LETTER TO THE EDITOR /Poster de la SFO

Corneal confocal microscopy and familial amyloidotic polyneuropathy

Microscopie confocale cornéenne et polyneuropathie amyloïde familiale

Purpose
To describe a case of familial amyloidotic polyneuropathy (FAP) with corneal amyloid deposits found using corneal confocal microscopy (CCM).

Case description
A complete ophthalmological examination with glaucoma assessment and CCM (Heidelberg Retina Tomograph II with Rostock cornea module) were performed in a patient with FAP. Color photographs of the anterior segment were also taken.

Clinical case
A 47-year-old man with an uncontrolled glaucoma of the left eye (LE) under maximal medical treatment has FAP linked to the Val30Met mutation of the transthyretin (TTR) gene. The diagnosis was made 15 years earlier during a liver transplant. The visual acuity is 1.0 without correction in both eyes. Under fixed combinations of brinzolamide—brimonidine and timolol—travoprost on top of 3 tablets of acetazolamide 250 mg per day, the intraocular pressure (IOP) of the LE is 18 mmHg. Color vision using Böstrom and Kugelberg boards is pathological for the LE and normal for the right eye (RE). The other parameters are normal. The slit lamp shows a clear cornea with fine keratic precipitates and a whitish superior temporal nodule of the bulbar conjunctiva of the LE (Fig. 1). The iris surface has pigmented deposits and the pupillary margin is scalloped over 360° (Fig. 2). White deposits on the anterior stromal denser in the pupillary area, are easily revealed after dilatation (Fig. 3). The fundus examination of the LE shows a vertical cup disc ratio of 0.9 and is otherwise normal. The angle is open with diffuse white deposits and hyperpigmented trabeculum (Fig. 4). The visual field is normal in the RE and shows inferior arcuate scotoma with superior nasal step in the LE. The CCM reveals hyper-reflective and punctiform deposits in all corneal layers mainly in the LE and also some clusters in the RE. At the stroma level, only punctiform deposits are visible. Clump deposits are probably masked by the nuclei of keratocytes (Fig. 5). Corneal nerves appear thinner and less numerous as compared to a normal cornea (Fig. 6). Trabeculectomy was performed, resulting in IOP of 10 mmHg without any medication. The decline is 28 months.

Discussion

FAP is an autosomal dominant neurodegenerative disease induced in the majority of cases by a mutation in TTR. This mutation is most commonly due to the substitution of valine by methionine at position 30 of the TTR gene (Val30Met) \[^{[1]}\]. The mutated TTR aggregates in the form of amyloid deposits in the peripheral nerves and various organs including the eye. The early ocular manifestations are due to circulating TTR and autonomic neuropathy: dry
eye and conjunctival vessel abnormalities. Then, secondary to ocular production of TTR by the ciliary pigment epithelium, deposits on the iris, the pupillary margin and the anterior crystalloid appear; also, scalloped iris and glaucoma develop. Finally, abnormalities due to the production of TTR by the retinal pigment epithelium are observed, including vitreous amyloidosis and amyloid retinal angiopathy [2]. Other ophthalmological manifestations have been reported: corneal hypoesthesia, pupillary light-near dissociation and more rarely bilateral optic neuropathy [3]. As the TTR is mainly produced by the liver, hepatic transplantation slows or even stops disease progression and increases the survival of patients with FAP [4]. The local production of TTR by the retinal and ciliary pigment epithelium explains the appearance or the progression of ocular involvement despite liver transplantation [5]. The incidence of glaucoma in patients with FAP, which varies from one study to another, is estimated to be 24% for all mutations, with a lower incidence for the Val30Met mutation (17%) as compared to the others (57%) [6]. Very few articles describe the CCM of patients with FAP [7]. In cases of familial amyloidosis of Finnish type, CCM showed hyper-reflective deposits between basal epithelial cells and immediately below them [7]. In our patient, hyper-reflective deposits are present in the epithelium, stroma and endothelium. These deposits progressively lead to a decrease in corneal sensitivity and alteration of epithelium and stroma, contributing to the development of dry eye, epithelial lesions and parakeratosis [8]. Hyper-reflective deposits are also visible in some corneal dystrophies, contact lens wearers and after LASIK, but in these cases, they are associated with other abnormalities [9]. The severity of corneal nerves involvement may be correlated to that of the other nerves [10].

Conclusion

The immunohistochemical analysis is the sole method to confirm that these corneal deposits are amyloid. The evaluation of corneal nerves by CCM could serve as a tool in the assessment and monitoring of the peripheral neuropathy in patients with FAP.

Disclosure of interest

The authors declare that they have no competing interest.

References


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Figure 6. Corneal confocal microscopy of corneal nerves of the right eye (A) and corneal nerves of healthy cornea (B). Bar = 50 µm.
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