

MILIARY TUBERCULOSIS AND BILATERAL MULTIFOCAL CHOROIDAL INVOLVEMENT: PLACE OF INDOCYANINE GREEN ANGIOGRAPHY

KOÇAK N.¹, SAATCI A.O.², CINGIL G.²,
CIMRIN A.³, UCAR E.S.³

ABSTRACT

Purpose: To present the clinical features and angiographic findings of choroidal involvement in two cases with miliary tuberculosis.

Methods: 49-year and 23-year-old men were hospitalized for fever of unknown origin and they received a diagnosis of miliary tuberculosis following the systemic work-up. Both cases experienced mild visual acuity disturbances prior to initiation of systemic treatment. They underwent full ophthalmological examination including fluorescein and indocyanine green angiography.

Results: The visual acuity of first case was 20/30 in OD, and 20/25 in OS. There was trace of cells in the anterior chamber and mild vitritis OU. Visual acuity of the second case was 20/20 OU. Anterior segment was unremarkable OU. Ophthalmoscopy of both cases showed cream-colored patchy choroidal infiltrations especially located at the posterior pole OU. Fluorescein and indocyanine green angiographies were obtained with Heidelberg scanning laser ophthalmoscope. These lesions were hypofluorescent in early phases of fluorescein angiography and demonstrated gradually increased hyperfluorescence in late phases. Same lesions were hypofluorescent throughout the indocyanine green angiography and well delineated. Both patients received a systemic treatment of isoniazid, rifampicin, ethambutol and morphazinamide. Most of the choroidal lesions re-

solved without apparent changes whereas some healed as chorioretinal scars.

Conclusion: In patients with miliary tuberculosis, indocyanine green angiography seems to show choroidal involvement much better than the fluorescein angiography and may be a more important diagnostic tool than fluorescein angiography during the disease course.

RÉSUMÉ

Objectif: Nous rapportons l'observation de deux patients ayant présenté une tuberculose miliaire, avec des résultats cliniques et angiographiques.

Patients et méthodes: Il s'agit de deux patients de 49 et 23 ans. Ils sont hospitalisés à la suite d'une fièvre indéterminée. Après l'examen clinique et radiologique, le diagnostic de tuberculose miliaire a été posé. Chez les malades qui souffraient d'un trouble visuel, un examen ophtalmologique complet, une angiographie au vert d'indocyanine (ICG) et une angiographie à la fluorescéine ont été effectués.

Résultats: Le premier cas a une vision de 20/30 à l'oeil droit et de 20/25 à l'oeil gauche. L'examen à la lampe à fente a permis de constater un Tyndall minimal dans la chambre antérieure et une vitrite minimale. Pour le deuxième cas la vision est de 20/20 des deux côtés et le segment antérieur est sans particularité. L'examen du fond d'oeil des malades montre des lésions jaune-grisâtre comme plaques multifocales choroïdiennes dans le pôle postérieur. Des angiographies à la fluorescéine et à l'ICG ont été effectuées avec le Heidelberg Scanning Laser Ophthalmoscope. L'angiographie fluorescéinique montre au niveau des plaques une hypofluorescence pendant la phase précoce et pendant la phase tardive une hyperfluorescence qui augmente progressivement. Les mêmes lésions avec l'ICG montrent une hypofluorescence pendant tous les phases. Après le traitement antituberculeux avec Isoniaside, Rifampisin, Etambutol et Morfosinamide, les lésions choroïdiennes

.....

¹ Fellow, Dokuz Eylul University, Ophthalmology Department, Izmir- Turkey

² Professor, Dokuz Eylul University, Ophthalmology Department, Izmir- Turkey

³ Professor, Dokuz Eylul University, Department of Chest Medicine, Izmir-Turkey

received: 18.05.06

accepted: 15.07.06

nes ont disparu sans cicatrice ou avec quelques cicatrices choroïdiennes minimes.

Conclusion: L'angiographie au vert d'indocyanine a mieux démontré que l'angiographie fluorescéinique les lésions choroïdiennes de tuberculose miliaire. L'ICG est plus performant pour le diagnostic de cette maladie.

KEY WORDS

Choroidal tuberculosis, indocyanine green angiography, miliary tuberculosis

MOTS-CLÉS

Angiographie au vert d'indocyanine, tuberculose choroïdienne, tuberculose miliaire.

