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Central retinal vein occlusion: report of two familial cases

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ABSTRACT: The authors report a 46-year-old father and 17-year-old son who each presented with unilateral central retinal vein occlusion (CRVO) and bilateral abnormalities of retinal vascular perfusion. The son presented with a nonperfused CRVO in the left eye, developed traction-rhegmatogenous retinal detachment treated with vitreous surgery, and developed prolonged arteriovenous filling in the retina of the fellow eye. The father presented with progressive CRVO in the right eye, developed choroido-vitreal neovascularization following laser treatment to create a chorioretinal anastomosis, underwent vitrectomy for retinal detachment and vitreous hemorrhage in that eye, and developed prolonged arm-eye and retinal arteriovenous circulation times in the fellow eye. An extensive evaluation (including hematological studies and imaging of the major vessels of the neck) failed to reveal a predisposing cause in either patient although echocardiography disclosed a mitral valve thrombus in the father. After institution of coumadin therapy, the circulatory parameters in the fellow eye of each patient improved. (Eur J Ophthalmol 1999; 9: 181-95)

KEY WORDS: Retinal vein occlusion, Familial, Coumadin, Surgery

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INTRODUCTION

Central retinal vein occlusion (CRVO) usually occurs in older adults but does occur in young adults (1). Bilateral abnormalities of retinal venous perfusion often indicates an underlying systemic abnormality (1). Familial occurrence of CRVO is highly unusual. We report a middle-aged father and teenage son who each presented with unilateral CRVO and bilateral abnormalities of retinal vascular perfusion.

Case report

Son

A 17-year-old Portuguese man was referred by his ophthalmologist (JH) to rule out a CRVO in March 1996. The patient noticed decreased vision in his left eye after being hit by a wave while on a beach seven months earlier. The past medical and ocular history were unremarkable. Visual acuity was 20/20 OD and 2/200 OS. A left relative afferent pupillary defect was present. Slit lamp and fundus examination of the right eye were normal. Slit lamp examination of the left eye was unremarkable. No neovascularization was noted on the iris or in the angle by gonioscopy. The vitreous was syneretic with 1+ cells. Indirect ophthalmoscopy of the left eye disclosed clear media and a flat retina. Biomicroscopy of the left eye disclosed marked swelling of the optic nervehead, prominent macular edema, and retinal whitening interpreted as ischemic macular infarction. Moderate intraretinal hemorrhage surrounded the macula and the optic nervehead, and scattered dot and blot hemorrhages were present as

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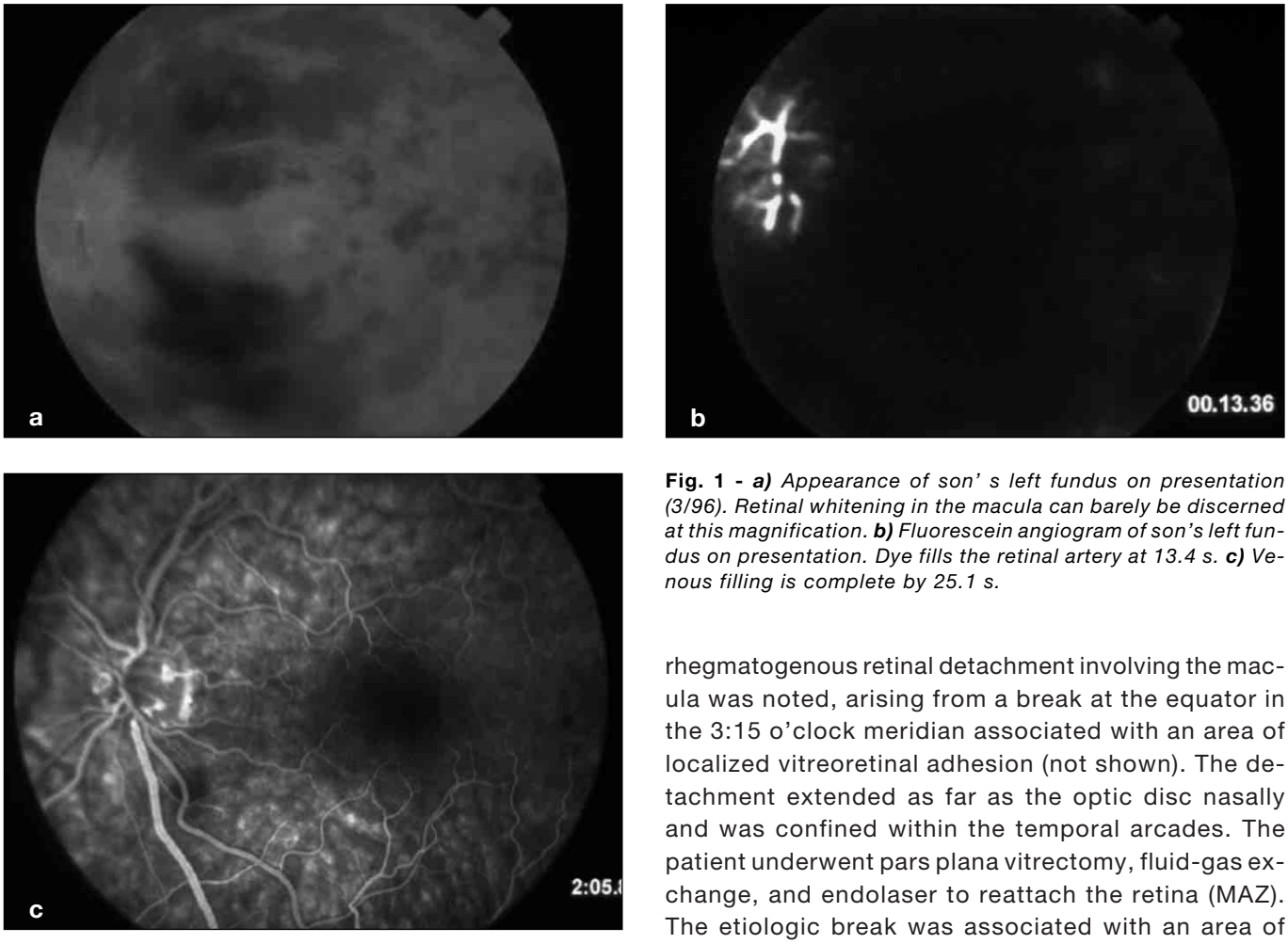


