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Subretinal neovascular membranes associated with chronic membranoproliferative glomerulonephritis type II

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Abstract. Subretinal neovascular membranes were observed in three patients with chronic membranoproliferative glomerulonephritis type II (dense deposit disease). The first signs of glomerulonephritis occurred at respective ages of 13, 10 and 10 years; subretinal neovascular membranes were noted at respective ages of 25, 32 and 32 years. All patients had bilateral, widespread retinal pigment epithelial abnormalities. Our findings indicate that subretinal neovascularization is a complication of dense deposit disease. In one patient, the early recognition and laser treatment of an extrafoveal subretinal neovascular membrane prevented further loss of vision.

Introduction

In September 1984 we observed multifocal subretinal neovascular membranes and extensive retinal pigment epithelial changes in a 32-year-old man suffering from chronic membranoproliferative glomerulonephritis type II (dense deposit disease). As similar fundus changes were recently observed in a second patient, a possible relationship between the two conditions was postulated. We therefore reviewed the ophthalmological records of all patients in our department known to have biopsyproven dense deposit disease. An association between subretinal neovascular membranes and this disease was found in three patients, who are described in the present paper.

Case reports

Case 1

Proteinuria was detected in a 13-year-old boy in August 1962. A renal biopsy performed in 1968 showed chronic membranoproliferative glomerulonephritis type II lesions, with dense deposits occurring in the glomerular and tubular basement membranes. The patient was treated with antihypertensive medication and indomethacin from August1968 until February 1969. There was a progressive evolution to renal failure, and chronic hemodialysis was started in October 1969.

An eye examination in March 1973 showed bilateral retinal pigment epithelial abnormalities, with multiple drusen-like lesions being observed in the macula as well as in the periphery (Fig. 1); however, the patient had no complaints and retained full vision. Repeated eye examinations in August 1973 and September 1974 did not show any change. In January 1975, at the age of 25 years, the patient mentioned reading difficulties for the first time; although he had full vision, a relative central scotoma was noted on both sides. Fundoscopy showed a fibrovascular scar inferior to the macula in the right eye; in the papillomacular area of the left eye, a small pigment epithelial detachment was noted. Fluorescein angiography showed marked window defects, which were spread over the macula and the peripheral retina (Fig. 2); there was mild leakage from the disciform lesions. No laser treatment was given. No ophthalmological follow-up was obtained, as a renal transplantation was performed in May 1975. The graft never functioned adequately. After multiple complications, a transplantectomy was performed in September 1975. The patient died a few days later at the age of 26.

Case 2

This man presented with a nephrotic syndrome at the age of 10 years. In January 1978, when the patient was 26 year old, a renal biopsy showed dense deposit disease. Blood pressure remained under control with methyldopa and salt restriction; no other medication was given. Renal function progressively deteriorated; chronic hemodialysis was started in March 1988 and was continued until July 1989, when the patient underwent a succesful renal transplant.

