European Journal of Ophthalmology / Vol. 16 no. 5, 2006 / pp. 779-781

SHORT COMMUNICATION

Clinical phenotype of an Italian family with a new mutation in the PRPF8 gene

F. TESTA[1], C. ZIVIELLO[2,3*], M. RINALDI[1], S. ROSSI[1], V. DI IORIO[1], E. INTERLANDI[1], A. CICCODICOLA[3], S. BANFI[2], F. SIMONELLI[1]*

[1]Department of Ophthalmology, Second University of Napoli
[2]Telethon Institute of Genetics and Medicine (TIGEM)
[3]Institute of Genetics and Biophysics "A. Buzzati-Traverso", CNR, Napoli - Italy

PURPOSE. *To report the clinical and functional characteristics of an autosomal dominant retinitis pigmentosa (ADRP) family with a novel point mutation (P2301S) in the PRPF8 gene.*
METHODS. *PRPF8 gene analysis and complete ophthalmologic examination in an ADRP family.*
RESULTS. *Clinical examination revealed the typical RP phenotype in all family members. Electroretinography showed preserved ERG photopic responses. Genetic analysis showed that the P2301S missense mutation segregated with the disease in all subjects.*
CONCLUSIONS. *Unlike previously reported families, the PRPF8 gene mutation in our family is associated with a mild phenotype in which cone function is partially preserved. (Eur J Ophthalmol 2006; 16: 779-81)*

KEY WORDS. *ADRP, PRPF8 gene, P2301S mutation*

Accepted: May 9, 2006

INTRODUCTION

Retinitis pigmentosa (RP) is an inherited degenerative disease of the retina that can be inherited in an X-linked, autosomal recessive, or autosomal dominant manner. To date, 12 autosomal dominant RP (ADRP)-causing loci have been cloned, namely RHO, RDS, RP1, IMPDH1, PRPF31, ROM1, PRPF8, HPRP3, NRL, FSCN2, CRX, and CA4 (RETnet, http://www.sph.uth.tmc.edu/Retnet/disease.htm).

PRPF8 mutations have been associated with type I or diffuse RP, with early onset of night blindness, nonrecordable electroretinogram (ERG), visual field loss, and partial loss of sight by age 30 years (1-6). Here we report the phenotypic manifestations of an Italian family affected by the recently reported P2301S mutation in the PRPF8 gene (7).

Case report

Molecular analysis showed that the P2301S mutation in the PRPF8 gene segregated with the disease in our family (Fig. 1). In our ADRP patients (5 females, 1 male), the disease started at a mean age of 10.3 years (±6.4 SD) with night blindness. Best-corrected visual acuity was between 1 and 0.2 (mean values 0.68±0.36 SD); myopic refraction was between –4 and –2 diopters in 4 of 6 patients. Color vision was normal in all patients except Patient III-3, who had achromatopsia. At fundus examination, Patients II-2, III-3, III-4, and III-6 showed atrophy of the retinal pigmented epithelium in the midperiphery. Bone-spicule pigmentation was diffuse in all retinal quadrants, and retinal vessels were narrowed (Fig. 2A). Optical coherence tomography examination re-