Fig. 1 - ***a)*** *Appearance of son' s left fundus on presentation (3/96). Retinal whitening in the macula can barely be discerned at this magnification.* ***b)*** *Fluorescein angiogram of son's left fundus on presentation. Dye fills the retinal artery at 13.4 s.* ***c)*** *Venous filling is complete by 25.1 s.*

far peripherally as the ora serrata for 360 degrees (Fig. 1). There was a small area of neovascularization inferonasally at the equator at 8:00 o'clock. Vascular sheathing was not present. B-scan echography did not show evidence of optic nerve drusen in either eye.

A diagnosis of CRVO was made. No significant past medical history was elicited. There was no family history of hypercoagulable disorders. An extensive medical evaluation was normal except for the eye findings. The complete blood count, blood chemistry, lipid profile, and erythrocyte sedimentation rate (ESR) were normal (Tab. I).

A fluorescein angiogram showed a normal arm-eye circulation time, and a normal arteriovenous transit time on the left, suggesting that there had been recanalization of the vein with reperfusion (Fig. 1). There was no evidence for vasculitis in either eye.

At a follow-up examination in May 1996, a traction-rhegmatogenous retinal detachment involving the macula was noted, arising from a break at the equator in the 3:15 o'clock meridian associated with an area of localized vitreoretinal adhesion (not shown). The detachment extended as far as the optic disc nasally and was confined within the temporal arcades. The patient underwent pars plana vitrectomy, fluid-gas exchange, and endolaser to reattach the retina (MAZ). The etiologic break was associated with an area of vitreoretinal traction arising from adherent retinal neovascularization.

One month later, visual acuity was 20/20 OD and HM OS. The intraocular pressure was 18 mm Hg OD and 12 mm Hg OS. The exam of the right eye was unchanged. Fundus exam of the left eye disclosed clear media and a flat retina with extensive panretinal photocoagulation. Marked macular edema persisted with newly evident subretinal fibrosis under the macula.

At a follow-up examination in September 1996, the central retinal artery of the right eye collapsed with minimal digital pressure. A fluorescein angiogram transiting the right eye revealed a slightly prolonged arteriovenous transit time with a normal arm-eye circulation time (Fig. 2). The patient was referred to a hematologist (PG) for further evaluation (Tab. I) and was started on 125 mg aspirin PO qAM.

In December 1996, the visual acuity was 20/20 OD and 20/200 OS. The intraocular pressure and slit lamp