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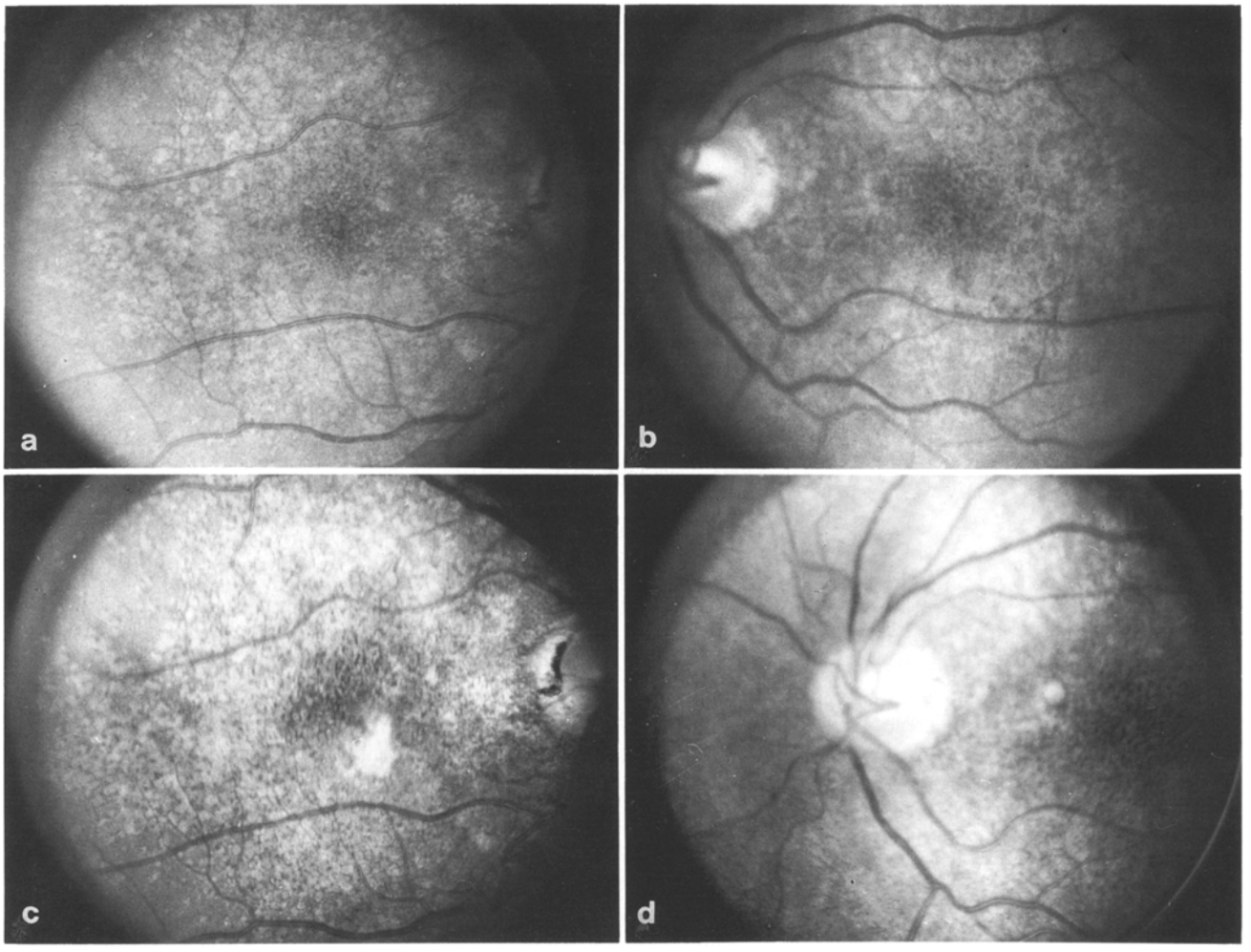

Fig. 1a–d. Case 1. **a** Right macula and **b** left macula show multiple small, drusen-like lesions and pigment dispersion (March 1973); 2 years later **c** the right macula has an inferofoveolar fibrovascular scar and **d** a small papillomacular pigment epithelial detachment can be seen in the left eye

