration was noted. In another patient aged 67 years, there were fewer deposits in the anterior stroma along with numerous deposits in deeper layers of peripheral cornea with a noticeably thickened Descemet membrane.

The OCT imaging showed hyperreflectivity in the anterior stroma corresponding to the deposits in the anterior stroma with thinning of the epithelium overlying the stromal deposits. The peripheral deposits were notably seen as hyperreflectivity in the deeper cornea at the posterior membrane level. In one patient aged 67 years with dense stromal haze, the posterior stroma was not very well characterised due to optical shadow effect from the dense anterior stromal deposits. Another patient aged 67 years had deposits in the deeper corneal layers, remarkably thickened Descemet membrane and few anterior stromal deposits on the OCT imaging.

Table 1 Clinical features and anterior segment-OCT characteristics of the study patients

Parameters	Central 8 mm	Central 8 mm + peripheral	Diffuse haze with spheroidal degeneration
No. of eyes	9	13	1
No. of patients	5	9	1
Age of onset of symptoms	Second decade	Second decade in all except 1 (fifth decade)	
Mean pachymetry (microns)	456 (390–495)	453 (407–553)	519
Mean age at presentation (years)	26 (20–31)	32.7 (21–54)	67
Mean vision (Snellen's)	20/125 (20/63–20/320)	20/200 (20/50–20/630)	20/630
Clinical and OCT features	Deposits in anterior stroma, thinning of epithelium at the site of deposits	Deposits in anterior stroma, thinning of epithelium over the site of deposits, Peripheral deposits in deeper layers of cornea, [a]patient had diffuse thickening of the Descemet membrane with few anterior stromal deposits	Dense stromal deposits causing an optical shadow in the posterior cornea

[a]Eye had a diffuse haze and hence characterised separately

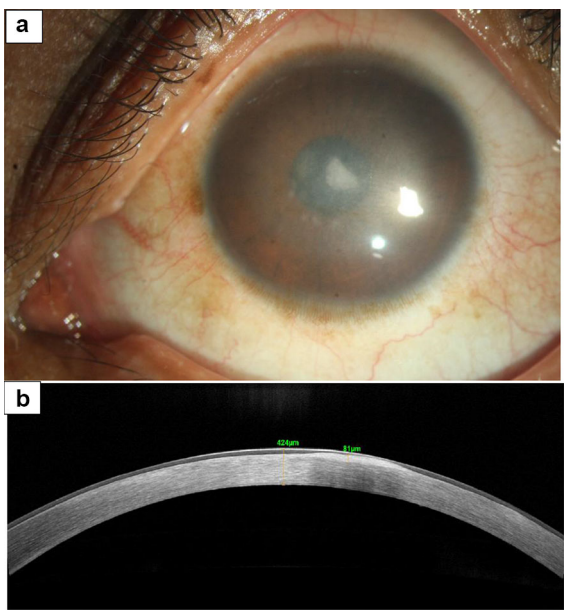

Fig. 1 Slit lamp photograph (**a**) and OCT image (**b**) of a 30-year-old patient showing anterior stromal lesions, with a clear peripheral cornea

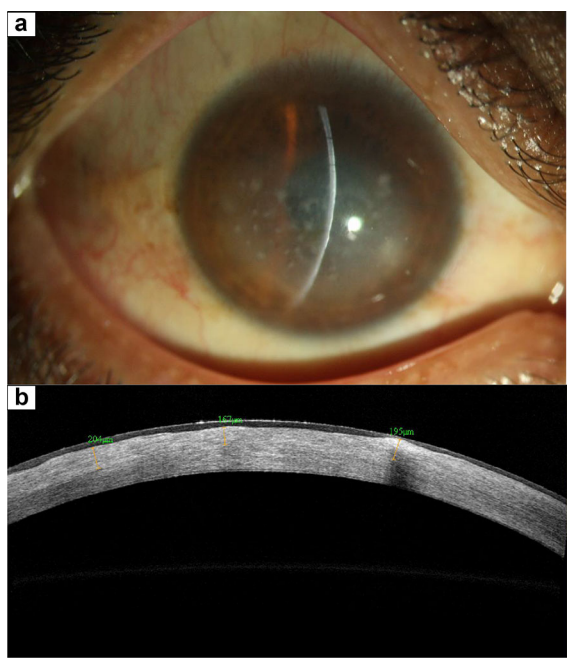

Fig. 2 Slit lamp photograph (**a**) and OCT image (**b**) of a 31-year-old patient showing anterior stromal deposits and haze in central cornea

