Graefe's Arch Clin Exp Ophthalmol (1992) 230:454–458

Graefe's Archive
for Clinical and Experimental
Ophthalmology

© Springer-Verlag 1992

Bullous retinal detachment and multiple retinal pigment epithelial detachments in patients receiving hemodialysis*

J. Donald M. Gass

Bascom Palmer Eye Institute, University of Miami School of Medicine, P.O. Box 016880, Miami, FL 33101, USA

Received November 25, 1991 / January 24, 1992

Abstract. Two patients receiving hemodialysis for chronic renal failure developed bilateral bullous retinal detachment associated with multiple underlying serous detachments of the pigment epithelium. Many of the detachments of the pigment epithelium were surrounded by subretinal whitish exudate that was probably fibrinous in type. There was fluorescein angiographic evidence of dehiscence of the pigment epithelium at the margin of some of the pigment epithelial detachments. Failure to recognize the nature of the retinal detachment in one patient resulted in an unsuccessful scleral buckling procedure

Introduction

In 1973, I reported 5 patients with a clinical syndrome characterized by (1) bilateral bullous exudative retinal detachment occurring in healthy middle aged males, (2) underlying multiple detachments of the retinal pigment epithelium (RPE), usually surrounded by a gray-white subretinal exudate, (3) absence of signs of inflammation, (4) angiographic evidence near the edge of the RPE detachments of RPE holes, through which fluorescein diffused into the subretinal space, (5) unresponsiveness to systemic corticosteroid treatment, and (6) rapid resolution of the retinal detachment after photocoagulation of the areas of RPE detachment [5]. The patients were believed to have a severe form of idiopathic central serous chorioretinopathy (ICSC). Others have confirmed these findings, including the predominance of males affected [1, 12, 17]. This report describes the syndrome in 2 women who were receiving hemodialysis because of chronic renal failure. The findings in one of these patients (case 2) and the clinicopathologic observations of Dr. Gilbert de Venecia of a third patient have been briefly reported previously [6].

* Presented on September 8, 1988, at the Gonin Society Meeting

Correspondence to: J. Donald M. Gass

Case reports

Case 1

In June 1987, a mentally handicapped, 35-year-old, Latin woman presented with a vague history of recent visual loss. She was unable to provide details of her past ocular history. In 1979, renal insufficiency caused by a congenital kidney defect and ureteral stenosis was detected. In 1980, she had surgical repair of a congenital heart defect. In 1981, she began receiving hemodialysis. Diverticulosis was diagnosed in 1983. Oral medications included benzene acetamide 25 mg q.i.d., Os-Cal one tablet b.i.d., and aluminum carbonate gel one capsule b.i.d. Visual acuity was 20/200 in both eyes with $+5.25+1.50\times090°$ OD and $+6.25+1.00\times090°$ OS. Except for marked limitation of the downward gaze and positive forced duction test involving both eyes, the anterior ocular segments were normal. There were no cells in the vitreous. There were several areas of mottling of the pigment epithelium in the macular and paramacular areas. There was attenuation of the retinal arterioles. In the left fundus, there was an inferior bullous retinal detachment that extended superiorly on the nasal side to the 11 o'clock meridian. There was no evidence of ciliochoroidal detachment. Preoperative evaluation revealed the following: blood pressure 120/70, mmHg arteriovenous shunt on the left forearm, blood urea nitrogen (BUN) 29 mg%, hemoglobin 9.6 g/dl, hematocrit 29 ml/dl, white blood cell count (WBC) 6400, and 3+ proteinuria. Although no retinal hole was identified, the configuration of the detachment suggested a diagnosis of rhegmatogenous retinal detachment, and a scleral buckling procedure and drainage of the subretinal fluid were done. On the second postoperative day, the subretinal fluid had partly reaccumulated, and there were two focal areas of RPE detachment enveloped by gray-white exudate superior to the left macula (Fig. 1A). Fluorescein angiography confirmed their presence and showed extension of the dye inferiorly toward the macular area (Fig. 1B). In addition, it showed evidence of a third area of shallow RPE detachment temporal to the macula. Because of the patient's inability to look downward, it was not possible to survey many areas of the fundus angiographically. Indirect ophthalmoscopy with cobalt blue filters in place failed to identify any other areas of late staining in the left eye. Argon laser was used to treat the areas of PRE detachment. During the next few weeks, there was incomplete resolution of the subretinal fluid. The patient returned in August, 1987. Visual acuity in the right eye was 20/300 and in the left eye, 20/200. In the right eye, there was bullous retinal detachment of the inferior half of the retina. In the macular area, there were multiple RPE detachments surrounded by white subretinal exudate (Fig. 1C). Peripherally, there were several local-