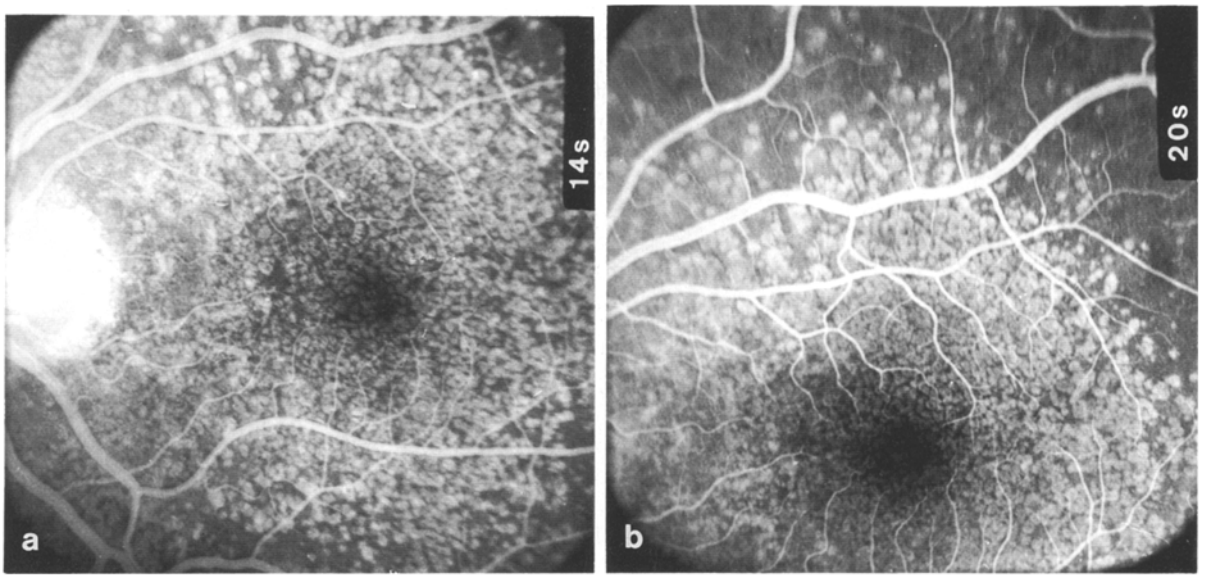

Fig. 2a, b. Case 1. In January 1975, the fluorescein angiogram of the left eye at **a** 14 s and **b** 20 s shows numerous small and larger window defects, according to the drusen-like deposits

