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SHORT COMMUNICATION

Macular involvement in secondary systemic amyloidosis

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PURPOSE. *A patient with subretinal and preretinal hemorrhage after secondary systemic amyloidosis due to familial Mediterranean fever is presented.*
METHODS. *Case presentation.*
RESULTS. *A 30-year-old woman with secondary systemic amyloidosis secondary to familial Mediterranean fever presented with painless visual loss in the right eye. The examination demonstrated multiple subretinal and preretinal hemorrhages, massive deposits which may represent amyloid material at the left macular region. After 6 months, the hemorrhages disappeared, but deposits persisted.*
CONCLUSIONS. *The macular deposition and hemorrhage is an uncommon manifestation of secondary systemic amyloidosis secondary to familial Mediterranean fever. Further evidence is necessary to understand the nature of these deposits and their relevance to secondary systemic amyloidosis and/or familial Mediterranean fever. (Eur J Ophthalmol 2008; 18: 459-61)*

KEY WORDS. *Amyloidosis, Familial Mediterranean fever, Retinal hemorrhage, Retinal exudate*

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INTRODUCTION

Ocular involvement in amyloidosis is uncommon. There are sporadic case reports of patients with systemic nonfamilial (AL) amyloidosis who present with ocular findings (1-4). Ocular involvement in a case with secondary systemic (AA) amyloidosis has not been described previously. A case with AA amyloidosis and retinal manifestations is presented.

Case report

A 30-year-old woman presented with painless visual loss in the left eye. The past medical history was positive for AA amyloidosis secondary to familial Mediterranean fever (FMF). The diagnosis had been made on renal biopsy (Fig. 1). The patient was on colchicine PO at the time of her examination. In her initial examination, visual acuity (VA) was 20/20 in the right eye and count fingers at 1 meter in the left. There was a mild afferent pupillary defect in the left eye (0.6 log units). The intraocular pressure (IOP) and the anterior segment evaluation were normal bilaterally. Fundus examination revealed marked narrowing and sheathing of the retinal arteries, multiple subretinal and preretinal hemorrhages accompanied by yellowish deposits which may represent amyloid material at the left macular region (Fig. 2A). On fundus fluorescein angiography (FFA), diffuse hypofluorescent areas representing the masking effect of the hemorrhages (Fig. 2B) were seen. These hypofluorescent areas persisted unchanged in the late phases. Optical coherence tomography (OCT) imaging (Stratus OCT, model 3000) of the macular region revealed hyperreflective material under the retinal pigment epithelium that may correspond to amyloid material and the central retinal

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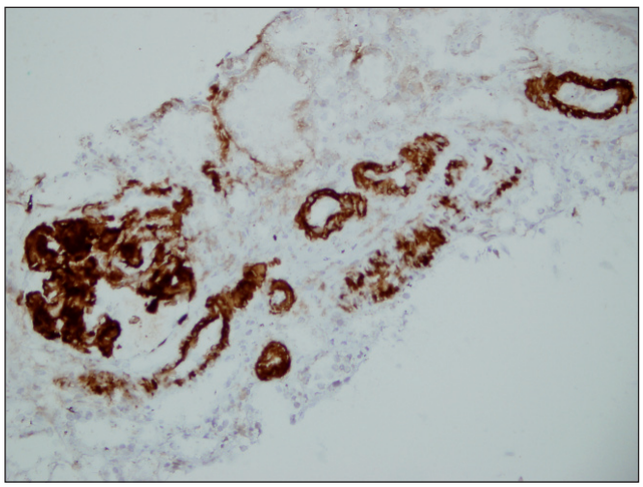

Fig. 1 - *Renal biopsy with immunostain for amyloid A. Amyloid A immunopositivity is seen in arteriolar walls and in glomeruli. Anti-amyloid A x200.*

thickness was normal (162±37 µm) (Fig. 2C).

The automated perimetry of the right eye was within normal limits.

Six months later, there was no change in the VA, IOP, or color vision in the left eye. The retinal hemorrhage had disappeared. However, the amyloid deposits persisted (Fig. 2D).

DISCUSSION

Ocular involvement in amyloidosis is uncommon. There are sporadic case reports of patients with systemic nonfamilial amyloidosis (AL amyloidosis) who present with ocular findings (1-4). Purcell et al described a patient with recurrent subconjunctival hemorrhages; histologically,

