Congenital Hypertrophy of the Retinal Pigment Epithelium as Biomarker for Familial Adenomatous Polyposis

FAMİLYAL ADENOMA TÖZ POLİPOZİSİN TANISINDA RETINA PIGMENT EPİTELİ KONJENİTALIIİPERTROEİSİNİN YERİ

Doç.Dr.Saadettin ÇETİNER, Prof.Dr.Derviş ŞEN, Prof.Dr.Sabri DEVECİOĞLU

GATA Genel Cerrahi A.B.D. Etlik/ANKARA

SUMMARY

Familial adenomatous polyposis (FAP), a rare and premalignant disease of the gastrointestinal tract, is inherited by Mendelian-dominant gene to a descendant, but the disorder may represent 20 and 25 percent spontaneous mutation.

Ten patients were investigated for congenital hypertrophy of the retinal pigment epithelium (CHRPE) as a biomarker for FAP. Of these, three had a colon cancer and FAP, seven were first-degree relatives of one of them.

Three patients with colon cancer have been found FAP endoscopicly. Three of four offspring at risk showed CHRPE. None of them had extracolonic manifestations. The youngest offspring at risk showing CHRPE was aged 4.

CHRPE appears to be transmitted from one generation to another and to be present after birth. Identifying CHRPE as a marker would facilitate diagnosis and management of FAP.

Key Words: Congenital hypertrophy of the retinal pigment epithelium Familial polyposis

Turk J Gastroenterohepato! 1991, 2: 19 23

ÖZET

Familyal adenomatöz polipozis (FAP) gastrointestinal sistemin nadir görülen ve kanserleşme riski olan bir hastalığıdır. Mendelin dominant geni ile kalıtımı olur, fakat % 20-25 oranında spontan mutasyon gösterebilir.

FAP tanısında retina pigment epiteli konjenital hipertrofisi (RPEKH) 10 olguda araştırıldı. Bunların üçü FAP ve kolon kanserli olgu, yedisi bunlardan birinin birinci derece akrabaları idi.

FAP ve kolon kanserli üç olguda RPEKH izlendi. RPEKH'de gözlenen üç olguda da endoskopik olarak FAP saptandı. Risk grubundaki dört çocuğun üçünde RPEKH gözlendi. Bunların hiçbirinde ekstrakolonik bulgular mevcut değildi. RPEKH gözlenen risk grubundaki çocukların en genci 4 yaşında idi.

RPEKH'nin bir nesilden diğerine geçtiği ve doğumdan sonra mevcut olduğu görülmektedir. RPEKH'nin saptanması FAP'in tanı ve tedavisini kolaylaştıracaktır.

Anahtar kelimeler. Retina pigment epiteli konjenital hipertrofisi, Familyal adenomatöz polipozis

T Klin Gastroenterohepatoloji 1991, 2: 19-23

Familial adenomatous polyposis (FAP) is a rare disease of the gastrointestinal tract, but an important one, because cancer develops before age 40 in nearly all untreated patients. It is a hereditary disorder, characterized by the development of large numbers of adenomatous polyps within the colon. There are always more than 100 polyp and sometimes thousand. The conditk n is said to occur in between 1 in 11.000 and 1 in 18.000 live births. The disease is inherited by Mendelian-dominant gene to a descendant and sex incidence is equal (1) Penetrance has been reported between 79 percent and 94 percent

Geliş Tarihi: 20.6.1990 **Kabul Tarihi: 20.8.1990**

Yazışma Adresi: Doç.Dr.Saadettin ÇETİNER GATA Genel Cerrahi ABD, ANKARA

(2). The affected child may in turn pass it on to a descendant, but the descendants of the unaffected children will be normal. In addition, the condition may arise as a genetic mutation in a previously normal family and 20-25 percent of all patients with FAP arise as such (1). Offspring and siblings at risk should be examined when adenomas are detected in colorectum. Regular rigid and flexible sigmoidoscopy should be performed on all first-degree relatives of the patients with FAP from 14 years of age or earlier. Whereas, it has been reported that congenital hypertrophy of the retinal pigment epithelium (CHRPE) as a biomarker for the genetic defect in FAP would facilitate diagnosis and management of the disease. Because this fundus lesion appears to be present at birth or shortly thereafter (2,6).