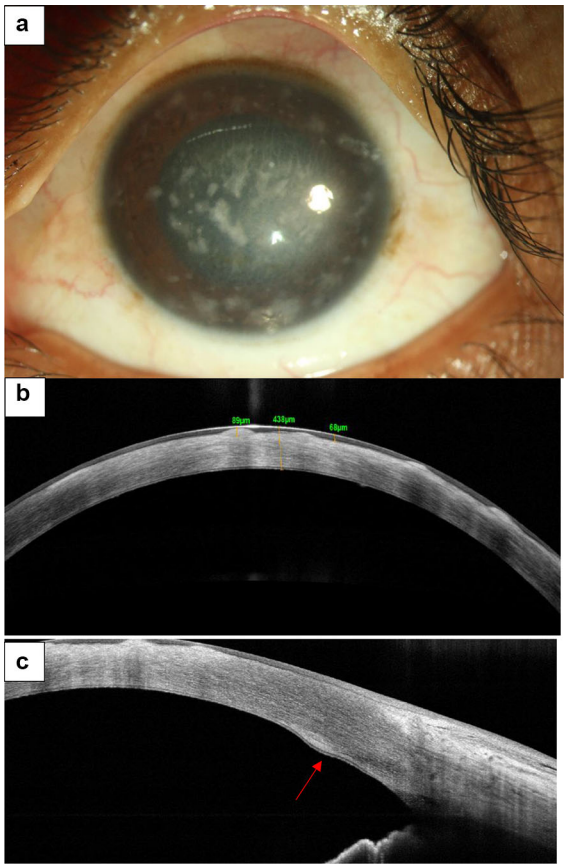

Fig. 3 Slit lamp photograph (**a**) and OCT image (**b**, **c**) of a 28-year-old patient showing anterior stromal deposits and haze in central cornea; **b** OCT imaging of the central cornea showing the deposits in the anterior to mid stroma; **c** the peripheral cornea shows deposits in the deep stromal layers

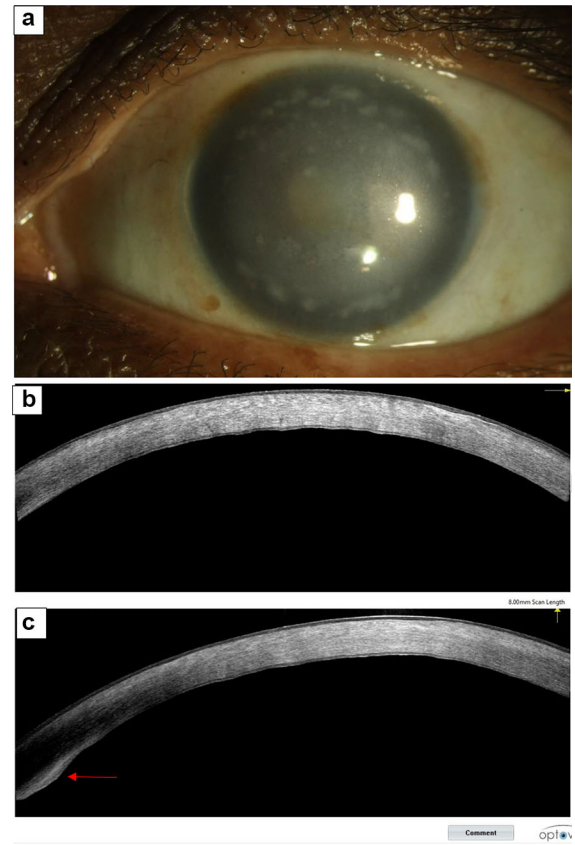

Fig. 4 Slit lamp photograph (**a**) and OCT image (**b**) of a 54-year-old patient showing anterior stromal deposits and haze in central cornea; **c** the peripheral cornea shows deposits in the deep stromal layers (red arrow)

