A Young Man with Multiple Bilateral Retinal Lesions

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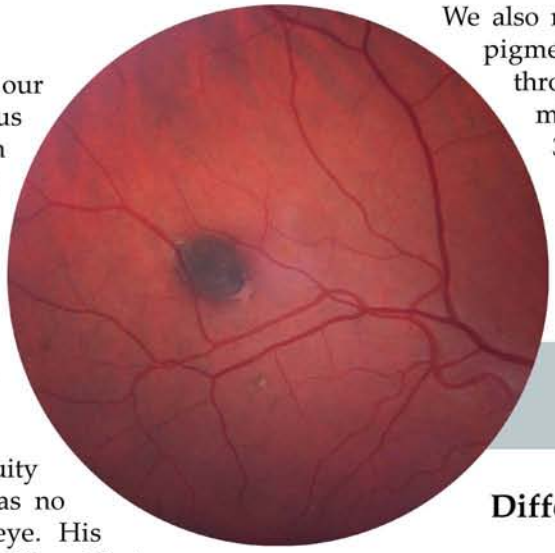
Introduction:

A 32-year-old man was referred to our office for further evaluation of suspicious lesions found in both of his retinas on routine dilated exam. The patient had no visual complaints, but was anxious about the discovery. He was mildly myopic, but his ocular history was otherwise unremarkable. His only other medical history included a previous hernia repair and previous bowel surgery.

The patient's best-corrected visual acuity was 20/20 in both eyes, and there was no afferent pupillary defect in either eye. His intraocular pressure by applanation was 19 mmHg in the right eye and 20 mmHg in the left eye. His anterior segment examination was unremarkable. On dilated funduscopic examination, his vitreous was clear in both eyes.

The primary lesion of concern was located in the midperiphery along the superotemporal arcade in the right eye (Fig. 1). Optical coherence tomography (OCT) over the lesion showed a hyperreflective retinal pigment epithelial (RPE) layer with thinning of the overlying neurosensory retina (Fig. 2).

Figure 2: OCT over this pigmented lesion, showing hyperreflectivity of the retinal pigment epithelium and overlying thinning of the neurosensory retina.



We also noted multiple similar darkly pigmented lesions scattered throughout the posterior pole and midperiphery in both eyes (Figs. 3, 4). Closer examination revealed that they were oval in shape, with a tapered area of depigmentation at the margins of the lesions (Fig. 5).

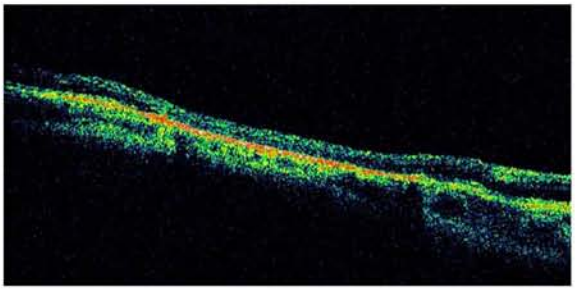
Figure 1: A hyperpigmented lesion along the superotemporal arcade in his right eye.

Differential Diagnosis:

The differential diagnosis for multiple hyperpigmented lesions in the fundus includes choroidal nevi, RPE hyperplasia secondary to previous trauma or inflammation, pigmented lattice degeneration, congenital hypertrophy of the retinal pigment epithelium (CHRPE), multifocal CHRPE ("bear tracks"), malignant melanoma of the choroid, and retinal pigment epithelium hamartomas related to familial adenomatous polyposis (FAP).

Upon further questioning of the patient, he revealed that he has a strong family history of FAP, and he had a prophylactic colectomy a few years ago. Both his brother and his father had numerous colonic polyps, and his uncle was treated for colorectal cancer.