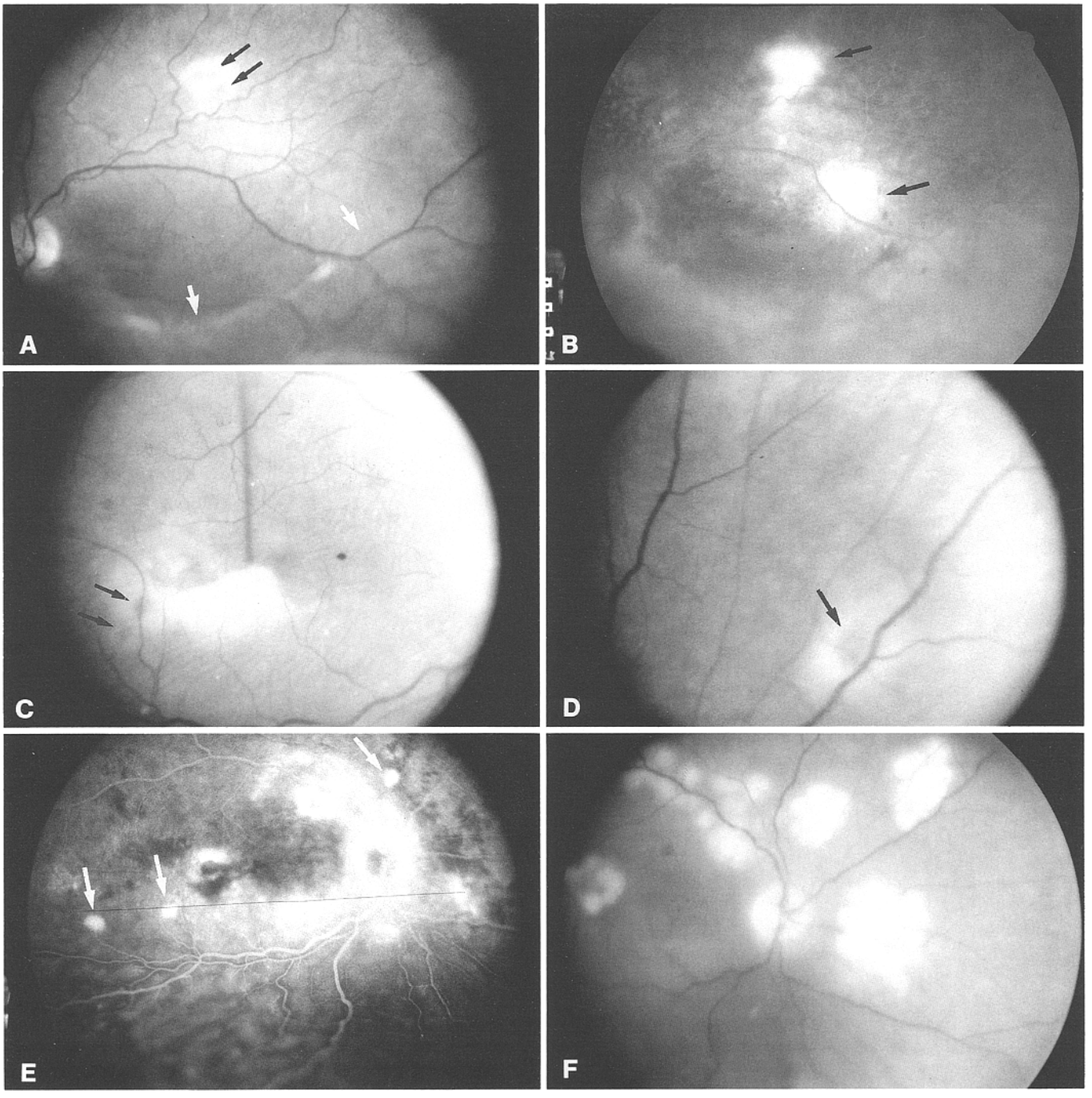

Fig. 1A–F. Case 1. **A** Left eye, June 12, 1987. Note two retinal pigment epithelium (RPE) detachments (*black arrows*) largely hidden by white subretinal exudate. There is a bullous retinal detachment inferiorly (*white arrows*). **B** Late phase angiogram showing staining of subretinal exudate in the vicinity of the small RPE detachments (*small arrow*) as well as evidence of another area of staining of subretinal exudate (*large arrow*). **C, D** Right eye, August 4, 1987. Note bullous retinal detachment with white subretinal exudate adjacent to and surrounding RPE detachments (*arrows*). **E** January 20, 1988, angiography reveals multiple RPE detachments (*arrows*). The mottled fluorescence inferiorly and that along the major vascular arcades is caused by leaking retinal capillaries. **F** Argon laser photocoagulation

ized RPE detachments partly enveloped by white subretinal exudate (Fig. 1D). The retina inferiorly in the left eye was detached. By January 1988, there was total bullous detachment in the left eye and persistence of the bullous detachment inferiorly in the right eye. Multiple RPE detachments as well as subretinal fibrous metaplasia were present near the center of the right macula in the area of previous white subretinal exudation. Fluorescein angiography in the right eye demonstrated multiple areas of RPE detachment, focal areas of subretinal staining, as well as retinal capillary leakage along the major retinal vascular arcades and inferiorly in the area of bullous detachment (Fig. 1E). Angiography in the left eye was unsatisfactory because of the highly elevated retina. Argon laser treatment was applied to the areas of RPE detachment in the right eye (Fig. 1F), and by March 1988, the subretinal fluid had partly resolved. The patient was scheduled to receive a kidney transplantation in the near future.