Discussion

MCD is an autosomal recessive dystrophy that arises because of various mutations in CHST6 gene [1, 2]. While one study reported a more severe phenotype in those with frameshift mutations when compared to missense mutations [7], another study on phenotype–genotype correlation was inconclusive [8]. A study by Rubenstein et al. [5] inferred that there may be some relationship between phenotype and genotype based upon the clinical observation that there were differences in the age of onset of the dystrophy. Although genotype heterogeneity is apparent in a few studies on the genetics of MCD, the phenotypic heterogeneity is not yet certain.

As per the classical description of this stromal dystrophy, the deposits of macular dystrophy begin in the central corneal stroma that later spread to the periphery to reach the limbus. The description and level of peripheral stromal deposits are not very well characterised and have only received an incidental mention in few reports [3, 5]. In our study, we observed that 9 eyes of 5 patients (mean age 26 years) had stromal deposits in the central 8 mm of the cornea. Thirteen eyes of 9 patients (mean age 32.7 years) also had discrete peripheral deposits localised to the deep stromal layers in addition to central anterior stromal deposits as seen on clinical slit lamp examination, and

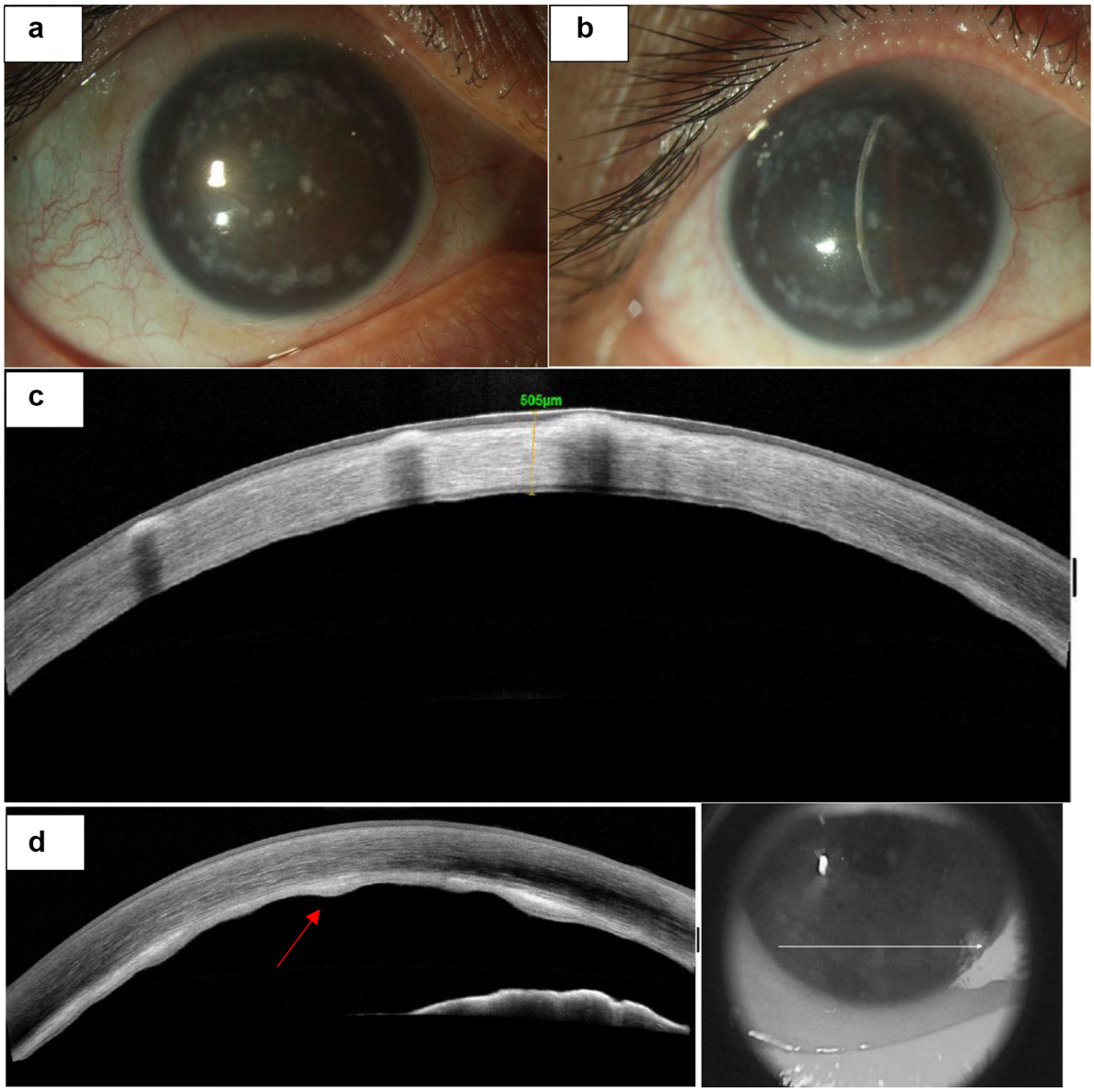

Fig. 5 Diffuse (**a**) and slit view (**b**) photograph and OCT image (**c**) of a 47-year-old patient showing anterior stromal deposits and haze in central cornea; **d** the peripheral cornea shows dense deposits in the deep stromal layers (line scan passing through the peripheral corneal deposits)