Discussion:



FAP vs. CHRPE

FAP is an autosomal dominant condition caused by a mutation in the adenomatous polyposis coli (APC) tumor suppressor gene located on chromosome 5q21.[1] Affected patients have hundreds to thousands of adenomatous

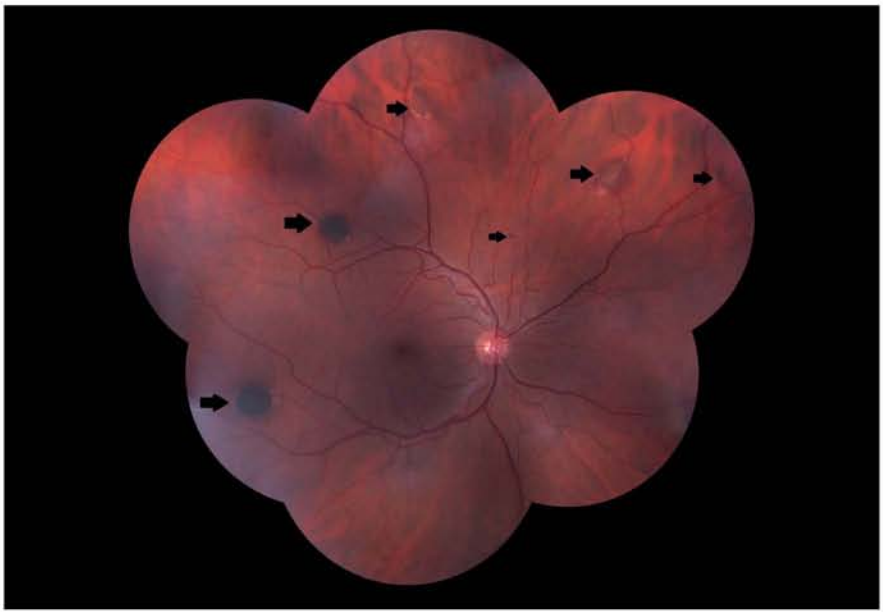


Figure 3: Multiple hyperpigmented lesions randomly distributed throughout the fundus in the right eye (arrows).

polyps, mostly in the large intestine that have nearly 100 percent progression to colorectal cancer if left untreated. When there are extracolonic manifestations (such as desmoid tumors, osteomas, dental anomalies, and soft-tissue tumors) in addition to intestinal polyps, a diagnosis of Gardner syndrome can be made.[1]

FAP has commonly been associated with CHRP E in the literature.1 However, histopathologic comparison of the fundus lesions in FAP and CHRPE shows distinct differences between the two entities.[2,3]

Histopathologic Differences

On microscopy, CHRPE lesions appear as tall RPE cells filled with large hypertrophic melanosomes. Histopathologic study of the pigmented fundus lesions in FAP shows three basic configurations:

- A monolayer of hypertrophic cells,
- A mound of RPE cells interposed between basement membrane of the RPE and the inner collagenous layer of Bruch's membrane, or
- A multilayered mound of hyperplastic cells.[2,3]

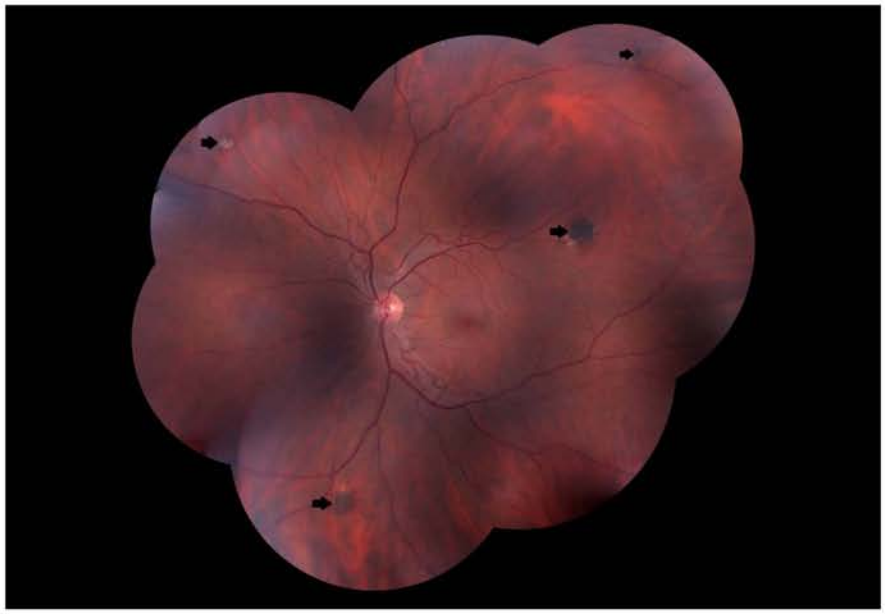
All three configurations are thought to be a result of a generalized defect in melanogenesis from the underlying APC gene mutation.