Ocular tuberculosis was first described in 1740 and ocular involvement was first reported in 1855 (2). *Mycobacterium tuberculosis* may cause multifocal choroidal granulomas and occasionally multifocal choroidal hemorrhages in patients with severe miliary tuberculosis (4,7,10). Choroidal tubercles may range from 1/4 to several disc-diameters in size and number from one to 50, with most eyes having fewer than five. Choroidal tubercles are the result of direct infection via hematogenous seeding from a systemic focus (7). Diagnosis is mostly presumptive and based on clinical appearance, systemic evaluation and response to treatment. Fundus fluorescein and indocyanine angiography are routinely used to delineate retinochoroidal involvement and are superior to clinical examination (6,12).

We describe the clinical features and angiographic findings of two cases with miliary tuberculosis and bilateral choroidal involvement.

CASE REPORTS

CASE I

A 49-year-old man was hospitalized with atypical pneumonia and high fever. A meticulous systemic work-up was carried out and a diagnosis of miliary tuberculosis was made. Ophthalmic examination was performed due to bilateral blurred vision just prior to initiation of anti-tuberculous treatment. His visual acuity was 20/

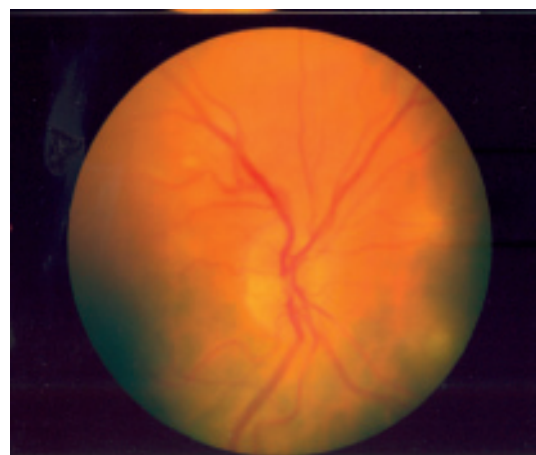


Figure 1: Case 1, Color fundus picture of the right eye showing multifocal choroiditis.

30 in OD and 20/25 in OS. There was trace of cells in the anterior chamber and mild vitritis was present OU. Ophthalmoscopy showed flat whitish scattered choroidal lesions especially located at the posterior pole OU (Figure 1). Fluorescein and indocyanine green angiographies were obtained with Heidelberg scanning laser ophthalmoscope. These lesions were hypofluorescent in the early phases of fluorescein angiography and hyperfluorescence increased gradually in the late phases. The same lesions were hypofluorescent throughout the course of indocyanine green angiography (Figure 2a, 2b)

and were more prominent as compared to fluorescein angiography.

A treatment combining isoniazid, rifampicin, ethambutol and morphazinamide was initiated. Two months later, his visual acuity was 20/20 OD and 20/25 OS. Anterior segment examination was unremarkable OU. Most of the choroidal lesions resolved without apparent changes. Some healed as chorioretinal scars. Control indocyanine green angiography was obtained (Figure 2c, 2d). Systemic treatment was discontinued after 24 months.