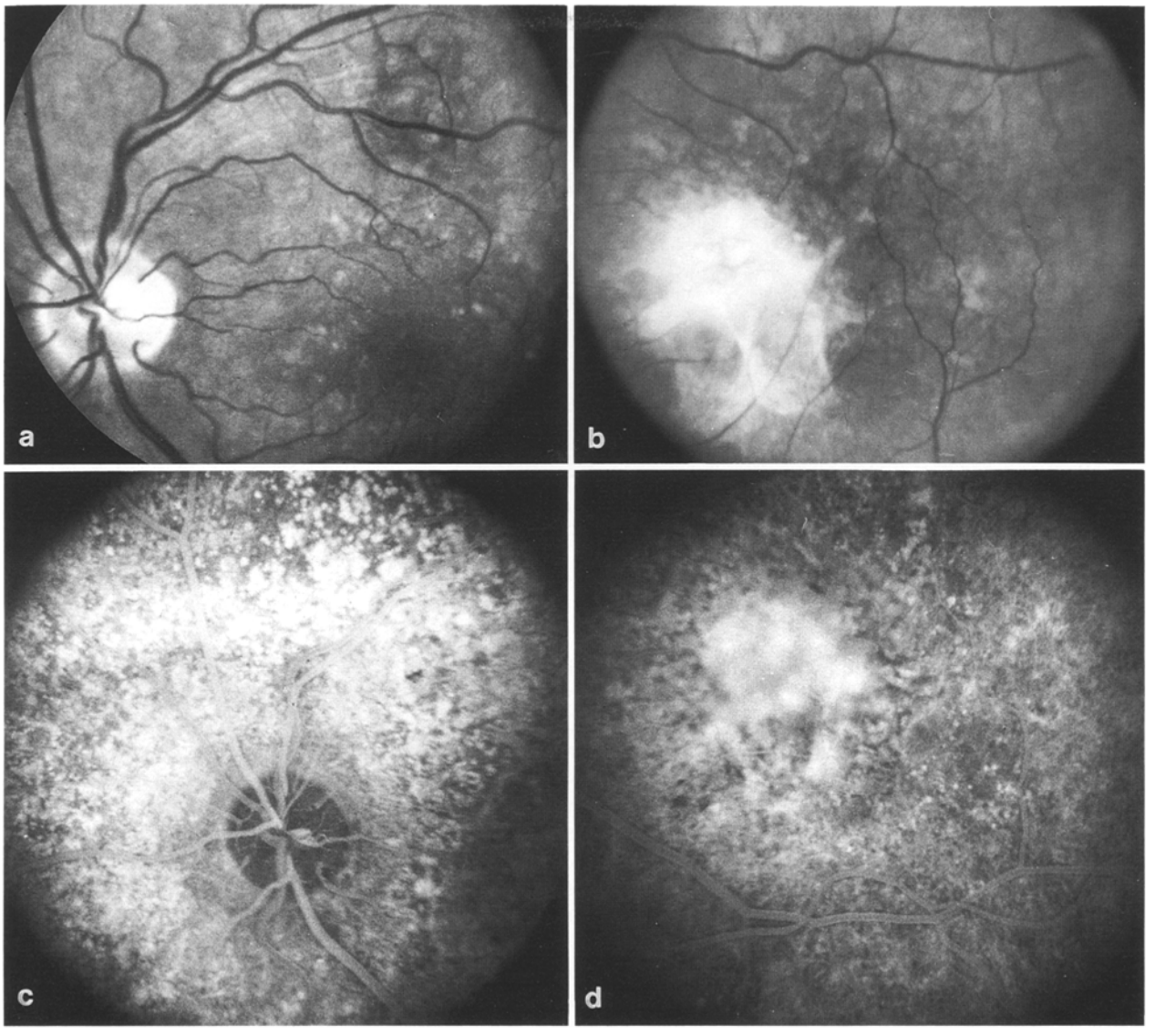

Fig. 3a–d. Case 2. **a** Left eye: flecked retina (December 1977); a choroidal nevus can be seen at the upper border of the macula (photograph courtesy of D. Van Germeersch). **b** In September 1984 the same macula has a central fibrovascular membrane. **c** Early and **d** late angiograms demonstrate numerous small and larger window defects, with leakage being confined to the central fibrovascular membrane

In December 1977 an eye examination was performed, revealing a left hypertrophia and amblyopia. Visual acuity was 20/26 OD and 20/100 OS, and anterior segments were normal. Fundoscopy showed widespread pigment epithelial abnormatilities, with multiple small flecks appearing in both eyes (Fig. 3). The eye problems occurred in 1984, when the patient was 32 years old, at which point a central scotoma suddenly prevented his being able to read. We examined the subject after his problem had persisted for 4 months. Visual acuity was limited to 20/200 OD and 20/300 OS, and both eyes had subfoveal fibrovascular membranes. An additional fibrovascular scar was noted near the equator in the left eye. Pigment epithelial abnormalities were more clearly demonstrated by fluorescein angiography. There were no retinal vascular changes. The electro-oculogram was reduced (Arden ratio: 160%, left and right eyes). The electroretinogram was subnormal in both eyes: subnormal phototopic and scotopic b_1 waves indicated disturbed cone function. An additional eye examination in November 1988 revealed fresh hemorrhages over the borders of the previously diagnosed subretinal neovascular membranes, and an additional focus of new vessels was observed in each eye (Fig. 4). Another evaluation in July 1989 revealed unchanged visual acuity and visual fields. Reading was possible with low-vision aids. In both eyes the subretinal neovascular membranes showed no gross changes; subtle hemorrhages and exudation indicated that they remained active.

Case 3

A 9-year-old girl developed a nephrotic syndrome in September 1965. The first renal biopsy performed in No-