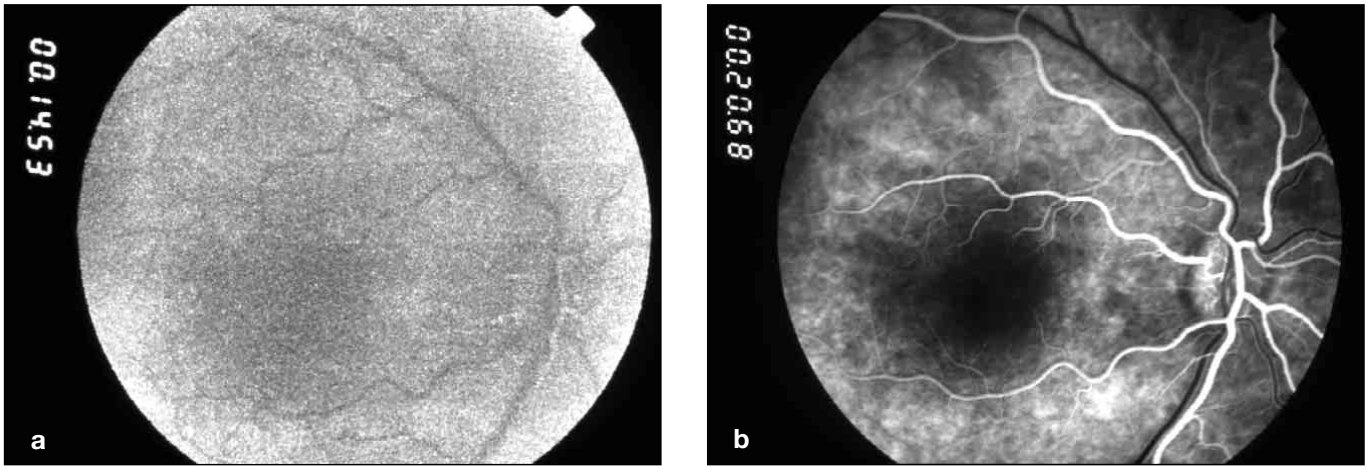


Fig. 2 - *Fluorescein angiogram of son's right eye in September 1996.* ***a)*** *Dye is first evident in the retinal artery at 14.5 s.* ***b)*** *Laminar venous filling is evident in the next frame at 20.7 s.* ***c)*** *Laminar venous filling is evident at 32.3 s.*

exam were normal in each eye. Funduscopic exam of the right eye was normal. Funduscopic exam of the left eye disclosed clear media, a flat retina, stable submacular fibrosis, and an epiretinal membrane along the superotemporal arcade with some foveal traction (Fig. 3). A repeat fluorescein angiogram showed abnormally prolonged arteriovenous transit time in the right eye (Fig. 4). Because of the progressive abnormalities in the right eye, the patient was started on coumadin titrated such that the international ratio (INR) was between 1.5-2.0, at the suggestion of his hematologist (PG).

In February 1997, the visual acuity was 20/20 OD and 20/200 OS. A repeat fluorescein angiogram of the right eye (with the patient anticoagulated), showed mild improvement in the arteriovenous transit time (Fig. 5).

Father

In May 1996, the 46-year-old father was referred by his general ophthalmologist (JH) for evaluation of three episodes of amaurosis fugax OD. Each episode lasted from 1.5 to 3 hours and was not associated with other systemic symptoms.

The visual acuity was 20/20 in each eye. Amsler grid testing, color vision (Ishihara pseudoisochromatic plates), and slit lamp examination were normal in both eyes. The intraocular pressure (applanation) was 13 mm Hg

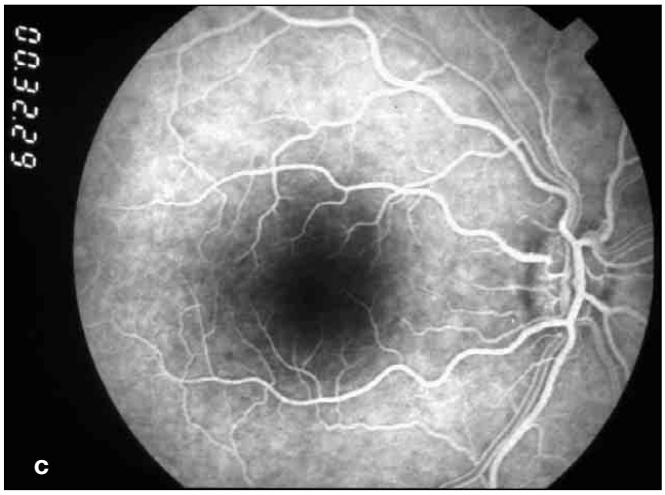


Fig. 3 - *Appearance of son's left fundus 7 months after vitreous surgery. Prominent peripapillary epiretinal fibrosis and submacular fibrosis are evident.*