Unlike those seen in CHRPE, the pigmented fundus lesions in FAP represent benign hamartomatous malformations of the RPE. In a review of 132 patients previously diagnosed with solitary or multifocal CHRPE, Shields and coworkers found that none of these patients had a history of FAP, Gardner syndrome, or intestinal cancer.[4] In an effort to correctly differentiate the pigmented fundus lesions in FAP from CHRPE, the same authors have suggested calling these lesions "retinal pigment epithelial hamartomas associated with familial adenomatous polyposis," or RPEH-FAP.5

Clinical differences

Clinically, there are several differences in appearance between CHRPE and RPEH-FAP lesions. CHRPE lesions are flat and darkly pigmented, have well-delineated smooth borders, and are often surrounded by a halo of depigmentation. With time, they may show scalloping or depigmented lacunae within the lesion. Multifocal CHRPE are grouped in a sector or quadrant of the fundus and are characterized by a larger lesion surrounded by several smaller ones. This appearance resembles an animal paw or footprint, and thus they are commonly referred to as "bear tracks."

Figure 4: Multiple hyperpigmented lesions randomly distributed throughout the fundus in the left eye (arrows).



Both solitary CHRPE and its multifocal variant are unilateral in the majority of cases, and the potential for malignant transformation is extremely rare.[5] RPEH-FAP lesions are bilateral and haphazardly distributed throughout the fundus. They are generally smaller and more ovoid than CHRPE and have an irregular border. These lesions also have a characteristic area of depigmentation at one edge of the lesion in the shape of a comma or fish tail (Fig. 5).

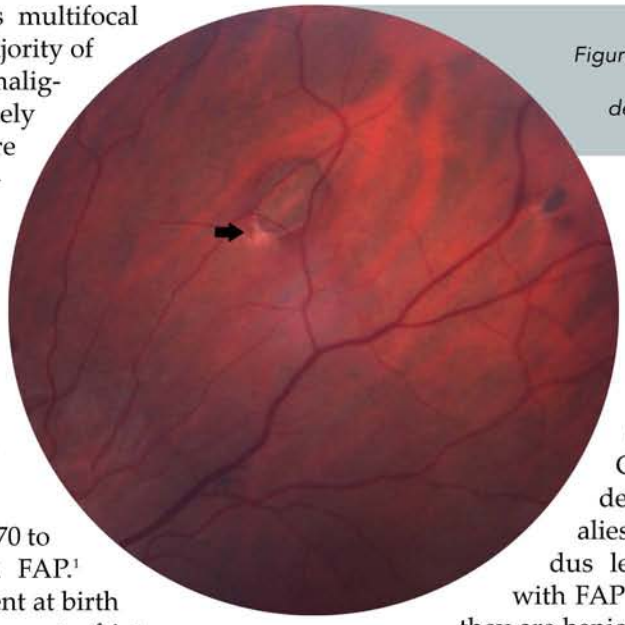


Figure 5: A higher magnification of one of the fundus lesions showing fish-tail depigmentation of the margins (arrow).

RPE hamartomas are found in 70 to 80 percent of patients with FAP.[1] These lesions are usually present at birth and often precede the development of intestinal polyps; thus, their presence on funduscopic examination can be a valuable aid in the diagnosis of FAP in at-risk family members.[1,2] When there are multiple pigmented lesions in both eyes (usually four or more in each eye), these clinical markers have 95 to 100 percent specificity for FAP.[1]

Patient counseling

Although the difference between CHRPE and RPEH-FAP is subtle clinically, it is nonetheless important to make the distinction because of its implications for patient counseling. Patients found to have solitary or multifocal CHRPE on ophthalmoscopy can be counseled that they do not have an increased risk of colon cancer compared to that of the general population. However, patients who have multiple bilateral pigmented lesions with characteristic fish-tail margins should undergo a thorough family history evaluation in addition to recommendation for a screening colonoscopy.

Conclusion:

By the time our presented to our office, he had already been treated with a colectomy for a known diagnosis of FAP, but he did not have any other extracolonic manifestations of Gardner's syndrome such as desmoid tumors or dental anomalies. We informed him that his fundus lesions are a known association with FAP and he was relieved to hear that they are benign in nature. Routine follow-up in one year or as needed was recommended.

References:

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