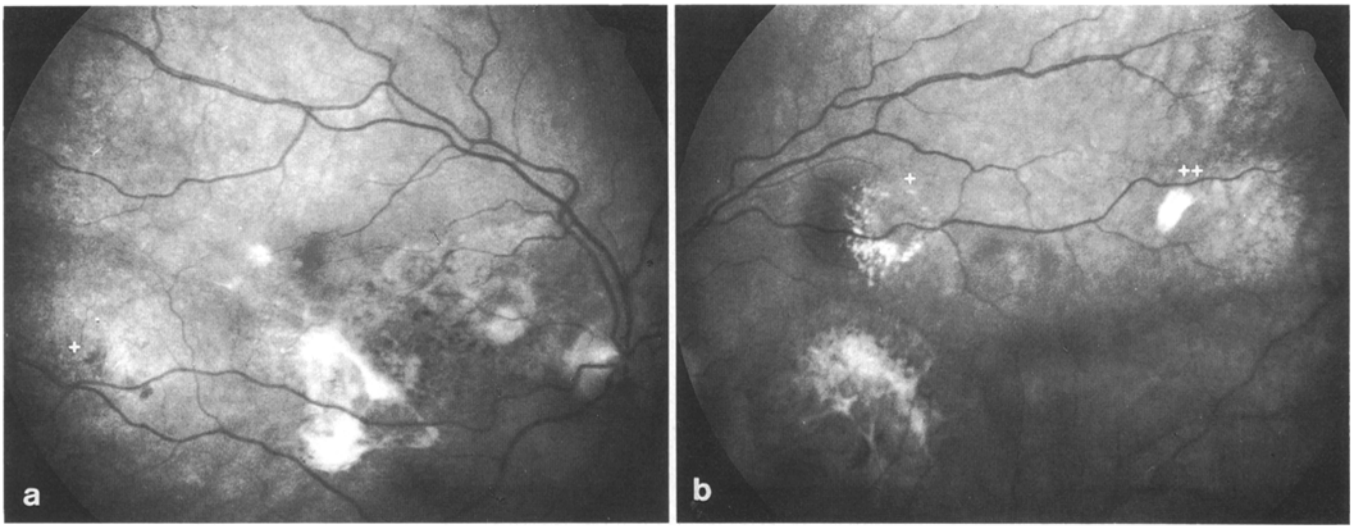

Fig. 4a, b. Case 2. New areas of subretinal membrane formation (+) as seen in November 1988 in the **a** right eye and **b** left eye. The central macular lesions and the scar near the equator (++) in the left eye remain almost unchanged in September 1989

vember 1965 demonstrated intra- and extracapillary proliferative glomerulonephritis; a subsequent biopsy in August 1969 showed a marked thickening and dense deposits in the basement membrane. In the period from November 1965 until April 1966, the patient was treated with prednisone; indomethacin was subsequently given for 10 years. In 1976 cyclophosphamide (50 mg/day) was added for a 2-year period. Under this treatment, the proteinuria disappeared and renal function remained stable. The patient never presented with arterial hypertension.

A fundus examination in November 1965, when the patient was 9 years old, was considered to be normal; in August 1969, when she was 13 years of age, bilateral inferotemporal retinoschisis was detected. The patient had full vision in both eyes, and no maculopathy was noted. In July 1976 there was no change; the patient was subsequently lost to follow-up until February 1989, when she was referred for laser treatment of a subretinal neovascular membrane. The subject had noticed metamorphopsia and poor vision of the right eye for a few weeks. Ophthalmoscopy and fluorescein angiography revealed an infrafoveolar subretinal neovascular membrane in the right eye, and both eyes had widespread pigment migration and granular pigment epithelial defects (Fig. 5). The retinal vessels had a normal aspect. The inferotemporal retinoschisis was unchanged. The electro-oculogram was abnormal (Arden ratio: 150%, right eye; 169%, left eye). The electroretinogram and the dark-adaptation curve were normal. The subretinal neovascular membrane was coagulated using an argon green laser. Post-treatment fluorescein angiograms revealed a flat, atrophic scar that enlarged somewhat during the follow-up period of nearly 1 year. The patients visual acuity was 20/30 OD and 20/20 OS.

Discussion

Membranoproliferative glomerulonephritis usually starts in childhood and has a chronic, progressive course; it is also called mesangiocapillary glomerulonephritis. Both terms refer to the mesangial proliferation and to the thickened, 'membranous' appearance of the glomerular capillary wall in this condition [6]. Three distinct types are identifiable based on light and electron microscopic differences. In type II membranoproliferative glomerulonephritis (dense deposit disease), the lamina densa of the glomerular basement membrane is largely replaced by electron-dense material, which does not include immunoglobulin or complement [6]. Dense deposits similar to those in the glomerular capillary walls are found in the basement membranes of Bowman's capsule and of the tubules [6]; they have also been identified in the basement membrane of the spleen [3–5] and, recently, in Bruch's membrane [1].

Specific fundus changes were recently recognized in membranoproliferative glomerulonephritis type II. Duvall-Young and co-authors [1] described dense deposits in Bruch's membrane that were similar to the renal lesion observed in a case of dense deposit disease. In subsequent reports, these authors described extensive pigment epithelial abnormalities in four other patients with biopsy-proven membranoproliferative glomerulonephritis type II [2–4]. The specific retinal pigment epithelial abnormalities in dense deposit disease were also observed in our patients; we report for the first time the association of the former with subretinal neovascular membranes as a complication of this disease.