Because of these reports, eases with FAP and members of a family at risk have been investigated for this fundus lesions.

MATERIALS AND METHODS

Ten patients were studied. Of these, three had FAP and a colon cancer, seven were first-degree relatives (mother, mother's sister and brother, cousins and doughter) of one of them.

Ophthalmologic examinations were performed by Department of Ophthalmology of Gulhane Military Medical Academy. Following pupil dilatation with cyclopenlolate (1 percent) and phenilcphrine (2.5 percent), the eyes of each patient were viewed 360 with indirect ophlhalmos-copy. Fundus fluoresccin angiography (FFA) was per-

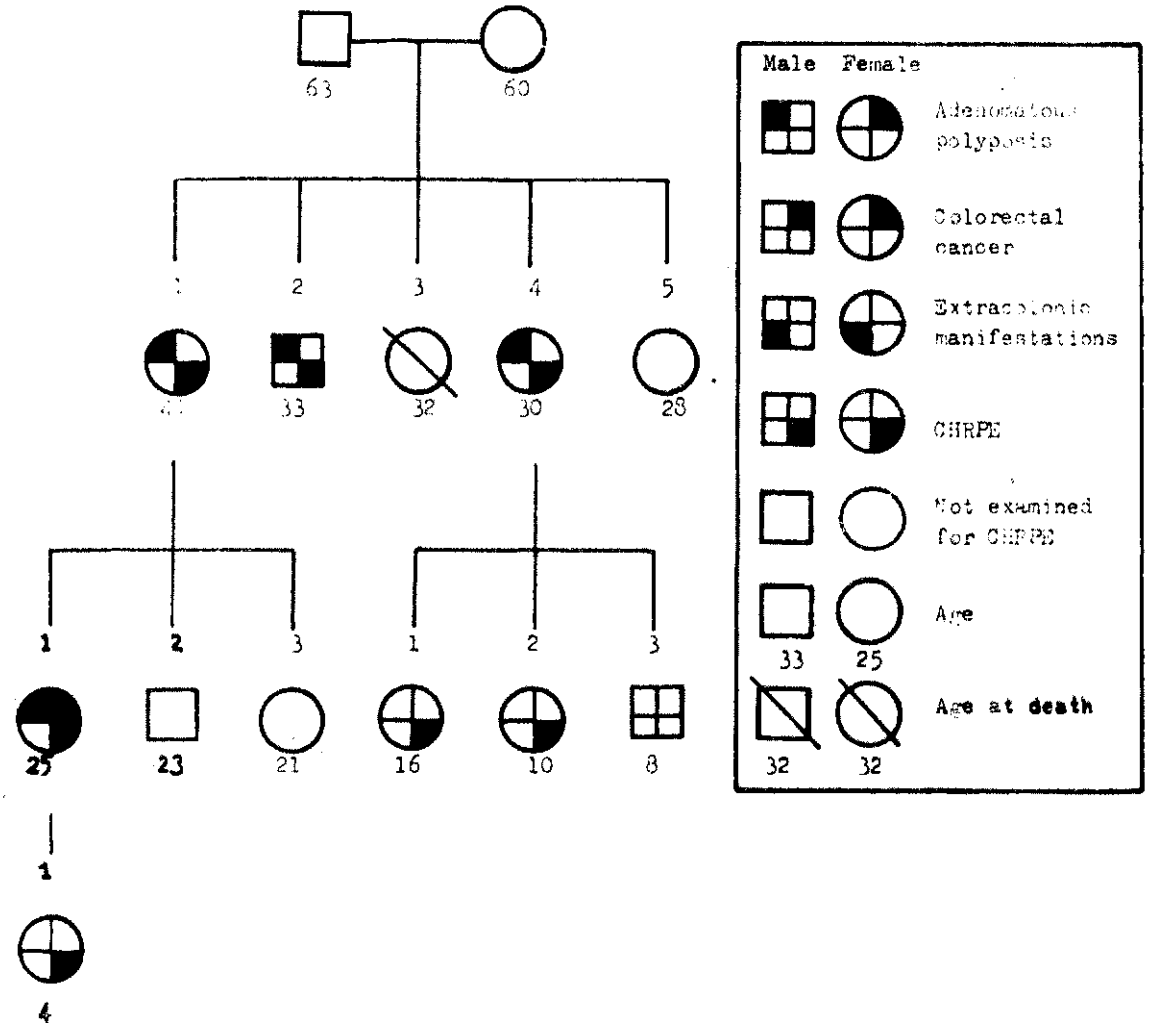

Figure 1. Pedigree of the subjects with FAP and offspring at risk and fundus lesions.

formed on each patient. Then, patients having fundus lesions were examined endoscopicly for FAP.

RESULTS

A patient (III -1), aged 25 years, having a colon cancer and FAP showed fundus lesions. Her mother and mother's sister and brother had also fundus lesions and FAP. Three of four offspring at risk having fundus lesions have refused examination for FAP (Fig. 1). Other two patients who had a colon cancer and FAP showed fundus lesions (Fig. 2).

Figure 2 : Two patients, had colon cancer and FAP, and fundus lesions.

Fundus lesions were ranged from 0.4 to 2 mm. in diameter and were round - pigmented wilh a surrounding pale halo, small and large round-pigmented and round - depig - mcnlcd in shape (Fig. 3). Patches of CHRPE were showed in FFA (Fig. 4)

None of the subjects had extracolonic manifestations (ECM).

DISCUSSION

In 1980 Blaire and Trempe, in 1984 Lewis at all and in 1987 Traboulsi at all have described CHRPE as a possible precursor for patients with FAP and ECM or at risk members of kindreds wilh documanted ECM. According to their findings, CHRPE occurs only in those patients with the classic findings described by Gardner (4,5,6).

Most recently, Llpois and Menczo have examined 24 patients from six families wilh FAP. They

