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MULTIFOCAL CHOROIDITIS WITH PANUVEITIS AND PUNCTATE INNER CHOROIDOPATHY: A MINI REVIEW

DE MEYER V.,[1] LAFAUT B.A.,[1] VAN DE SOMPEL W.,[2] AND DE LAEY J.J.,[1]

SUMMARY

Multifocal choroiditis and punctate inner choroidopathy cause scattered acute chorioretinal lesions in the fundus. Secondary choroidal neovascularization and, more rarely, diffuse subretinal fibrosis without obvious neovascularization are associated with both syndromes and cause severe visual loss. Both disorders are of unknown etiology and have many similarities. It is our purpose to present four such cases with emphasis on their fluorescein and indocyanine green angiographic appearance. We review shortly the literature on the subject.

SAMENVATTING

Multifocale choroiditis en punctiforme choroidopathie van de interne lagen veroorzaken acute chorioretinale letsels verspreid in de fundus. Secundaire chorioidale neovascularizatie en, minder frequent, diffuse subretinale fibrose zonder duidelijke neovascularizatie, zijn complicaties van beide ziektebeelden die een ernstig visusverlies kunnen veroorzaken. De oorzaak van deze ziekten die goed op elkaar lijken is niet bekend. Wij stellen vier gevallen voor met nadruk op de fluoresceïne en indocyanine groen angiografie. We bespreken kort de ziektebeelden aan de hand van de literatuur.

RESUME

La choroidite multifocale et la choroidopathie interne punctiforme causent des lésions choriorétiniennes aiguës, dispersées dans le fond d'oeil. Des néovaisseaux choroidiens secondaires et, moins fréquemment, de la fibrose sous-rétinienne diffuse sans néovascularisation évidente sont des complications de ces deux maladies qui peuvent provoquer une importante baisse de l'acuité visuelle. Nous présentons quatre patients en mettant l'accent sur les aspects de la fluoangiographie et de l'angiographie au vert d'indocyanine. Nous discutons brièvement ces maladies, en nous basant sur la littérature récente.

KEY WORDS

Multifocal choroiditis with panuveitis (MCP), punctate inner choroidopathy (PIC), ICG angiography.

MOTS CLES

La choroidite multifocale avec panuvéite, la choroidopathie interne punctiforme, l'angiographie au vert d'indocyanine.

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[1] *Department of Ophthalmology, University Hospital Ghent*
[2] *Department of Ophthalmology, Middelheim Hospital Antwerp.*

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INTRODUCTION

Multifocal choroiditis and punctate inner choroidopathy cause acute chorioretinal lesions scattered in the fundus. Secondary choroidal neovascularization and more rarely diffuse subretinal fibrosis without obvious neovascularization are associated with both syndromes and cause severe visual loss. Both disorders are of unknown etiology and have many similarities. It is our purpose to present a few cases and review shortly the literature on the subject.

CASE REPORTS

Case 1 (figure 1): A 27-year-old myopic female was referred for visual loss and metamorphopsia in the left eye. Her visual acuity was 1.0 in the right eye and 0.4 in the left. Multiple focal chorioretinitis lesions were scattered in the posterior pole and in the nasal midperiphery of both eyes; more lesions were found in the right eye. In the left eye an extrafoveal choroidal neovascular membrane was identified by fluorescein as well as by indocyanine green angiography. On indocyanine green angiography several more hypofluorescent spots were found than could be suspected clinically or on fluorescein angiography. The neovascular membrane was treated by laser photocoagulation and additionally subtenon steroids injections were given. Four months later, the visual acuity was 1.0 in both eyes and the metamorphopsia had almost entirely disappeared. Fluorescein angiography showed an atrophic chorioretinal scar, indicating successful laser treatment.