this corroborated with the findings on OCT imaging. The peripheral deposits in the deeper layer were non-contiguous with the central anterior stromal lesions. This clinical presentation probably represents a distinct clinical presentation of macular corneal dystrophy as it is seen in many patients even in the early ages (second and third decade) and therefore, not necessarily a feature of progression of the dystrophy with age from the central cornea to the peripheral cornea. In fact, in one patient who presented at the age of 67 years, the peripheral deposits were more prominent than the central anterior stromal deposits. This patient had complaints of reduced vision much later in life (fifth decade) compared to the rest others.

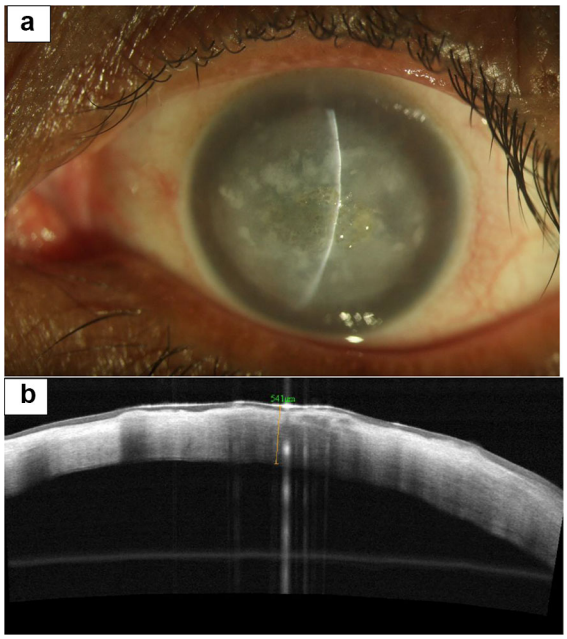

Fig. 6 Slit lamp photograph (**a**) and OCT image (**b**) of a 67-year-old patient showing diffuse anterior stromal deposits, haze and spheroidal degeneration in cornea. There is sparing of peripheral 2 mm of cornea from the limbus. The dense anterior stromal deposits cause an optical shadow in the posterior part of the cornea

The clinical findings of our study show that MCD has a diverse clinical spectrum. We could not perform genetic analysis or immunophenotype in our patients. The phenotype−genotype correlations and immunophenotype studies in MCD would be insightful.

Compliance with ethical standards

Conflict of interest All authors declare that they have no conflict of interest.

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