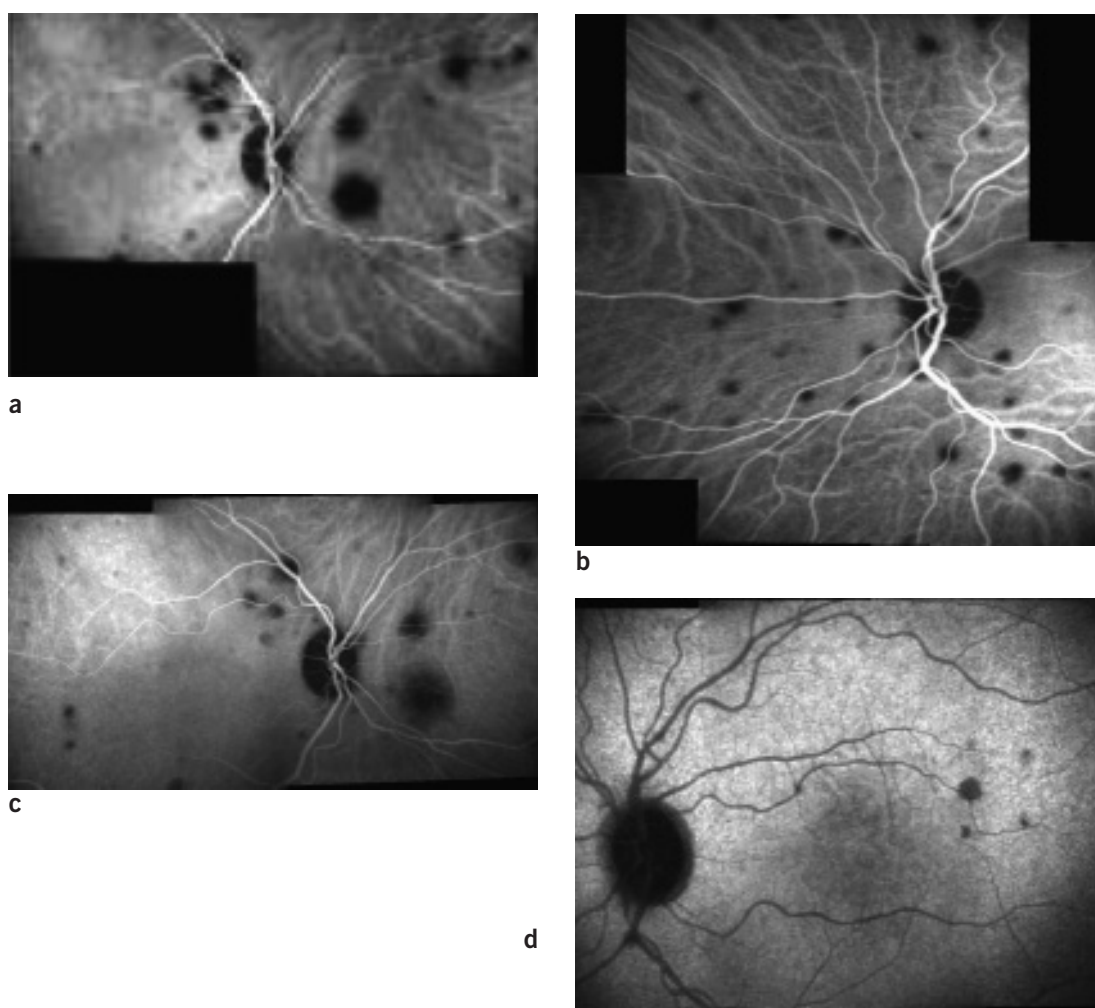


Figure 2a-2b-2c-2d: Case 1, Indocyanine green angiography. Composite picture of the right (a) and left (b) eyes showing hypofluorescent spots prior to treatment. Composite picture of the right (c) and left (d) eyes after systemic treatment, fewer hypofluorescent areas corresponding now to inactive chorioretinal scars.

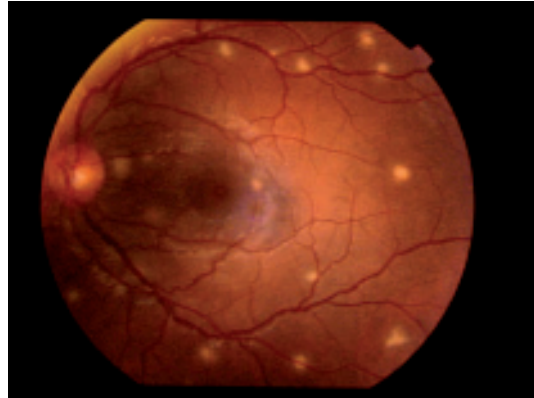
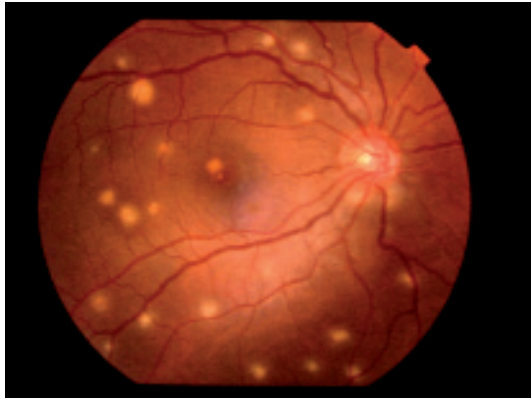


Figure 3a-3b: Case 2, Color fundus picture of the right (a) and left (b) eyes showing bilateral multifocal choroiditis.