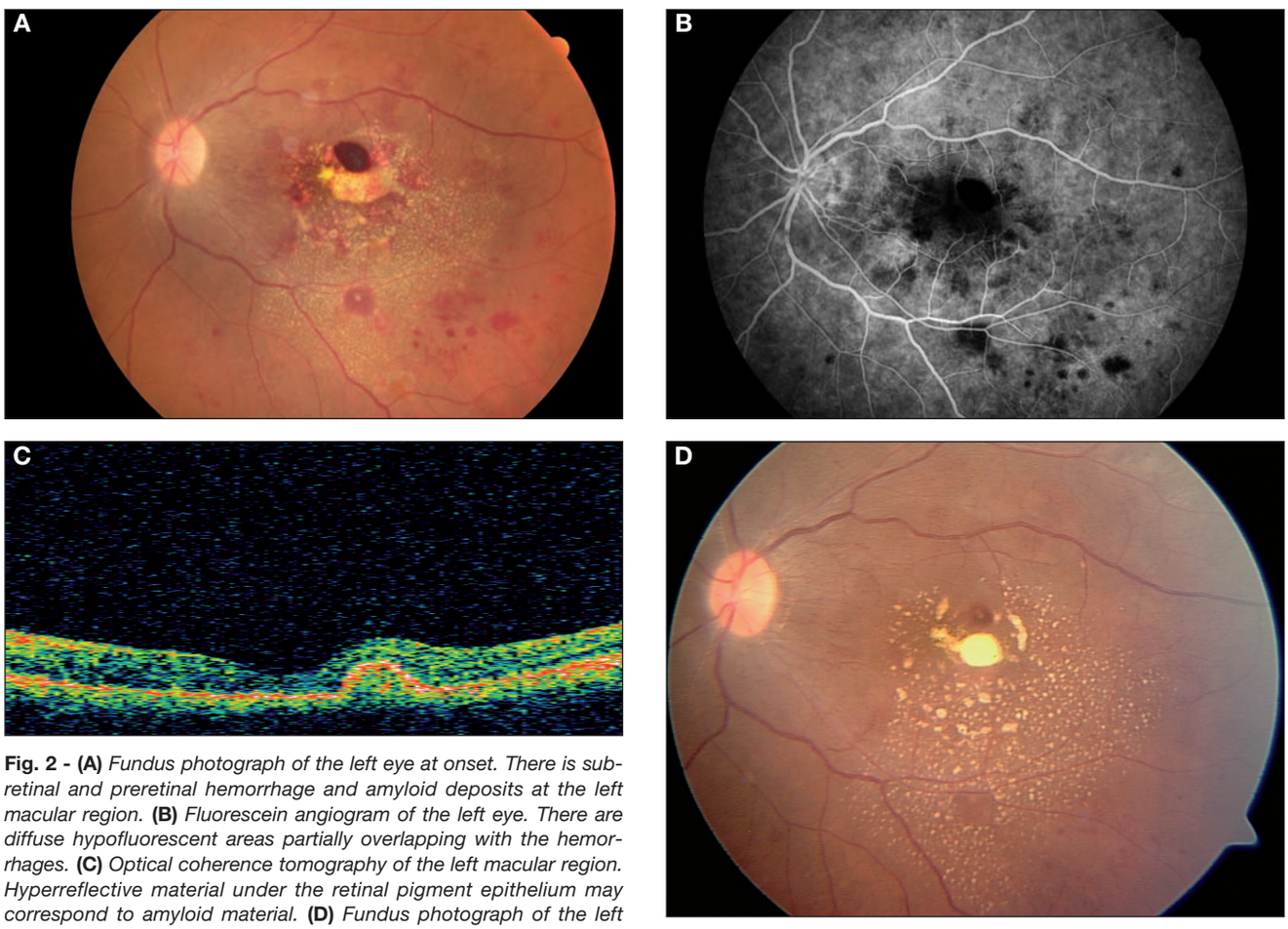

Fig. 2 - (A) *Fundus photograph of the left eye at onset. There is subretinal and preretinal hemorrhage and amyloid deposits at the left macular region.* **(B)** *Fluorescein angiogram of the left eye. There are diffuse hypofluorescent areas partially overlapping with the hemorrhages.* **(C)** *Optical coherence tomography of the left macular region. Hyperreflective material under the retinal pigment epithelium may correspond to amyloid material.* **(D)** *Fundus photograph of the left eye after 6 months. The retinal hemorrhage disappeared; however, macular deposits persisted.*

amyloid deposits were found in the conjunctiva with involvement of blood vessels (2). Ts'o and Bettman reported a case of AL amyloidosis with diffuse occlusion of the choriocapillaris; amyloid substance was found around and inside the vessels (3). Vitreous deposits of amyloid are found in primary familial amyloidosis but are sporadically reported in nonfamilial amyloidosis (4). Pece et al described a case of AL amyloidosis with diffuse bilateral chorioretinal abnormalities including hemorrhages and pigmentary mottling at the posterior pole, with hypofluorescent areas on fluorescein and indocyanine green angiography. In their report, the exact nature of these hypofluorescent areas was unclear but the authors speculated that these could be amyloid deposits or the result of previous intraretinal or subretinal hemorrhages (1).

Acute hemorrhages into the retina and subretinal space can be seen with a retinal macroaneurysm. Chronic leakage from a macroaneurysm may present with lipid exudates and macular edema, similar to this case. Although chronic damage to the vascular wall (by hypertension, sclerotic changes, or emboli) is the most likely cause of macroaneurysm formation, peripheral multifocal chorioretinitis (PMC), which has a strong association with sarcoidosis, may also cause macroaneurysm formation. The cause of macroaneurysm formation in PMC patients is presumably periphlebitis, which causes damage to the vascular wall and results in leakage. The FFA of our patient did not reveal the presence of a macroaneurysm. However, the deposition of amyloid in and around the vessels has been demonstrated in patients with AL amyloidosis (2,3) and one can speculate that this deposition may cause sclerotic damage to the vessel wall or induce breakdown of the blood–retinal barrier and hence leakage at least in selected patients.

Familial Mediterranean fever is a disease characterized by recurrent episodes of fever and peritonitis. In the Middle East and Europe, FMF is frequently complicated by amyloidosis and progressive renal failure. Ocular involvement is rare in FMF and mostly presents with episcleritis and anterior uveitis. Involvement of the outer eye and uveal tract in FMF was reported previously in two siblings. Panuveitis and episcleritis were also present in this case series and FFA revealed staining of both discs with early and late hyperfluorescence of the retinal lesions (5). FMF was not complicated by amyloidosis in the same case series (5).

It is not clear in this case whether this presentation is a result of amyloid-related damage to retinal vessels and secondary leakage or direct amyloid deposition into retinal and subretinal areas. We also do not know if this presentation is a result of FMF-related damage. This clinical entity has not been described in AA amyloidosis or FMF. Further studies with clinicopathologic correlation are necessary in order to clarify the underlying pathogenesis in such pathologies.

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