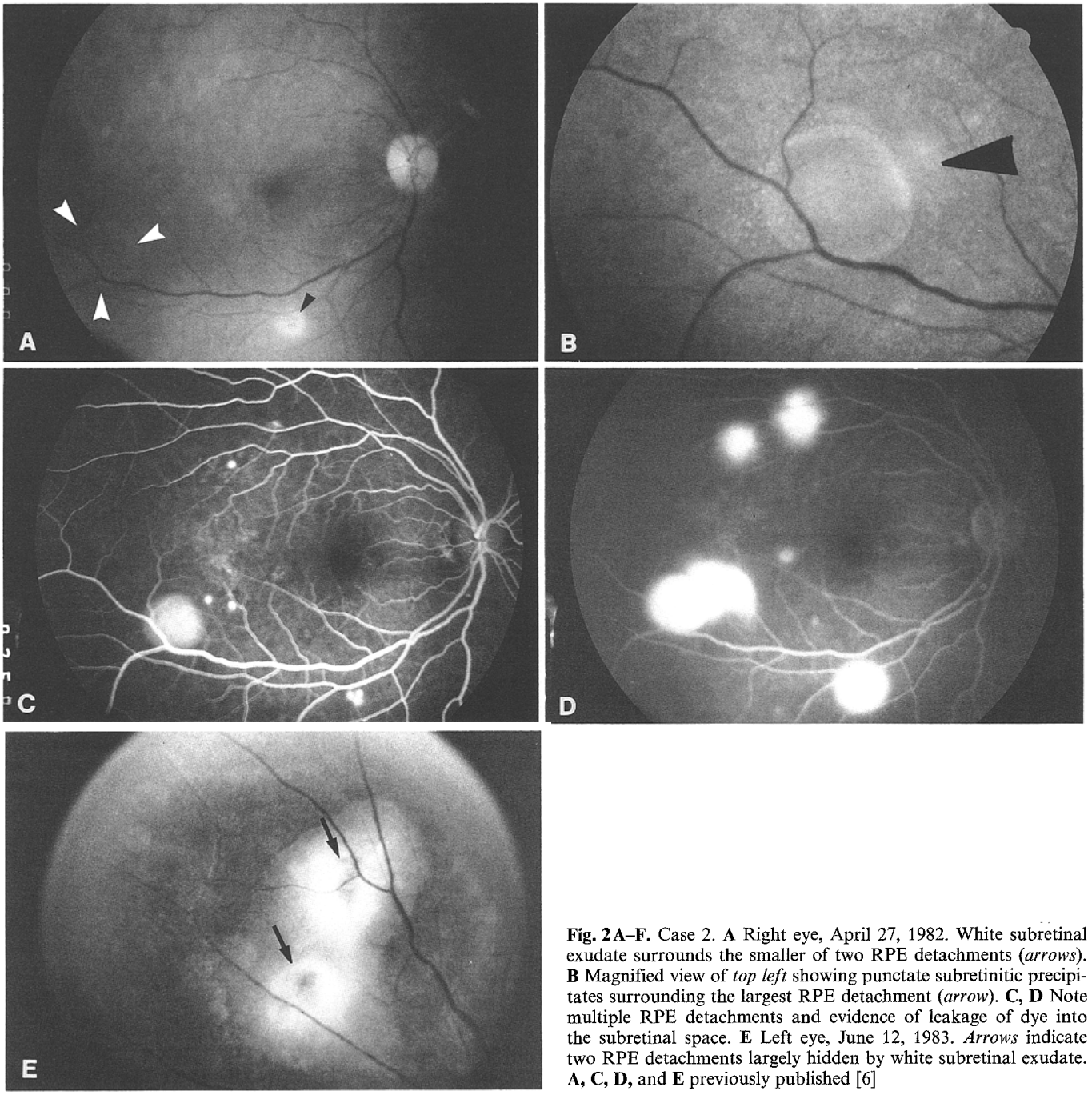

Fig. 2A–F. Case 2. **A** Right eye, April 27, 1982. White subretinal exudate surrounds the smaller of two RPE detachments (*arrows*). **B** Magnified view of *top left* showing punctate subretinitic precipitates surrounding the largest RPE detachment (*arrow*). **C, D** Note multiple RPE detachments and evidence of leakage of dye into the subretinal space. **E** Left eye, June 12, 1983. *Arrows* indicate two RPE detachments largely hidden by white subretinal exudate. **A, C, D,** and **E** previously published [6]

Case 2

In March 1982, a 36-year-old, American Indian woman was examined by her local physician because of redness of the eyes and headache. She had a history of chronic renal failure caused by glomerulonephritis and had received hemodialysis for 6 years. Examination revealed evidence of anterior scleritis in the left eye. Medical evaluation revealed well controlled hypertension and normal physical examination. Abnormal laboratory findings included erythrocyte sedimentation rate 94, slightly depressed complement 56 CH 100 units (normal above 70 units), polyclonal increase in serum immunoglobulin G-(IgG) β-globulin 1.33 (normal 0.54) and γ-globulin 2.26 mg% (normal 0.69–169 mg%), and ANA 1:40 (normal 1:20), and roentgenographic evidence of parenchymal lung changes and thickening of the inferior wall of the maxillary sinuses. Complete blood count and electrolytes were within normal limits except for a BUN of 42 mg%. Negative studies included LE prep, serum cryoglobulins, enhanced computerized tomography (CT) of the brain, electrocardiogram, and HLA B27, A1, A2, A9, B7, B8, B12, B14. After oral prednisone 40 mg/day and antituberculous medication, the ocular symptoms improved. In April 1982, she noted a superior scotoma in the right eye. When examined at the Bascom Palmer Eye Institute (BPEI), her visual acuity was 20/20 OU (in each eye). There was minimal evidence of anterior scleritis in the left eye. In the right eye, there was an inferior bullous retinal detachment associated with multiple focal serous RPE detachments, many of which were surrounded by gray-white subretinal exudation and punctate subretinal precipitates (Fig. 2A, B). The left fundus was normal. Fluorescein angiography confirmed the presence of multiple serous RPE detachments and