1120-6721/779-03$15.00/0

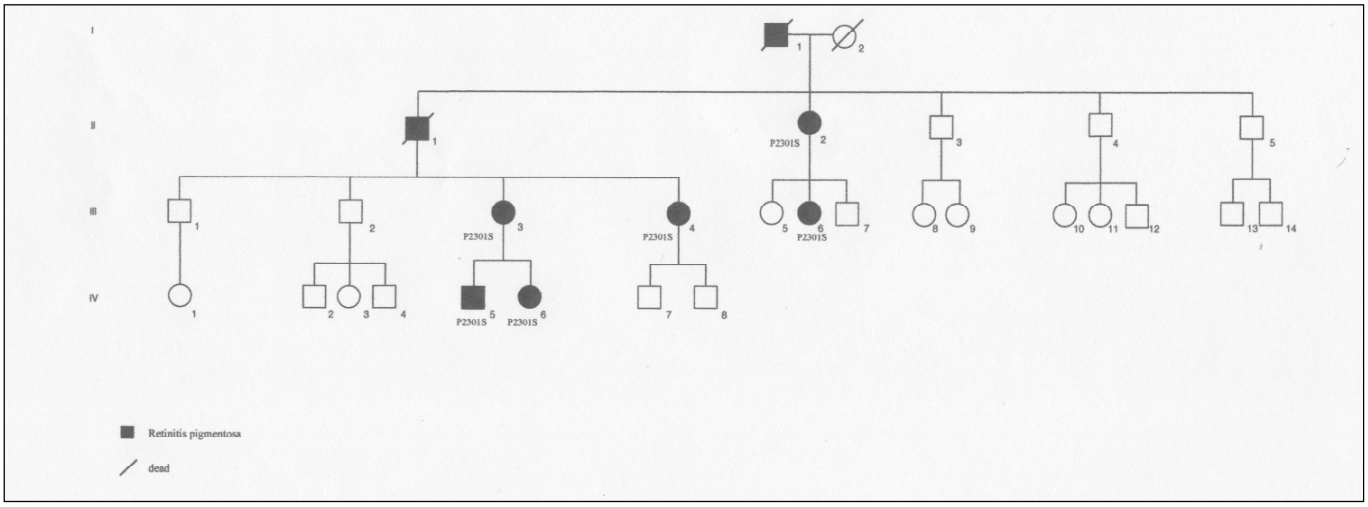

Fig. 1 - *Pedigree of the autosomal dominant retinitis pigmentosa family and the mutation identified in the PRPF8 gene.*

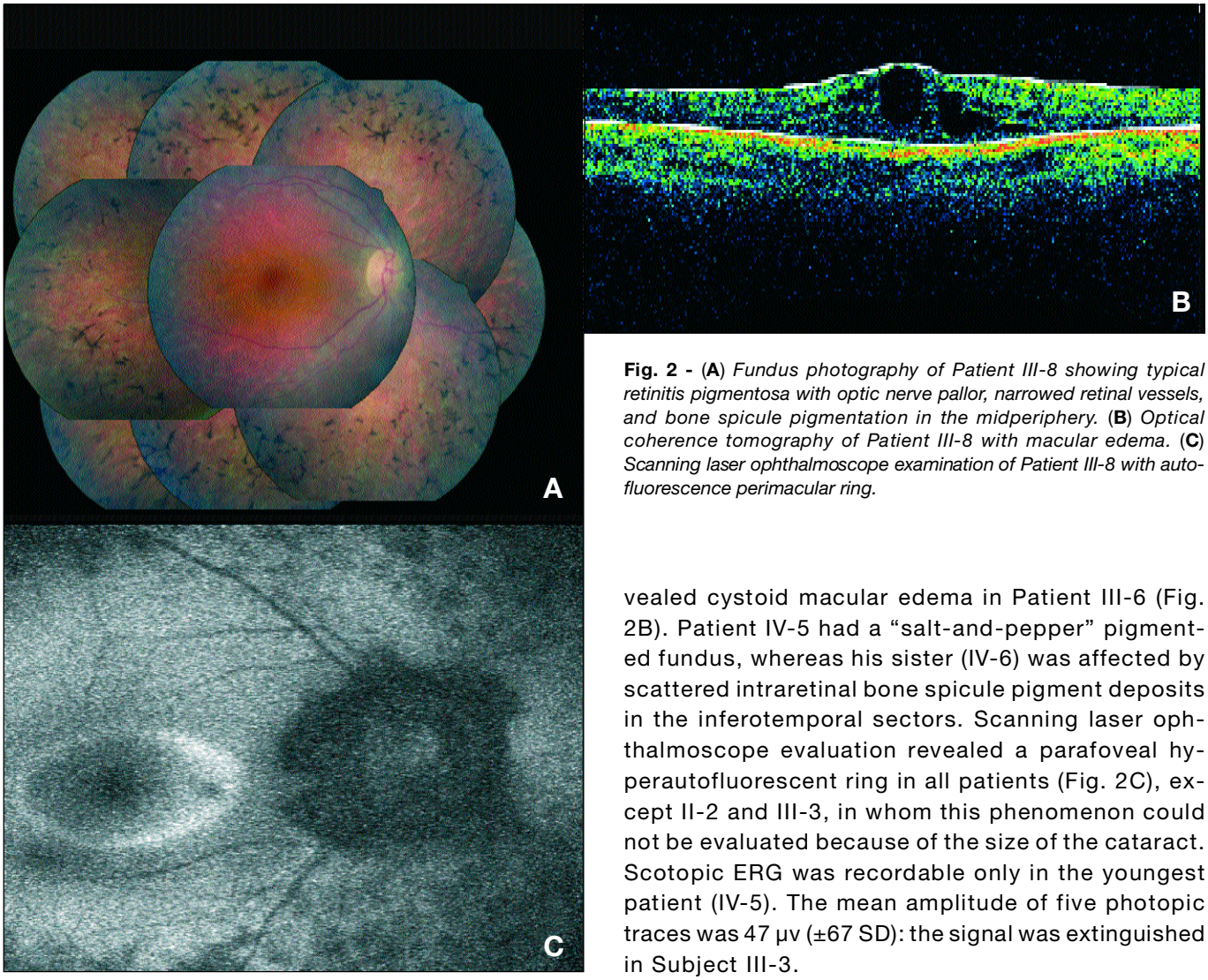

Fig. 2 - (**A**) *Fundus photography of Patient III-8 showing typical retinitis pigmentosa with optic nerve pallor, narrowed retinal vessels, and bone spicule pigmentation in the midperiphery.* (**B**) *Optical coherence tomography of Patient III-8 with macular edema.* (**C**) *Scanning laser ophthalmoscope examination of Patient III-8 with autofluorescence perimacular ring.*