Case 2 (figure 2,3): A 26-year-old myopic female was evaluated for a sudden onset of metamorphopsia in her right eye. The visual acuity was 0.6 in the right eye and 0.8 in the left. The anterior segments and vitreous did not show signs of inflammation. Fundus examination of the right eye revealed a few yellowish lesions at the level of the RPE in the macular region. The left eye was normal. On fluorescein angiography, the lesions in the right eye were hyperfluorescent in the early phase with dye leakage in the late phase. Indocyanine green angiography revealed large hypofluorescent lesions from the early phase on; this hypofluorescence persisted in the late phase and was surrounded by slight, ill-defined hyperfluorescence. Additionally much smaller hypofluorescent spots were observed that could not be identified by fluorescein angiography. Two weeks later the visual acuity in the right eye had dropped to 0.2. Ophthalmoscopically, the size of the macular lesions had considerably increased. A few small hemorrhages were also seen. Fluorescein angiography revealed punctate hyperfluorescence in the early phase that became confluent in the late phase. The indocyanine green angiography was comparable to the previous angiogram in the early phase, but in the late phase the macular area of hypofluorescence was more extensive. A hypofluorescent ring was observed around the optic disc as well as several smaller hypofluorescent spots in the late phase. A general evaluation including blood tests and lip biopsy for sarcoidosis were negative. An oral steroid therapy of 64 mg methylprednisolon daily was initiated, but this did not lead to any improvement. Three months later a fibrotic choroidal neovascular membrane was removed. Visual acuity did not recover as chorioretinal atrophy had developed under the entire foveal area.

Case 3 (figure 4): A 33-year-old emmetropic female consulted an ophthalmologist because of decreased vision in her left eye since a few days. She suffered from a flu-like illness a couple of weeks earlier at presentation. The visual acuity was 1.0 in the right eye and 0.1 in the left. The anterior segments were normal and no vitreous cells were seen. Fundus examination of the right eye appeared normal. In the posterior pole of the left eye some deeply located intraretinal white dots were seen that stained minimally during the fluorescein angiography. Additionally, fluorescein angiography demonstrated papiledema and a granular aspect of the macular area. An enlarged blind spot was found with static perimetry (Humphrey 30-2). Multiple evanescent white dot syndrome (MEWDS) was suspected. Systemic steroids (64 mg methylprednisolon daily) were prescribed. Five weeks later, the visual acuity had normalized and the yellow dots had disappeared.

During the follow-up of 7 years, she experienced several episodes of blurred vision in the left eye with subsequently spontaneous regression of subjective complaints. The right eye remained unaffected. More chorioretinitis foci