showed evidence of the dye leaking through defects at the margin of some of these detachments into the subretinal fluid (Fig. 2C, D). Soon afterward, she experienced a marked loss of vision in the right eye because of progressive retinal detachment. Her local physician treated the areas of RPE detachment with argon laser. The retinal detachment resolved in the right eye but subsequently developed in the left eye. When she returned to the BPEI in October 1982, the visual acuity was 20/200 in the right eye and 20/20 in the left eye. There was no evidence of active scleritis, although there was some focal thinning of the perilimbal sclera in the left eye. There were scattered chorioretinal scars in the areas of previous photocoagulation in the right eye and exudative detachment of the retina nasally and inferiorly in the left eye. This was associated with multiple focal RPE detachments, each enveloped in gray-white subretinal exudate (Fig. 2E). She was lost to follow-up until April, 1984, when she presented because of decreased vision in both eyes. Visual acuity was 20/200 bilaterally. She had a superficial corneal pannus and evidence of an active anterior scleritis in the left eye. There were bilateral posterior subcapsular cataracts. Ultrasonography revealed no evidence of retinal detachment or uveal tract thickening. In December, 1984, ultrasonography revealed thickening of the ciliary body and retinal detachmant superiorly in the left eye. Bilateral cataract extractions were done. Postoperatively, visual acuity was 20/60 OD and finger counting OS. The vitreous was clear, and there was no retinal detachment in the right eye. The left fundus could not be visualized because of corneal opacification and a pupillary membrane. Ultrasonography revealed further thickening of the ciliary body in the left eye, which was enucleated because of the possibility of melanoma.

Histopathologic examination revealed a funnel-shaped retinal detachment, proteinaceous subretinal fluid, and a necrotizing granulomatous anterior scleritis and cylitis. Posterior to the pars plicata, there were a few scattered foci of mild degeneration and proliferation of the pigment epithelium. There was no evidence of intrachoroidal exudation. The choroidal vessels were normal. There were a few foci of lymphocytic and plasma cell infiltration of the choroid. A review of the patient's original kidney biopsy specimen failed to show evidence of vasculitis. The patient died of unknown cause approximately 6 months later.

Her clinical and histopathologic findings suggested that the retinal detachment that occurred in her left eye shortly before it was removed was probably caused by the anterior scleritis and cyclitis. Nothing was found histopathologically to explain the cause of her episodes of exudative detachment of the retina and RPE 2 years previously in both eyes.

Discussion

The exudative retinal detachment overlying multiple RPE detachments, most of which were surrounded by gray-white subretinal exudation, the angiographic evidence of defects or tears at the edge of the RPE detachments, and the response to photocoagulation in these 2 patients are findings identical to those previously reported in healthy, predominantly middle-aged men with severe bilateral ICSC [5]. In 1967, I reported a cloudy white exudate surrounding RPE detachments in patients with more typical ICSC with retinal detachment confined to the macular region and postulated that it was caused by leakage of proteins from the choriocapillaries through RPE defects that were often evident angiographically [4]. Additional evidence for this hypothesis was provided by Dr. Gilbert de Venecia, who at the 1982 Verhoeff Ophthalmic Pathology Society Meeting presented the clinical and histopathologic findings in one eye removed from a 40-year-old American Indian man who presumably had received hemodialysis and who, 5 weeks after receiving a renal transplant, noted visual loss caused by bilateral retinal detachment, multiple RPE detachments surrounded by gray-white subretinal exudate, and "smoke stack" leaks angiographically [6]. On histopathological examination, Dr. de Venecia found fibrinous exudate beneath the detached RPE and surrounding subretinal space and no evidence of choriocapillary occlusion or choroiditis. His findings suggest that the RPE and retinal detachments, whether occurring in patients receiving hemodialysis or with ICSC, are caused by a severe focal alteration in the choriocapillary permeability sufficient to permit escape of molecules as large as fibrinogen into the sub-RPE and subretinal spaces. The cause for the capillary permeability alteration in both groups of patients is unknown.