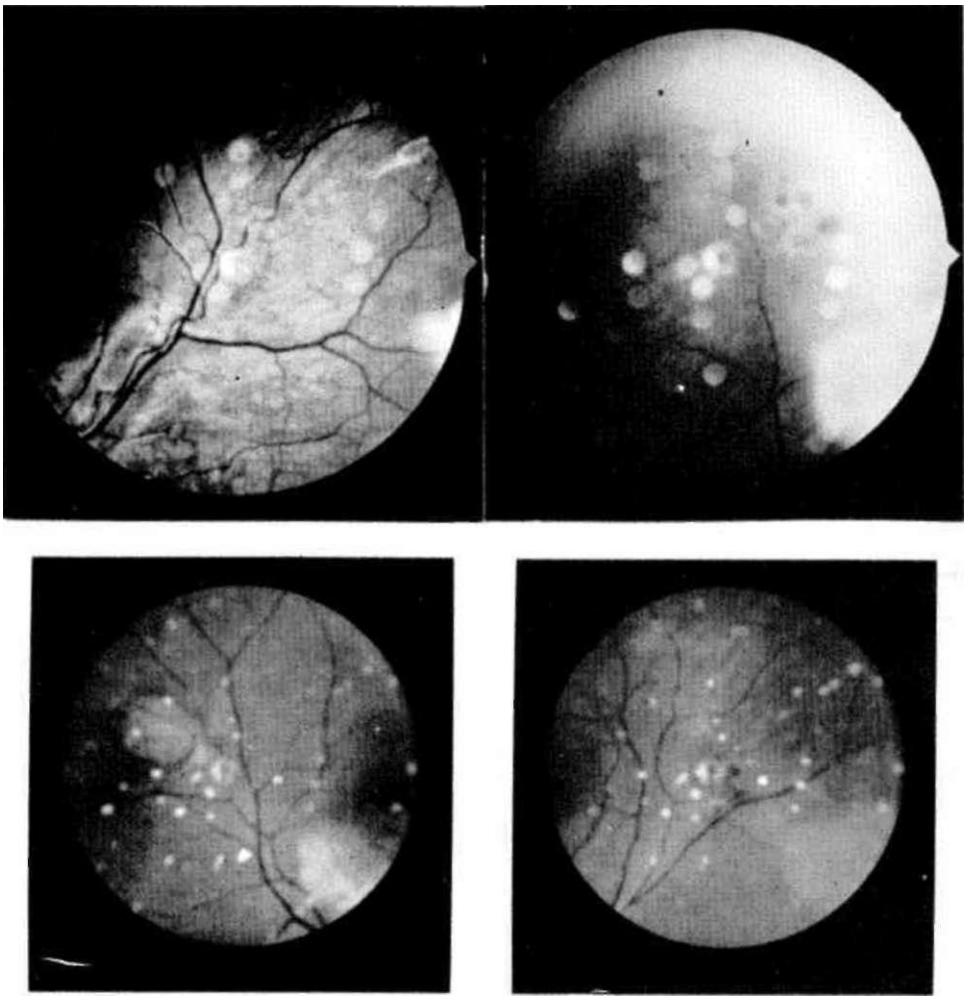

Figure 3. Fundus fluorescein angiography of patches of congenital hypertrophy of retinal pigment epithelium.

found that 11 patients were free of the intestinal disease and normal ocular fundi. Ten patients with polyposis showed patches of C H R P E . The remaining three patients showed pigmentation of the fundus, but no polyps of the colon. These three patients were less than 25 years of age (3).

Berk at all have reported in 40 patients with F A P and 11 offspring at risk for F A P . 35 (87.5 percent) of cases with F A P had retinal lesions, 22 of 25 patients with F A P alone had retinal lesions while 13 of 15 patients with F A P and E C M were similarly affected. Other 8 of offspring at risk for F A P (72.7 percent) had retinal lesions (2). According to them, the gene responsible for C H R P E appears to be transmitted from one generation to another, demonsrated by the high sensitivity of the retinal lesions in patients with F A P alone and with other E C M (2,3).

A11 of six subjects with F A P and three of four offspring at risk had fundus lesions. None of them had E C M .

Approximately 20 and 25 percent of patients with F A P have no family history and in these cases, the disorder represents spontaneous mutation (1).

Grandparents, aged 63 and 62 years, were healthy, but they couldn't be examined. Siblings in