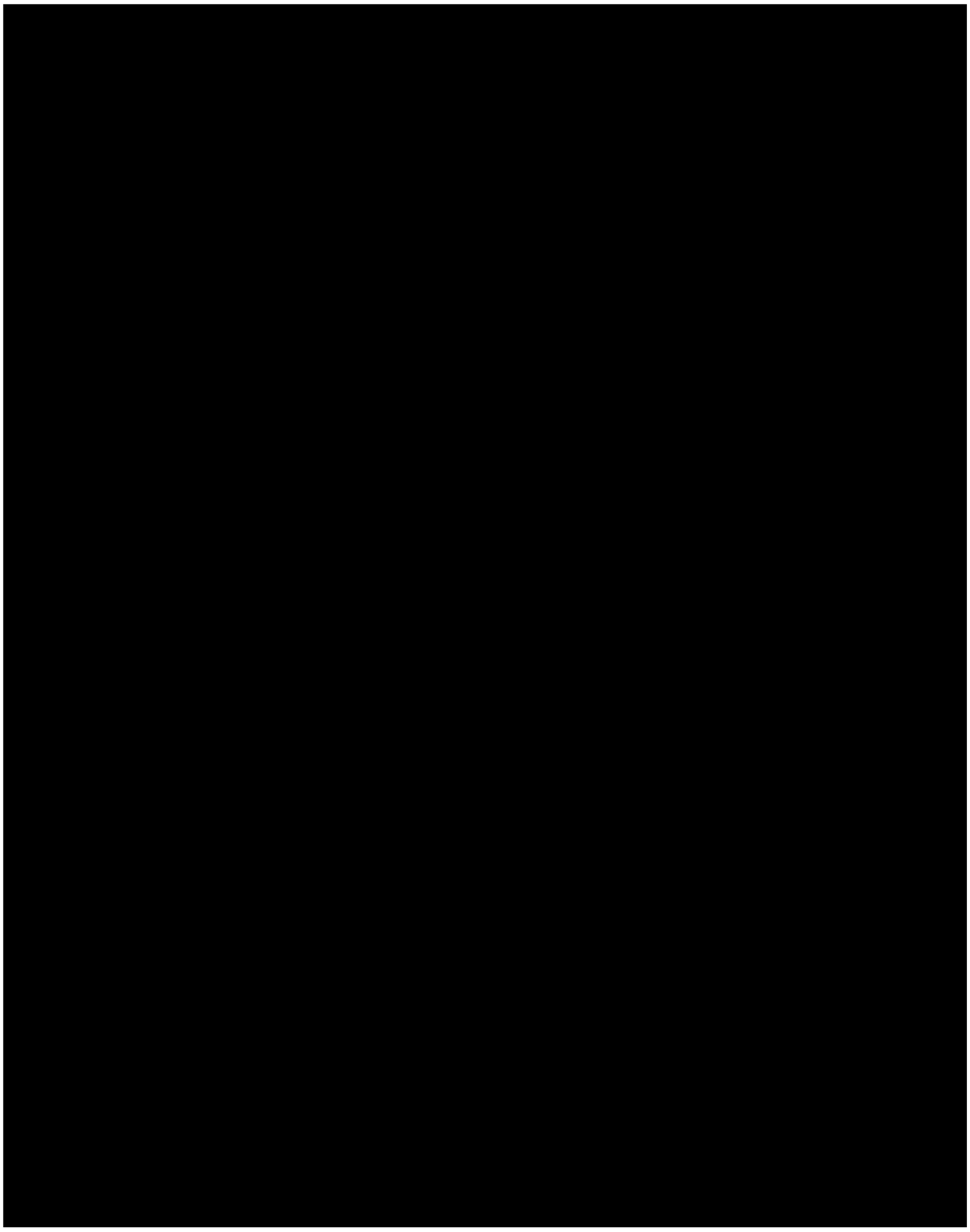

Figure 1, case 1: A: venous phase fluorescein angiogram of left eye, indicating leakage from a neovascular membrane and a few focal lesions in the interpapillomacular area; B: venous phase fluorescein angiogram 4 months after laser photocoagulation of the neovascular membrane; CD and EF: venous and late phase indocyanine green angiogram of right eye and left eye respectively, note the hypofluorescence of the local lesions in the late phase. The neovascular membrane is slightly hyperfluorescent, surrounded by a darker rim.

appeared in the left eye, not only in the macular area but some also nasally and subsequently the lesions atrophied. Ultimately, in the left eye, macular subretinal fibrosis developed resulting in severe and permanent visual loss (visual acuity 0.02). The subretinal fibrosis stained on fluorescein angiography from the early phase on but dye leakage was not ob-

served. Multiple focal lesions were visible as window defects. The fibrosis caused hypofluoresecence in the early and middle phase of the indocyanine green angiography but could not be distinguished anymore in the late phase. During the entire follow-up no inflammation neither in the anterior segment nor in the vitreous was observed. The subretinal fibrous tissue was surgically removed, visual acuity improved to 0.3 and the metamorphopsia disappeared.

Case 4 (figure 5): A 43-year-old emmetropic male was referred for bilateral blurred vision of six months duration. The visual acuity was 1.0 in the right eye and 0.3 in the left. Slitlamp examination revealed some old keratic precipitates as well as a few cells in the vitreous. Fundus examination of both eyes showed several yellowish lesions at the level of the retinal pigment epithelium, scattered in both posterior poles. In the left eye, a few chorioretinal lesions were also hyperpigmented. Fluorescein angiography revealed a minimal diffusion of dye within all of the lesions in the late phase. In the left macula, a neovascular net was demonstrated by fluorescein angiography. The patient was treated by repeated subtenon steroid injections in the left eye. Inactivation of inflammation and choroidal neovascularization was observed; the visual acuity recovered to 0.9. Eight years later, the patient consulted again with complaints of blurred vision in the right eye. At that moment, the visual acuity was 0.5 in the right eye while the visual acuity in the left eye remained unchanged at 0.9. Several scarred lesions were seen in both eyes as well as a subfoveal choroidal neovascular membrane in the right eye. This finding was confirmed by fluorescein as well as indocyanine green angiography. The choroidal neovascular membrane did not regress within 3 months under systemic steroid treatment, 64 mg of methylprednisolon daily, and was surgically removed. Visual acuity unfortunately failed to improve postoperatively because of a central choroidal defect.