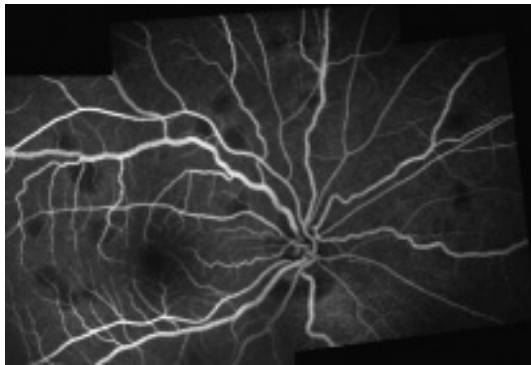


Figure 4a-4b: Case 2, Fundus fluorescein angiographic picture showing early hypofluorescence due to blocking (a) and late hyperfluorescence corresponding to areas of choroidal infiltrates (b).

CASE II

A 23-year-old man with fever of unknown origin was hospitalized. His systemic work-up revealed miliary tuberculosis. Histopathologic evaluation of needle liver biopsy confirmed the diagnosis. He was examined by us for blurred vision just prior to anti-tuberculous treatment. His visual acuity was 20/20 in both eyes. The anterior segments were unremarkable OU. Ophthalmoscopy showed multifocal cream-colored relatively well-defined choroidal infiltrations especially located at the posterior pole OU (Figure 3a, 3b). Fluorescein and indocyanine green angiographies were obtained with the Heidelberg scanning laser ophthalmoscope. These lesions were hypofluorescent in the early phases

of fluorescein angiography and demonstrated gradually increased hyperfluorescence in the late phases (Figure 4a, 4b). The same lesions remained hypofluorescent throughout the indocyanine green angiography (Figure 5a, 5b) and indocyanine green angiographic features were more striking than fluorescein angiographic features.

The patient received a systemic treatment of isoniazid, rifampicin, ethambutol and morphazinamide. Eight months later, most of the choroidal lesions seemed to resolve without apparent changes. Some healed as chorioretinal scars. Control indocyanine green angiography was obtained (Figure 5c, 5d).