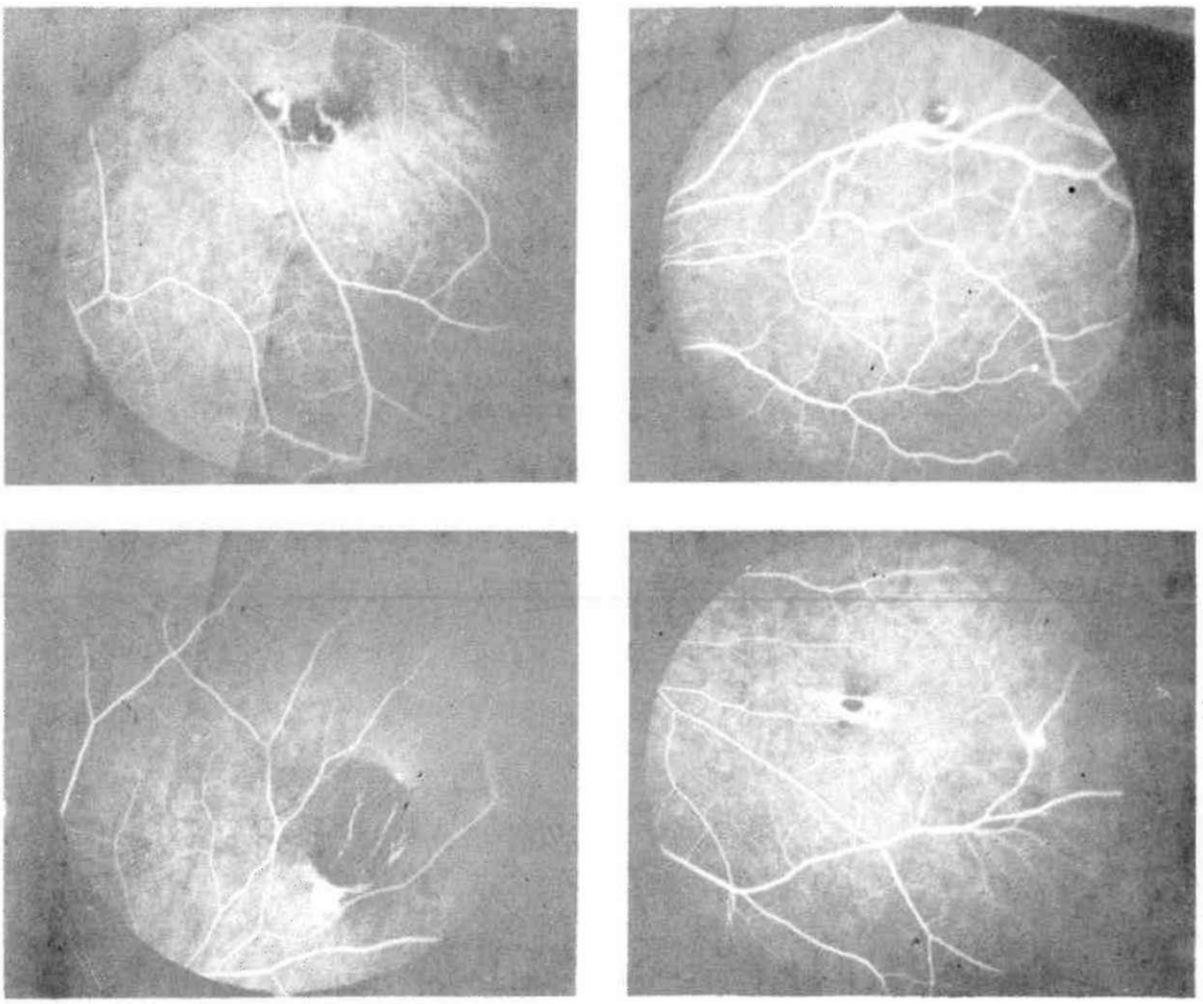

Figure 4. Fundus lesions; round pigmented with a surroinding pale halo, small and round pigmented and raund depigmented in shape.

proband II probablyrepresent spontaneous mutation. But CHRPE appears to be inherited in proband III and IV.

Fundus lesions appears to be present at birth or shortly there after (2,6). The youngest of offspring at risk showing CHRPE was aged 4 years (Fig.l).

Berk at all have classified four distinct combination of fundus lesions : oval pigmented with surrounding pale halo, small round-pigmented, large round-pigmented and round-depigmcntcd (2). Our findings were similar to that of Berk's (Fig. 3-4).

Conclusion

CHRPE appears to be transmitted from one generation to another and to be present after birth. Identifying CHRPE as a marker is a direct and noninvasive method and would facilitate early diagnosis and management of patients withFAP.

LITERATURE

Schwartz SI, Ellis II: Maingot's abdominal operations Appleton-Century-crofts/Norwalk-Connecticut. pp: 1366-71, 1985.

Berk T, BA, **MSSA,** Cohen Z, Mcleod RS, Parker JA. Congenital hypertrophy of the retinal pigment epithelium as a marker for familial adenomatous polyposis. Dis Col Rcct 31:253-7,1988.

I.lpois MD, Menczo JE: Congenital hypertrophy of the retinal pigment epithelium and familial polyposis of the colon. Am .1 Ophthal 103:235-6,1987.

Blair NP, Trempe CI.: Hypertrophy of the retinal pigment epithelium associated with Gardner's syndrome. Am J Ophthal 90: 661-7, 1980.

Ixwis RA, Crowdcr WE, Eierman LA, Nussbaum RE, Ferrel RE: ITic Gardner syndrome. Significance of oculcr features. Ophthal 91: 916-25,1984.

Traboulsi EI, Krush AI, Gardner EI. Prevalance and importance of pigmented ocular fundus lesions in Gardner's syndrome. N Engl .1 Med 316: 661-7, 1987.