DISCUSSION

Two inflammatory syndromes, multifocal choroiditis and panuveitis (MCP) and punctate inner choroidopathy (PIC) cause multifocal small yellow fundus lesions that become chorioretinal atrophic scars. These two syndromes are predominantly seen in young, mildly myopic women that complain of blurred vision and/or scotomata. They characteristically experience photopsia.

In MCP[6, 14, 16, 20], the fundus lesions are round and predominantly found in the posterior pole or nasal quadrant. The lesions have a diameter from 100-1000 μm and are often grouped in clusters or have a linear distribution. The acute lesions are creamy and leak fluorescein. The majority of patients have vitreal cells often associated with mild to moderate anterior uveitis. The active disorder may be complicated by a hot disc, retinal vasculitis and cystoid macular edema. The active multifocal choroidal lesions evolve into atrophic chorioretinal scars with variable hyperpigmentation that appear as window defects on fluorescein angiography. Secondary choroidal neovascularization, from scars or sometimes from active lesions in the macular area are the main cause of severe visual loss in these patients. The majority of patients has bilateral disease with recurrences.

In PIC[26], on the other hand, the acute lesions are creamy yellow and become atrophic and pigmented as in MCP but tend to be somewhat smaller (100-300 μm) and are rather concentrated in the posterior pole. There is no anterior segment inflammation; vitritis and cystoid macular edema have not been reported in this disorder. Unless the disorder is complicated by choroidal neovascularization, the prognosis is usally good. Recurrences are rarely seen.

Both MCP or PIC can be associated with diffuse subretinal fibrosis[4, 6, 26]. Several scattered choroiditis lesions over the posterior pole with overlying turbid subretinal fluid are seen in the active phase. Fluorescein angiography indicates diffuse leakage from the lesions. Subretinal fibrosis gradually develops from the focal lesions without obvious choroidal neovascularization, forms a placoid subretinal scar and may cause severe visual loss. Recurrences with aggravation of fibrosis have been reported.

Differential diagnosis:

It must be pointed out that many ocular inflammatory and infectious conditions can develop