In our patients, we examined the retina prior to the growth of subretinal neovascular membranes. In two eyes with subretinal neovascular membranes and long

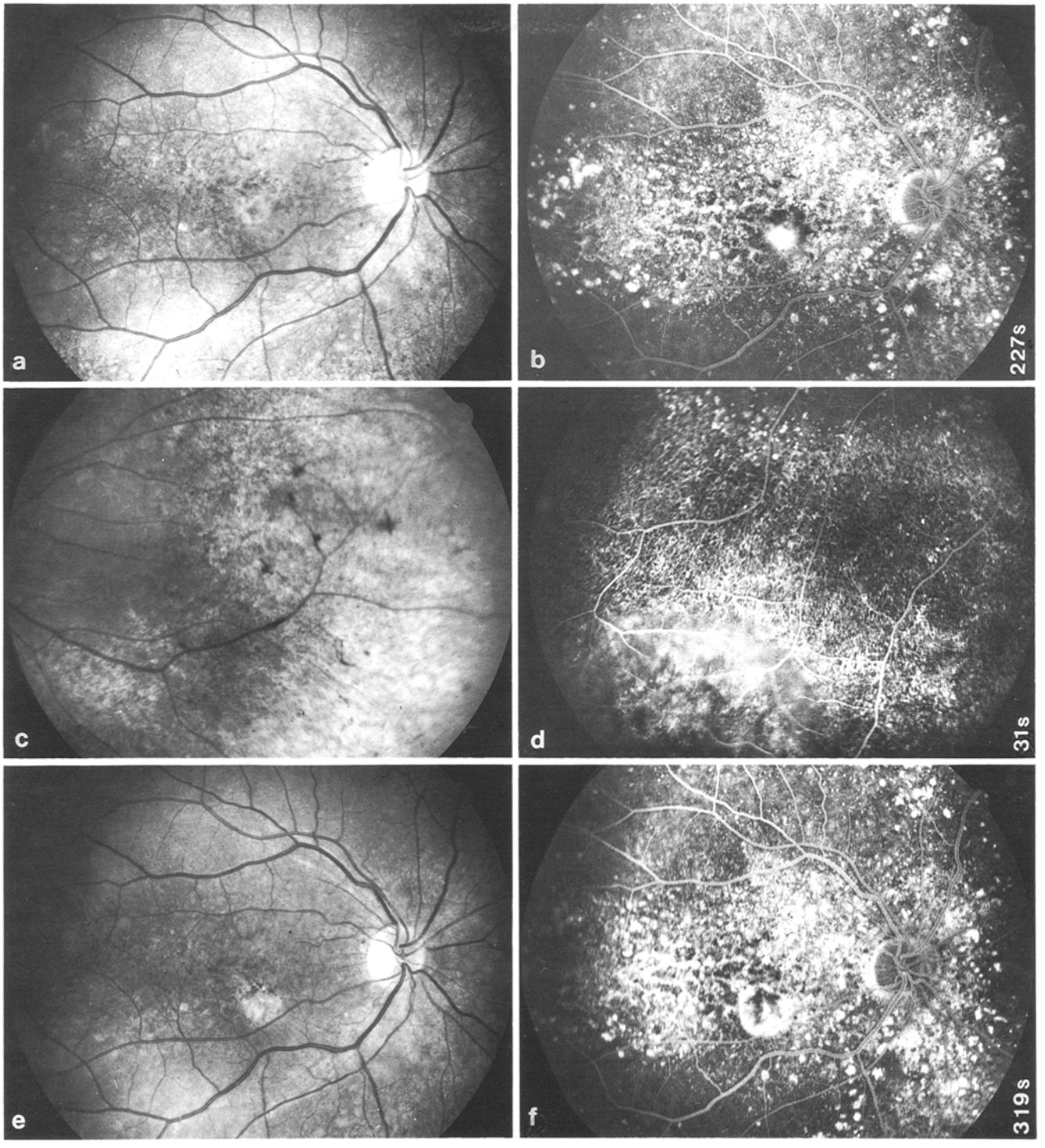

Fig. 5a–f. Case 3. Macular and peripheral pigment abnormalities, drusen-like lesions and a small infrafoveolar subretinal neovascular membrane **a** as noted in the right eye and **b** as confirmed by fluorescein angiography. **c** The nasal retina shows marked pigment migration and early choroidal atrophy. **d** In the inferotemporal area, retinoschisis is clearly demonstrated on the fluorescein angiogram. **e** At 1 month after argon laser treatment the macular scar is flat and atrophic. **f** Fluorescein angiography performed 3 months after treatment shows some enlargement of the scar

follow-ups, the visual outcome was poor. One eye with an extrafoveolar subretinal neovascular membrane was successfully treated with argon laser coagulaton. Our findings indicate that follow-up of patients with membranoproliferative glomerulonephritis type II is indicated, in view of a possible complication with subretinal neovascular membranes, which can be treated by laser therapy.

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