Sir,

Unusual macular findings in a known choroideremia carrier

Choroideremia is a very rare, progressive, X-linked choroidal degeneration. The clinical appearance of an affected male is highly characteristic and usually easily recognised.[1] However, the clinical appearance of a carrier female is much more subtle, resembling that of a very young male sufferer.[2,3] In these patients, detectable changes are usually restricted to the retinal mid-periphery, with occasional fine pigmentary mottling at the macula.[1,2] Normal visual acuity is retained.[4,5] We report a known carrier female with macular as well as peripheral retinal changes, together with marked unilateral reduction in visual acuity.

Case report

Our patient is a 64-year-old white woman who is an obligate heterozygote from an extended family with choroideremia (Fig. 1). She manifests bilateral, peripheral retinal pigment epithelial mottling through 360°, these findings being consistent with those previously described.[1,2,4] In addition, she also demonstrates asymmetric macular changes. The visual acuity on the right has been reduced to counting fingers level for the last 4 years, and there is a large area of retinal pigment epithelial disruption centred on the macula, and with no evidence of drusen (Fig. 2). The left visual acuity is 6/6, and a small area of chorioretinal atrophy with drusen is present inferotemporal to the fovea (Fig. 3). The peripheral visual fields are normal bilaterally, while the right central visual field shows a large paracentral scotoma. The flash electroretinogram, electro-oculogram and visual evoked potentials are all within normal limits bilaterally for the laboratory in which they were conducted (Burdon Institute, Bristol).

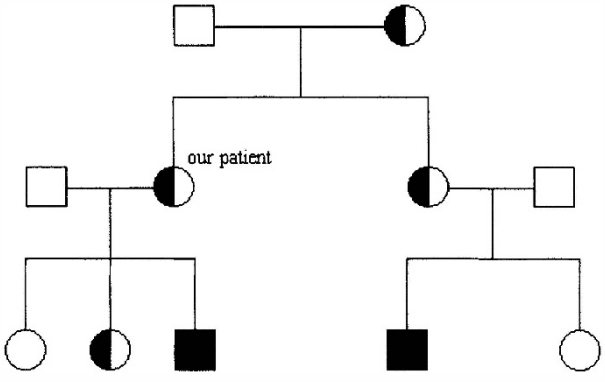

Fig. 1. *Pedigree of the patient's extended family. Squares, male; circles, female; open symbols, unaffected; filled symbols, severely affected; half-filled symbols, carriers.*

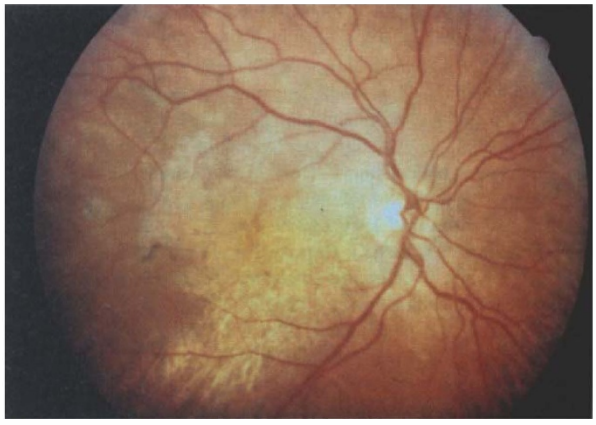

Fig. 2. *Right fundus photograph. A large area of macular pigment epithelial disruption can be seen.*

Comment

Macular changes in choroideremia carriers have been previously described.[1,4,6] These usually take the form of fine pigmentary mottling without loss of acuity or peripapillary atrophy,[1,4,5] though diminished visual acuity has been reported.[6,7] Interestingly, our carrier patient has suffered a severe unilateral reduction in acuity, due to unilateral choroidal atrophy. To our knowledge this has not previously been reported in association with the carrier state of choroideremia.

The genetic mutation causing choroideremia is known to involve the long arm of chromosome X (Xq21.1–Xq21.33).[8–10] The changes noted in our patient could be explained by the Lyon hypothesis of unbalanced X chromosome inactivation.[5,11–13] In order to equalise the genetic contribution of the sex chromosomes, all female somatic cells inactivate one X chromosome, a random process termed Lyonisation. This may result in biased inactivation towards one X chromosome. Should a mutation-carrying X

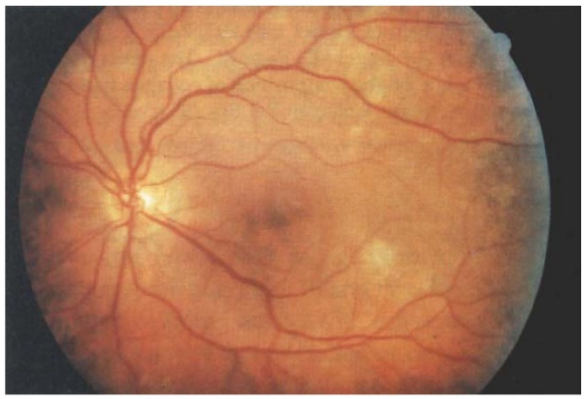

Fig. 3. *Left fundus photograph. A small area of chorioretinal atrophy infero-temporal to the fundus is present. Note the peripheral pigmentary changes characteristic of a choroideremia carrier.*

chromosome be active in a sufficient proportion of cells in a tissue in which the gene is expressed then a female may manifest the disease in that tissue. If cells of only parts of that tissue are affected then a mosaic pattern may be demonstrated. The X-inactivation ratio determines the degree to which the tissue is affected and in our patient could explain the laterality of involvement.

It might be argued that these changes are due to other causes. Age-related macular degeneration is a possibility; however, the relatively early age of onset, paucity of drusen and marked asymmetry of the macular findings are somewhat atypical. Serpiginous choroiditis commencing at and involving solely the macular region has been described.[14,15] Involvement is bilateral, although its extent is frequently asymmetrical.[14,16] Our patient's condition has remained essentially unilateral for more than 4 years now, with no signs of acute inflammation at any stage. Geographical atrophy of the macula is also described in Stargardt's disease,[17] a heredo-macular disorder. Onset is usually bilateral and in the teenage years.[18,19] Fundus flavimaculatus, a variant, has onset in the fourth or fifth decade. Retinal flecks are not always present,[17,20] but the visual prognosis is generally good. Other fundal dystrophies have been reported to give a similar appearance to choroideremia;[12,21] these include gyrate atrophy, diffuse choriocapillaris atrophy, central areolar choroidal dystrophy and retinitis pigmentosa.

We feel the family history and carrier status of our patient are important when considering the cause of her eye disease. Mechanisms by which an obligate heterozygote for an X-linked condition may manifest disease uniocularly and to varying degree within the same eye have been postulated. We believe manifest choroideremia is the most likely cause of our patient's visual disability, and would be interested to hear of any similarly affected female carriers.

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Sir,

Darkening of eyelashes in a patient treated with latanoprost

Latanoprost, a prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$) analogue, is the first in a new class of drugs for the treatment of open angle glaucoma. Its primary mode of action is by increasing uveoscleral aqueous outflow. Iris pigmentation is a well-documented association with topical latanoprost treatment.[1,2] We report a case of darkening of the eyelashes in a patient treated with latanoprost.

Case report

A 78-year-old woman attended the Birmingham and Midland Eye Centre with a diagnosis of pseudoexfoliative glaucoma in her right eye. Her right