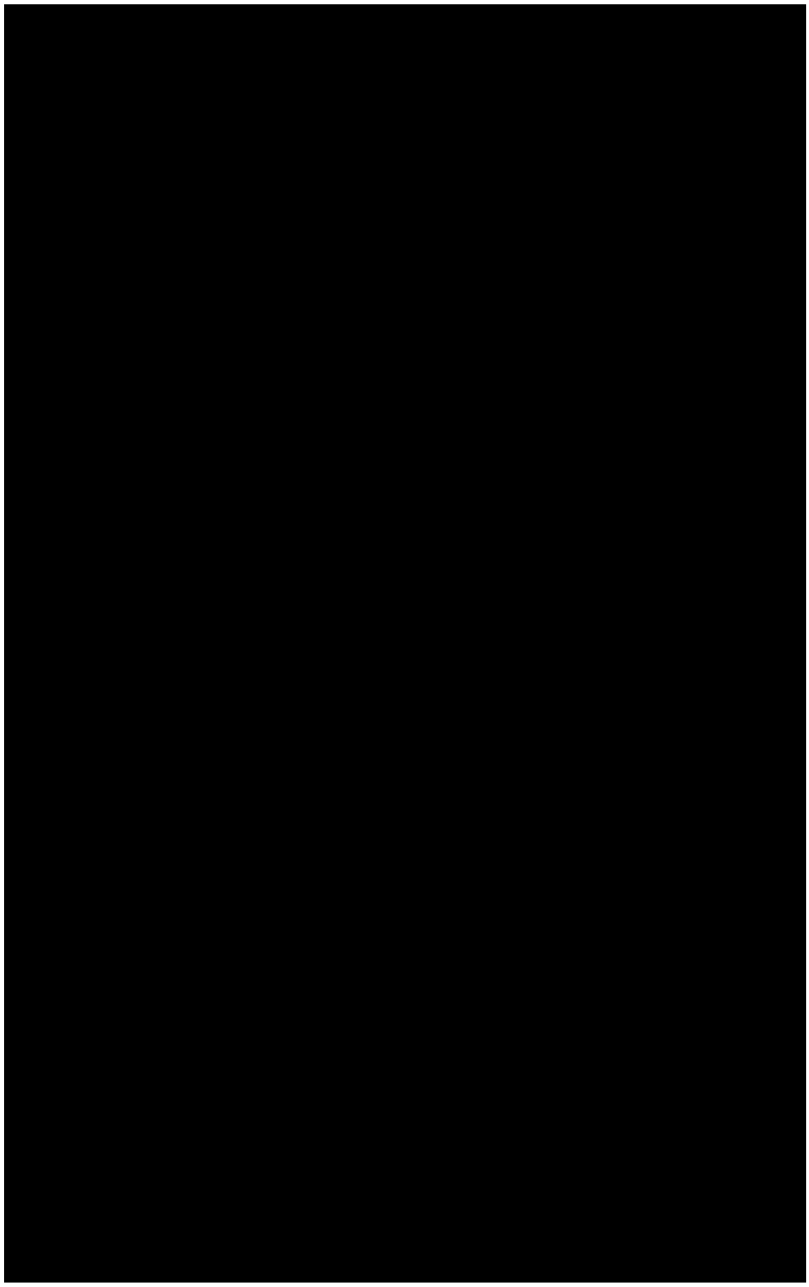

Figure 2, case 2: A and B: red-free fundus photograph at presentation and 2 weeks later. C: early venous phase fluorescein angiogram at presentation. D: two weeks later, the punctate hyperfluorescent lesions have almost become confluent. E and F: late phase fluorescein angiogram at presentation and 2 weeks later, showing fluorescein leakage in the subretinal space. G and H: red-free fundus photographs, respectively 2 and 3 months later, show subretinal fibrosis.

subretinal fibrosis. MCP or PIC associated with diffuse subretinal fibrosis should be differentiated from the rare condition, 'subretinal fibrosis and uveitis syndrome' described by Palestine et al.[17, 18] in Afro-Americans. In the latter syndrome, the multitude of spots over the retina

Figure 3, case2: A and B: early and venous phase indocyanine green angiogram at presentation, macular areas of hypofluorescence are seen in the venous phase that persist as more punctiform spots and areas of hypofluorescence in the late phase; C and D: early and venous phase indocyanine green angiogram 2 weeks later. The hypofluorescence in the venous phase has remained almost unchanged, in the late phase however, a much larger area of hypofluorescence is observed as well as the appearance of new focal hypofluorescent spots.

is not observed, the fibrosis develops in the absence of serous or serohemorrhagic subretinal fluid and the vitritis is more severe. Punched out chorioretinal spots, peripapillary atrophy, peripheral curvilinear chorioretinal atrophy and macular choroidal neovascularization are also characteristic findings in presumed ocular histoplasmosis syndrome (POHS). In the latter syndrome previous, subclinical infection with Histoplasma capsulatum is suspected. Positive histoplasmin skin testing confirms the diagnosis but has been replaced by specific lymphocyte stimulation in vitro to avoid unwanted reactivation of the disease[1, 5]. This syndrome is endemic in certain areas of the United States but has not been described in Europe[24], although a condition with similar ophthalmoscopic characteristics without previous contact with Histoplasma capsulatum is known. In MCP and PIC the etiology is essentially unknown[22, 23]. Slakter et al. have reported different indocyanine green angiographic characteristics for both disorders[21]. In MCP or PIC hypofluorescent lesions of various size are found in the posterior pole while in POHS intensely hyperfluorescent spots are seen as well as small hypofluorescent spots. Others have reported the combined presence of hypo- as well as hyperfluorescent spots in MCP and PIC[7].