Emotional stress, type A personality, and pregnancy appear to be risk factors for developing ICSC in otherwise healthy individuals [4, 7, 18]. The experimental production of ICSC in monkeys by an intravenous injection of epinephrine suggests that hyperactivity of the adrenomedullary system may be important in the pathogenesis of ICSC in otherwise healthy individuals, as well as in patients with chronic renal failure undergoing hemodialysis [19, 20].

I could find no previous report of exudative retinal detachment and RPE detachments occurring in patients undergoing hemodialysis. Friberg et al. reported a 60-year-old woman who developed bilateral bullous retinal detachment and RPE detachments 4 months after a renal transplant [3]. She had received hemodialysis for 6 weeks following the transplant. Jabs et al. [11] reported these findings in 2 patients with lupus erythematosus, 1 a hypertensive woman with lupus nephritis and the other, a normotensive man. Neither were receiving hemodialysis. I have recently seen a young hypertensive woman with lupus nephritis with the same ocular findings. She, too, was not undergoing hemodialysis. The findings in these 3 patients, 2 of whom were hypertensive, and the 2 subjects of this report, both of whom had normal or near normal blood pressure, suggest that renal insufficiency is more important than either blood pressure or hemodialysis in the causation of the fundus picture resembling severe ICSC.

Since the onset of symptoms in Dr. de Venecia's case began within 5 weeks after renal transplantation, it is possible that factors associated with renal failure antedating the transplant were primarily responsible for the RPE and retinal detachment. The same might be said for the case of Friberg et al. Miyake et al. reported uveal effusion developing acutely during hemodialysis in a 15-year-old girl [15]. Evidence of ciliochoroidal exudative detachment did not occur in either of the subjects of this report.

Neither case 1 nor case 2 presented with evidence of uncontrolled hypertension or other disorders associated with disseminated intravascular coagulopathy (DIC), both of which are recognized causes for retinal detachment in patients with renal disease. Exudative retinal detachment, when caused by accelerated hypertension, e.g., in patients with severe toxemia of pregnancy [8,

14], or by DIC [2], is associated with ophthalmoscopic and angiographic evidence of multifocal areas of choroidal vascular occlusion and acute RPE damage, but not with exudative RPE detachment. In these latter patients, there is histopathologic evidence that focal areas of fibrin-platelet occlusion of the choriocapillaris and choroidal arterioles are the cause of RPE changes and exudative retinal detachment [2, 14]. Focal clumping of the RPE (Elschnig's spots) and linear areas of RPE atrophy and choroidal vascular wall opacification (Siegrist's streaks) are premanent telltale scars of this process [14]. These late RPE changes unaccompanied by retinal detachment have been noted in some patients receiving hemodialysis, but it is uncertain as to whether they were present prior to the commencement of hemodialysis [9, 10, 13].

I have seen the development of bilateral exudative retinal detachment associated with disruption and clumping of the RPE in the macular area similar to that seen in patients with accelerated hypertension, and disseminated intravascular coagulopathy in patients after renal and heart-lung transplantation [9]. The mechanism responsible for retinal detachment in the latter patients who require immunosuppressive therapy for maintenance of their homograft may be different than that occurring in patients receiving hemodialysis.