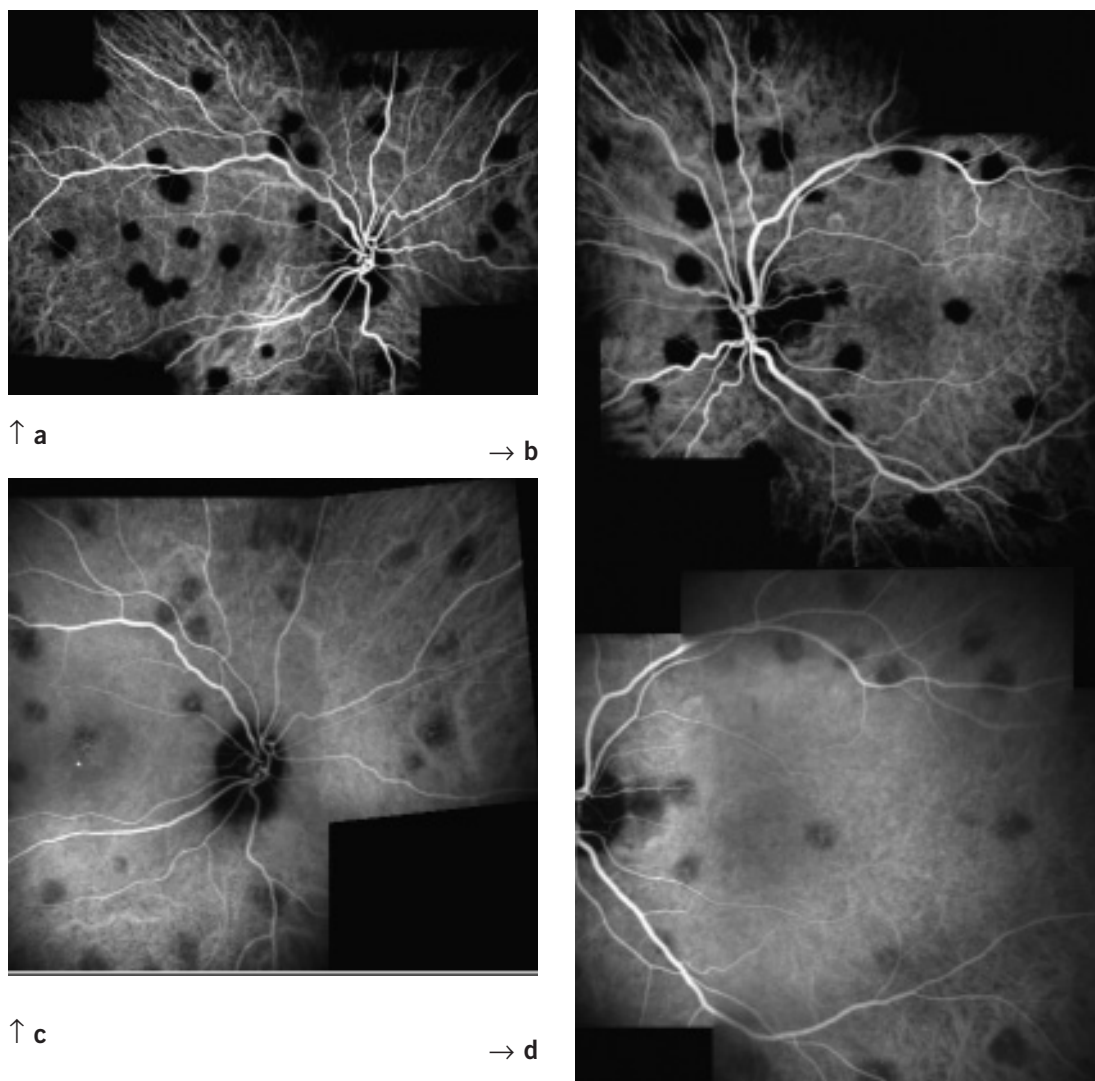


Figure 5a-5b-5c-5d: Case 2, Indocyanine green angiography. Composite picture of the right (a) and left (b) eyes showing hypofluorescent spots prior to treatment. Composite picture of the right (c) and left (d) eyes after systemic treatment, fewer areas of hypofluorescence corresponding to inactive chorioretinal scars.

DISCUSSION

Tuberculosis may involve conjunctiva and cornea and present as ulceration, tumor-like mass, phlyctenular keratoconjunctivitis, and interstitial keratitis (11). Episcleritis, scleritis, chronic iridocyclitis, retinal vasculitis, retinal vascular occlusion, vitritis, and papillitis are among the other manifestations (1,8,11). The most common ocular presentation of pulmonary tu-

berculosis is choroiditis (8). Choroidal tuberculoma may accompany active or inactive tuberculosis and intraocular manifestations are usually associated with active systemic disease (8). Sheu et al (8) reported five cases of tuberculosis with various ocular manifestations such as panophthalmitis, endophthalmitis, posterior uveitis with choroidal tubercles, keratitis, and lid mass. Three of five patients had miliary tuberculosis as our two cases.

Choroidal tuberculosis may present as serpiginous choroiditis-like choroidal involvement. Gupta et al (5) reported eleven eyes of seven patients with choroidal tuberculosis resembling serpiginous choroiditis. All eyes responded well to anti-tuberculous treatment. Fluorescein angiography of the lesions showed hypofluorescence initially and hyperfluorescence in the late phases.

Many investigators believe that indocyanine green angiography is a very helpful method for detecting choroidal involvement in granulomatous chorioretinitis (10,12). Stanga et al (9) recommended indocyanine green angiography both for diagnosis and for monitoring the effect of treatment in inflammatory eye disorders affecting the choroid such as tuberculosis, posterior scleritis, sarcoidosis, toxoplasmosis and Behçet's disease. In Wolfensberger et al's (12) study, fluorescein and indocyanine green angiographies were performed in 15 eyes with presumed posterior segment ocular tuberculosis. One eye of eight patients was phthisic. Fluorescein angiography and fundus examination were able to show choroidal involvement only in nine (60%) eyes. Indocyanine green angiography revealed choroidal involvement in the remaining six (40%) eyes, in whom fundus examination and fluorescein angiography were considered as normal. They classified the indocyanine green angiographic findings into four main groups: 1) irregularly distributed, hypofluorescent lesions in the early and intermediate phases of angiography that either became isofluorescent or remained hypofluorescent in the late phase; 2) numerous, small, focal, hyperfluorescent spots; 3) choroidal vessels that appeared fuzzy in the intermediate phase because of leakage; 4) diffuse choroidal hyperfluorescence in the late phase. Moreover, focal hyperfluorescent spots were seen in eyes with more long-standing disease. The disparity between Topcon fundus camera and scanning laser ophthalmoscope indocyanine green angiography is a well-known fact and instrument type is important while interpreting the indocyanine green angiographic findings (3). In our patients, choroidal lesions remained hypofluorescent throughout the indocyanine green angiography sequences. However in Wolfensberger et al's (12) study, some of the choroidal lesions were reported to be bright as the images were ob-