Multiple evanescent white dot syndrome, MEWDS, predominantly seen in young females, is another inflammatory syndrome that causes

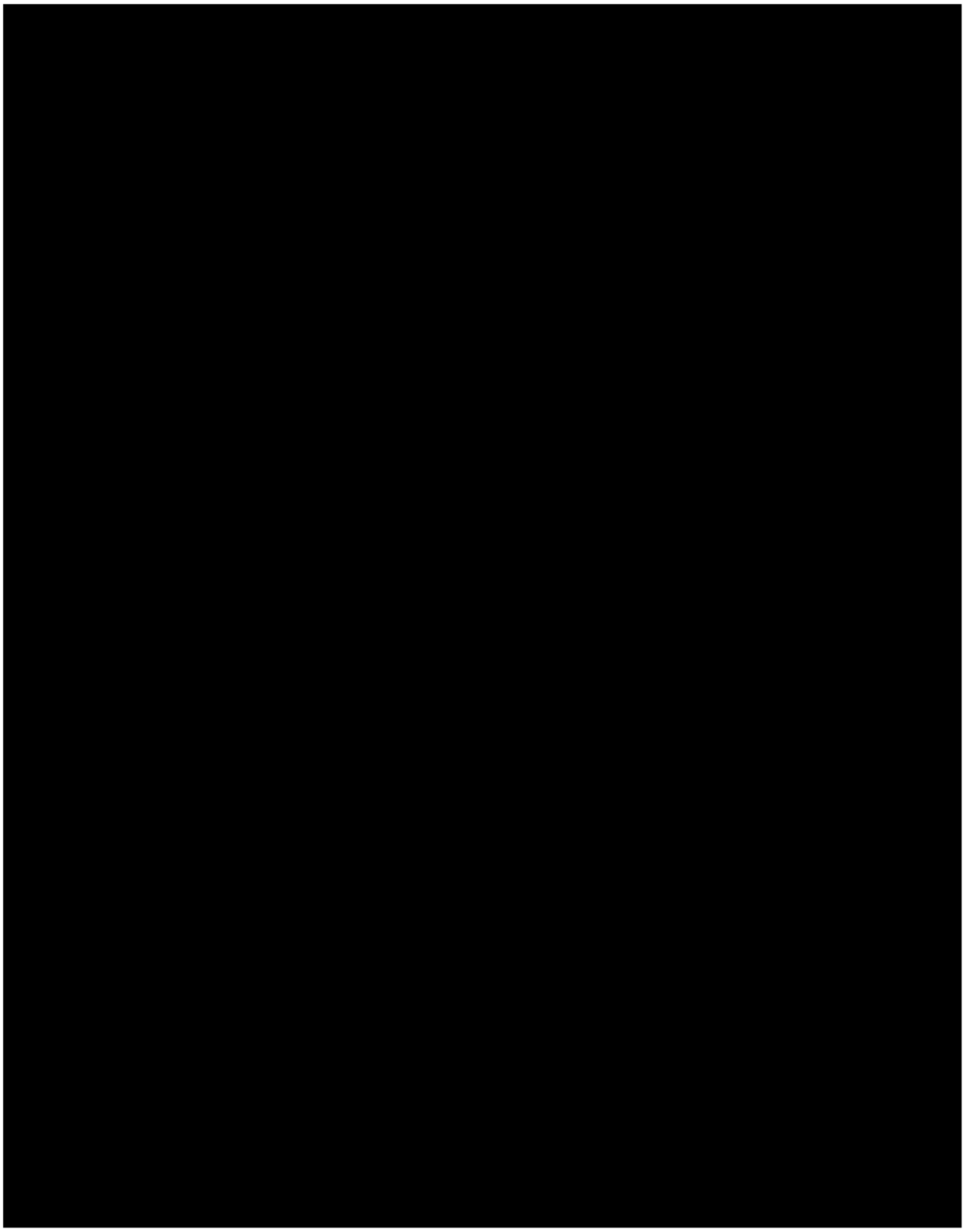

Figure 4, case 3: A and B: early venous and late phase fluorescein angiogram, indicates the presence of subretinal fibrous tissue that seems to connect several individual focal lesions; C and D: venous and late phase indocyanine green angiogram. The subretinal tissue blocks fluorescence in the venous phase and is almost isofluorescent in the late phase; E and F: venous and late phase indocyanine green angiogram nasal to the disc. Rather atropic chorioretinal lesions, which are hypofluorescent from the early phase of the angiogram.

unilateral, more rarely bilateral visual loss[10]. Small yellow lesions are seen at the level of the outer retina as well as a granular macular appearance. The yellow spots subsequently resolve spontaneously with recovery of visual acuity. Blind spot enlargement is often seen in

Figure 5, case 4: A: red-free fundus photograph; B: venous phase fluorescein angiogram, several atrophic focal lesions as well as a subfoveal neovascular network are seen. C and D: venous and late phase indocyanine green angiogram, a net is seen in the venous phase.