In conclusion, the clinician should be aware that patients either receiving hemodialysis or having undergone renal or other major organ transplantation may experience visual loss caused by exudative retinal detachment. When the detachment becomes bullous, it may be mistaken for a rhegmatogenous retinal detachment. Fluorescein angiography is helpful in avoiding this error. In some cases, photocoagulation is successful in causing resolution of the retinal detachment.

Acknowledgements. This investigation was supported in part by Public Health Service Research Grant EY02549 and Core Grant EY02180, Department of Health and Human Services, National Institutes of Health, National Eye Institute, and, in part, by Research to Prevent Blindness, Inc., New York City.

References

1. Benson WE, Shields JA, Annesley WH Jr, Tasman W (1980) Idiopathic central serous choroidopathy with bullous retinal detachment. Ann Ophthalmol 12:920–924
2. Cogan DG (1975) Ocular involvement in disseminated intravascular coagulopathy. Arch Ophthalmol 93:1–8
3. Friberg TR, Eller AW (1990) Serous retinal detachment resembling central serous chorioretinopathy following organ transplantation. Graefe's Arch Clin Exp Ophthalmol 229:305–309
4. Gass JDM (1967) Pathogenesis of disciform detachment of the neuroepithelium. II Idiopathic central serous choroidopathy. Am J Ophthalmol 63:587–615
5. Gass JDM (1973) Bullous retinal detachment. An unusual manifestation of idiopathic central serous choroidopathy. Am J Ophthalmol 75:810–82
6. Gass JDM (1987) Stereoscopic atlas of macular diseases. Diagnosis and treatment, 3rd edn. CV Mosby, St Louis, pp 46–59
7. Gass JDM (1991) Central serous chorioretinopathy and white subretinal exudation during pregnancy. Arch Ophthalmol 109:677–681
8. Gass JDM, Pautler SE (1985) Toxemia of pregnancy pigment epitheliopathy masquerading as a heredomacular dystrophy. Trans Am Ophthalmol Soc 83:114–130
9. Gass JDM, Slamovits TL, Gieser RG, Fuller DG (1991) Posterior chorioretinopathy and retinal detachment after organ transplantation.
10. Hilton AF, Harrison JD, Lamb AM, et al. (1982) Ocular complications of hemodialysis and renal transplant patients. Aust J Ophthalmol 10:247–253
11. Jabs DA, Hanneken AM, Schachat AP, Fine SL (1988) Choroidopathy in systemic lupus erythematosus. Arch Ophthalmol 106:230–234
12. Kayazawa F (1982) Central serous choroidopathy with exudative retinal detachment. Ann Ophthalmol 14:1035–1042
13. Kitaoka M, Hayasaka S, Mizuno K (1986) Localized chorioretinal degeneration in patients receiving hemodialysis. Ophthalmologica 193:200–206
14. Klien BA (1968) Ischemic infarcts of the choroid (Elschnig's spots): a cause of retinal separation in hypertensive disease with renal insufficiency. A clinical and histopathologic study. Am J Ophthalmol 66:1069–1074
15. Miyake K, Miyaki C, Ohno T, Kishi T (1976) A case of uveal effusion onset during hemodialysis. Folia Ophthalmol Jpn 27:1144–1149
16. Polak BC (1980) Ophthalmological complications of hemodialysis and kidney transplantation. Doc Ophthalmol 49:1–96
17. Tsukahara I, Uyama M (1978) Central serous choroidopathy with bullous retinal detachment. Albrecht von Graefe's Arch Klin Exp Ophthalmol 206:169–178
18. Yannuzzi LA (1986) Type A behavior and central serous chorioretinopathy. Trans Am Ophthalmol Soc 84:799–845
19. Yoshioka H, Katsume Y, Akune H (1981) Experimental central serous chorioretinopathy. I. Clinical findings. Jpn J Ophthalmol 25:112–118
20. Yoshioka H, Katsume Y (1982) Experimental central serous chorioretinopathy. III Ultra-structural findings. Jpn J Ophthalmol 26:397–409