tained with Topcon camera system. Tayanc et al.(10) performed indocyanine green angiography on two patients with tuberculosis and unilateral choroidal involvement. In the first case, two hypofluorescent lesions that corresponded to the choroidal tuberculomas were noted in the involved eye. However, only one of these two lesions was found during ophthalmoscopic examination and fluorescein angiography. These lesions persisted after treatment, but became less hypofluorescent. In the second case, indocyanine green angiography showed a hypofluorescent choroidal lesion corresponding to a choroidal tuberculoma that appeared larger in size than on fluorescein angiography. This lesion remained hypofluorescent in all phases of indocyanine green angiography and became less obvious after treatment. They explained the angiographic findings in two ways: 1) these lesions may be active choroidal granulomas still persisting after treatment; however, they become less hypofluorescent after treatment which may be interpreted as shrinkage of the granuloma and 2) this hypofluorescence may correspond to atrophic lesions.

In our cases, indocyanine green angiography showed the details of choroidal involvement more clearly than either fundus examination or fluorescein angiography. Indocyanine green angiography seems to demonstrate choroidal involvement much better than the clinical examination and fluorescein angiography in patients with military tuberculosis and also yields more information during the course of follow-up of choroidal lesions and their response to systemic treatment.

REFERENCES

- (1) BERINSTEIN D.M., GENTILE R.C, MCCORMICK S.A., WALSH J.B. – Primary choroidal tuberculoma. *Arch Ophthalmol* 1997; 115:430-431.
- (2) DONAHUE H.C. – Ophthalmologic experience in a tuberculosis sanatorium. *Am J Ophthalmol* 1967; 64:742-748.
- (3) FLOWER R.W., CSAKY K.G., MURPHY R.P. – Disparity between fundus camera and scanning laser ophthalmoscope indocyanine green imaging of retinal pigment epithelium detachments. *Retina* 1998; 18:260-268.
- (4) GASS J.D.M. – Stereoscopic atlas of macular disease; diagnosis and treatment. 4th ed. St. Louis: CV Mosby;1997;326-333.

- (5) GUPTA V., GUPTA A., ARORA S., BAMBERY P., DOGRA M.R., AGARWAL A. – Presumed tubercular serpiginous like choroiditis. Clinical presentations and management. *Ophthalmology* 2003; 110:1744-1749.
- (6) HELM C.J., HOLLAND G.N. – Ocular tuberculosis. *Surv Ophthalmol* 1993; 38:229-256.
- (7) MEHTA S. – Ocular lesions in acute disseminated tuberculosis. *Ocular Immunology and Inflammation* 2004; 12: 311-315.
- (8) SHEU S.J., SHYU J.S., CHEN L.M., CHEN Y.Y., CHIRN S.C., WANG J.S. – Ocular manifestations of tuberculosis. *Ophthalmology* 2001; 108:1580-1585.
- (9) STANGA P.E., LIM J.I., HAMILTON P. – Indocyanine green angiography in chorioretinal diseases: Indications and interpretation. An evidence-based update. *Ophthalmology* 2003; 110:15-24.
- (10) TAYANC E., AKOVA Y.A., YILMAZ G. – Indocyanine green angiography in ocular tuberculosis. *Ocular Immunology and Inflammation* 2004; 12: 317-322.
- (11) THOMPSON M.J., ALBERT D.M. – Ocular tuberculosis. *Arch Ophthalmol* 2005; 123:844-849.
- (12) WOLFENSBERGER T.J., PIGUET B., HERBORT C.P. – Indocyanine green angiographic features in tuberculous chorioretinitis. *Am J Ophthalmol* 1999; 127:350-353.

.....

Correspondence and reprints:

*Ali Osman SAATCI
Mustafa Kemal Sahil Bulvari No:73
A Blok Daire:9 Narlidere- Izmir 35320 Turkey
Tel: +90 532 7437071
Fax: +90 232 2782717
e-mail: osman.saatci@deu.edu.tr and
osman.saatci@yahoo.com*