MEWDS but also in MCP and PIC[11, 19]. Some patients, such as our case 3, that initially present as MEWDS, later develop characteristics of MCP/PIC[3].

Many other conditions should be ruled out in patients with multiple focal choroiditis lesions. In the presence of multiple punched-out chorioretinal lesions, especially in the inferior midperiphery, non-caseating sarcoid granulomas may be found in the conjunctival biopsy, even in the absence of elevated angiotensin converting enzyme or radiographic lung lesions[8]. MCP has been described in elderly patients as well[15]. Ocular non-Hodgkin lymphoma should however be excluded in the latter patient group with vitritis and multiple focal choroiditis lesions, often unresponsive to steroid treatment[2].

Treatment:

Some authors have reported the use of systemic or subtenon steroids in controlling the inflammation in MCP/PIC; beneficial effects have especially been reported in eyes with additional cystoid macular edema[6, 14]. Reduction in number and size, or even resolution, of hypofluorescent spots on indocyanine green angiography has been observed in response to steroid treatment in MCP[7, 21]. It has therefore been suggested that indocyanine green angiography could be of value in titrating anti-inflammatory treatment in this disorder. Secondary choroidal neovascularization is the major cause of permanent visual loss in these patients. Focal areas of inflammatory activity as well as choroidal neovascularization will leak fluorescein and might be difficult to differentiate by fluorescein angiography alone. Areas of inflamma-

tory activity will be hypofluorescent by indocyanine green angiography, while secondary choroidal neovascularization will likely be hyperfluorescent[7, 21]. Regression of small subretinal choroidal neovascular membranes may occur spontaneously or during steroid treatment[14]. Extra- and juxtafoveal neovascular membranes can be treated effectively by laser photocoagulation[12]. Therapeutic guidelines are however not available for choroidal neovascularization in MCP or PIC in contrast to the clear indications provided by the Macular Photocoagulation Study in POHS[12]. Surgical removal of subfoveal neovascularization may be of benefit as well[9, 13, 25].

REFERENCES

(1) American Thoracic Society. Clinical usefulness of skin testing in histoplasmosis, coccidiodomycosis and blastomycosis: the official statement. Am Rev Respir Dis 1988; 138: 1081-1082.

(2) Brown J, Reddy CV, Kimura AE, Folk JC. Long-term visual prognosis of multifocal choroiditis, punctate inner choroidopathy and the diffuse subretinal fibrosis syndrome. Ophthalmology 1996; 103: 1100-1105.

(3) Callanan D, Gass JDM. Multifocal choroiditis and choroidal neovascularization associated with the multiple evanescent white dot and acute idiopathic blind spot enlargement syndrome. Ophthalmology 1992; 99: 1678-1685.

(4) Cantrill HL, Folk JC. Multifocal choroiditis associated with progressive subretinal fibrosis. Am J Ophthalmol 1986; 101: 170-180.

(5) Check IJ, Diddie KR, Jay WM, Merker R, Hunter RL. Lymphocyte stimulation by yeast phase Histoplasma capsulatum in presumed ocular histoplasmosis syndrome. Am J Ophthalmol 1979; 87: 311-316.

(6) Dreyer RF, Gass JDM. Multifocal choroiditis and panuveitis. A syndrome that mimics ocular histoplasmosis. Arch Ophthalmol 1984; 102: 1776-1784.

(7) Giovanni A, Scasselati-Sforzolini B, D'Altobrando E, Mariotti C. Indocyanine green angiographic findings in multifocal choroidopathies. Bull Soc belge Ophtalmol 1998; 267: 45-53.