vealed cystoid macular edema in Patient III-6 (Fig. 2B). Patient IV-5 had a "salt-and-pepper" pigmented fundus, whereas his sister (IV-6) was affected by scattered intraretinal bone spicule pigment deposits in the inferotemporal sectors. Scanning laser ophthalmoscope evaluation revealed a parafoveal hyperautofluorescent ring in all patients (Fig. 2C), except II-2 and III-3, in whom this phenomenon could not be evaluated because of the size of the cataract. Scotopic ERG was recordable only in the youngest patient (IV-5). The mean amplitude of five photopic traces was 47 μv (±67 SD): the signal was extinguished in Subject III-3.

DISCUSSION

Previous studies of ADRP families with linkage and mutations of the PRPF8 gene revealed a severe type of RP with early onset of night blindness, diffuse retinal involvement, and a nonrecordable ERG (1-6). Differently, our family, which carries the P2301S mutation, presents a typical RP phenotype with quite good visual acuity until middle age, associated with normal color vision in all patients but one. Moreover, ERG responses were preserved in all patients, which indicates primary impairment of rod photoreceptors and partially preserved cone function. In addition, four of our ADRP patients showed a perimacular hyperautofluorescent ring. This finding indicates preserved central photopic sensitivity, which is typical of RP patients who have good visual acuity (8). In line with this finding, a histologic study of RP caused by a PRPF8 gene mutation revealed the absence of rod photoreceptors and a reduced number of cone photoreceptors in the affected retina of a 63-year-old woman (9).

The clinical expression of ADRP in our family could be due to the biological effect exerted by mutation P2301S on PRPF8 protein function. Based on our results, we would argue that a combined clinical and genetic analysis would allow a more careful and precise prognostic evaluation of ADRP patients.

ACKNOWLEDGEMENTS

This work was supported by grants from Regione Campania (Convenzione - art. 66 del D.P.R. 382/80).

Supported by the Italian Telethon Foundation. None of the authors has proprietary interest in this study.

We are grateful to Jean Ann Gilder for revising and editing the text.

None of the authors has a proprietary interest in this study.

Reprint requests to:
Prof. Francesca Simonelli
P.zza Leonardo, 14
80129 Napoli, Italy
franctes@tin.it

REFERENCES

1. Greenberg J, Goliath R, Beighton P, Ramesar R. A new locus for autosomal dominant retinitis pigmentosa on the short arm of chromosome 17. Hum Mol Genet 1994; 3: 915-8.
2. Kojis TL, Heinzmann C, Flodman P, et al. Map refinement of locus RP13 to human chromosome 17p13.3 in a second family with autosomal dominant retinitis pigmentosa. Am J Hum Genet 1996; 58: 347-55.
3. Tarttelin EE, Plant C, Weissenbach J, Bird AC, Bhattacharya SS, Inglehearn CF. A new family linked to the RP13 locus for autosomal dominant retinitis pigmentosa on distal 17p. J Med Genet 1996; 33: 518-20.
4. McKie AB, McHale JC, Keen TJ, et al. Mutations in the pre-mRNA splicing factor gene PRPC8 in autosomal dominant retinitis pigmentosa (RP13). Hum Mol Genet 2001; 10: 1555-62.
5. van Lith-Verhoeven JJ, van der Velde-Visser SD, Sohocki MM, et al. Clinical characterization, linkage analysis, and PRPC8 mutation analysis of a family with autosomal dominant retinitis pigmentosa type 13 (RP13). Ophthalmic Genet 2002; 23: 1-12.
6. Martinez-Gimeno M, Gamundi MJ, Hernan I, et al. Mutations in the pre-mRNA splicing-factor genes PRPF3, PRPF8, and PRPF31 in Spanish families with autosomal dominant retinitis pigmentosa. Invest Ophthalmol. Vis Sci 2003; 44: 2171-7.
7. Ziviello C, Simonelli F, Testa F, et al. Molecular genetics of autosomal dominant retinitis pigmentosa (ADRP): a comprehensive study of Italian families. J Med Genet 2005; 42: 47-50.
8. Robson AG, Egan CA, Luong VA, Bird AC, Holder GE, Fitzke FW. Comparison of fundus autofluorescence with photopic and scotopic fine-matrix mapping in patients with retinitis pigmentosa and normal visual acuity. Invest Ophthalmol Vis Sci 2004; 45: 4119-25.
9. To K, Adamian M, Berson EL. Histologic study of retinitis pigmentosa due to a mutation in the RP13 gene (PRPC8): comparison with rhodopsin Pro23His, Cys110Arg, and Glu181Lys. Am J Ophthalmol 2004; 137: 946-8.