(8) Hershey JM, Pulido JS, Folberg R, Folk JC, Massicote SJ. Non-caseating conjunctival granulomas in patients with multifocal choroiditis and panuveitis. Ophthalmol 1994; 101: 596-601.

(9) Holekamp NM, Thomas MA, Dickenson JD, Valluri S. Surgical removal of subfoveal choroidal neovascularization in presumed ocular histoplasmosis syndrome: stability of early visual results. Ophthalmology 1997; 104: 22-26.

(10) Jampol LM, Sieving PA, Fishman GA, Gilbert H. Multiple evanescent white dot syndrome. Clinical findings. Arch Ophthalmol 1984; 102: 671-674.

(11) Khorram KD, Jampol LM, Rosenberg MA. Blind spot enlargement as a manifestation of multifocal choroiditis. Arch Ophthalmol 1991; 109: 1403-1407.

(12) Macular Photocoagulation Study Group. Five-year follow-up of fellow eyes of individuals with ocular histoplasmosis and unilateral extrafoveal choroidal neovascularization. Arch Ophthalmol 1996; 114: 677-688.

(13) Melberg NS, Thomas MA, Burgess DB. Surgical removal of subfoveal choroidal neovascularization: ingrowth site as a predictor of visual outcome. Retina 1996; 16: 125-129.

(14) Morgan CM, Schatz H. Recurrent multifocal choroiditis. Ophthalmology 1986; 93: 1138-1147.

(15) Nölle B, Faul S, Jenisch S, Westphal E. Peripheral multifocal chorioretinitis with panuveitis: clinical and immunogenetic characterization in older patients. Graefe's Arch Clin Exp Ophthalmol 1998; 236: 451-460.

(16) Nozik RA, Dorsch W. A new chorioretinopathy associated with anterior uveitis. Am J Ophthalmol 1973; 76; 758-762.

(17) Palestine AG, Nussenblatt RB, Chan CC, Hooks JJ, Friedman L, Kuwabara T. Histopathology of the subretinal fibrosis and uveitis syndrome. Ophthalmology 1985; 92: 838-844.

(18) Palestine AG, Nussenblatt RB, Parver LM, Knox DL. Progressive subretinal fibrosis and uveitis. Br J Ophthalmol 1984; 68: 667-673.

(19) Reddy CV, Brown J, Folk JC, Kimura AE, Gupta S, Walker J. Enlarged blind spots in chorioretinal inflammatory disorders. Ophthalmology 1996; 103: 606-617.

(20) Schenk F, Böke W. Retinal vasculitis with multifocal retinochoroiditis. Int Ophthalmol 1990; 14: 401-404.

(21) Slakter JS, Giovannini A, Yannuzzi LA, Scassellati-Sforzolini B, Guyer DR, Sorenson JA, Spaide RF, Orlock D. Indocyanine green angiography of multifocal choroiditis. Ophthalmology 1997; 104: 1813-1819.

(22) Spaide RF, Skerry JE, Yanuzzi LA, DeRosa JT. Lack of HLA-DR2 specificity in multifocal choroiditis and panuveitis. Br J Ophthalmol 1990; 74: 536-537.

(23) Spaide RF, Sugin S, Yannuzzi LA, DeRosa JT. Epstein-Barr virus antibodies in multifocal choroiditis and panuveitis. Am J Ophthalmol 1991; 112: 410-413.
(24) Sultorp-Schulten MSA, Bollemeijer JG, Bos PJM, Rothova A. Presumed ocular histoplasmosis in the Netherlands: an area without histoplasmosis. Br J Ophthalmol 1997; 81: 7-11.
(25) Thomas MA, Kaplan HJ. Clinical experience with the surgical removal of subfoveal neovascular membranes. Short term postoperative results. Ophthalmology 1992; 99: 969-976.
(26) Watzke RC, Packer AJ, Filk JC, Benson WE, Burgess D, Ober RR. Punctate inner choroidopathy. Am J Ophthalmol 1984; 98: 572-584.
(27) Zamiri P, Boyd S, Lightman S. Uveitis in the elderly - is it easy to identify the masquerade? Br J Ophthalmol 1997; 81: 827-831.

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Request for reprints:
V. De Meyer
Oogziekten U.Z. Gent.
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