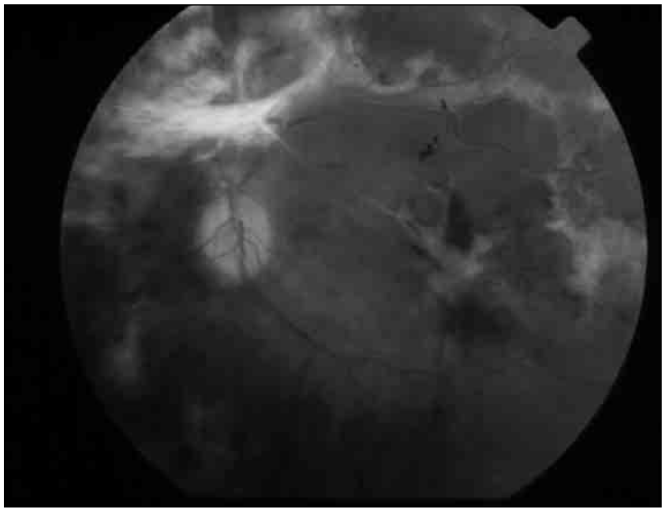


TABLE I - HEMATOLOGICAL EVALUATION OF THE SON

Test	Result	Normal range
CBC		
WBC	7.8 T/ul	4.3 - 11.0 T/ul
Hemoglobin	15.3 g/dl	14.0 - 16.5 g/dl
Hematocrit	43.4%	40.0 - 54.0%
Platelets	194 T/ul	150 - 375 T/ul
Chemistry		
Sodium	134 mEq/L	135 - 146 mEq/L
Potassium	4.0 mEq/L	3.5 - 5.3 mEq/L
Chloride	100 mEq/L	95 - 108 mEq/L
BUN	16 mg/dl	8 - 20 mg/dl
Creatinine	0.6 mg/dl	0.5 - 1.4 mg/dl
Glucose	90 mg/dl	60 - 120 mg/dl
Uric acid	4.9 mg/dl	2.6 - 7.2 mg/dl
SGOT	12 U/L	5 - 37 U/L
SGPT	11 U/L	0 - 48 U/L
LDH	123 U/L	100 - 190 U/L
Calcium	9.0 mg/dl	8.8 - 11.0 mg/dl
Phosphorus	2.9 mg/dl	2.5 - 4.0 mg/dl
PT	12.6 sec	11.5 - 12.5 sec
aPT	24.8 sec	25 - 35 sec
Cholesterol	147 mg/dl	100 - 200 mg/dl
Triglycerides	126 mg/dl	16 - 200 mg/dl
LDL	88 mg/dl	60 - 185 mg/dl
HDL	34 mg/dl	>34 mg/dl
Iron, total	82 mcg/dl	25 - 170 mcg/dl
Iron binding capacity	368 mcg/dl	200 - 450 mcg/dl
ESR	14 mm/hr	0 - 20 mm/hr
ANA	Negative	negative
Rheumatoid factor	Negative	negative
Hemoglobin A1c	6.8%	6.5%
Compliment CH100	116 U/ml	40 - 97 U/ml
Sickle cell screen	Negative	negative
Hemoglobin A	100%	100%
RPR	non-reactive	non-reactive
Protein C antigen	126%	70 - 140%
Protein S antigen	98%	70 - 140%
Protein S activity	93%	80 - 180%
Activated Protein C Resistance	4.05 ratio	2.49 - 4.49 ratio
Lupus-type anticoagulant	Negative	negative
Cardiolipin Ab IgG	<15 GPL	<15 GPL
Cardiolipin Ab IgM	<10 MPL	<10 MPL
Cardiolipin Ab IgA	<10 APL	<10 APL

Test	Result	Normal range
Antithrombin panel		
activity	120 %	78 - 117%
antigen	29 mg/dl	25 - 33 mg/dl
Phosphotidylserine Ab IgG	<2.0 SD	<2.0 SD
Phosphotidylserine Ab IgM	<2.0 SD	<2.0 SD
Phosphotidylserine Ab IgA	<2.0 SD	<2.0 SD
Fibrinogen	321 mg/dl	150-400 mg/dl
Factor V gene	no Arg 506 to Gln mutation	no Arg 506 to Gln mutation
Serum homocysteine	9.4 mcmol/L	5.1 - 13.9 mcmol/L
Carotid doppler	Normal	normal
Transesophageal	negative for cardiac clots or	normal
echocardiogram	any valvular abnormality	
Platelet aggregation		
collagen	26 ohms	11 - 32 ohms
arachidonic acid	20 ohms	4 - 32 ohms
ristocetin	27 ohms	5 - 35 ohms
Platelet release		
thrombin	1.9 nmoles of ATP	>0.5 nmoles of ATP
collagen	1.1 nmoles of ATP	0.5 - 1.7 nmoles of ATP
arachidonic acid	0.2 nmoles of ATP	0.6 - 1.4 nmoles of ATP

OD and 19 mm Hg OS. Funduscopic examination of the right eye disclosed that the veins were somewhat engorged at the optic nervehead, and there were scattered intraretinal hemorrhages along the temporal arcades and in the midperiphery, particularly superiorly (Fig. 6). The macula appeared normal. Fundus exam of the left eye also revealed clear media and a flat retina. The veins appeared slightly engorged in the posterior pole but were not tortuous. A venous shunt vessel was present at the optic nervehead (Fig. 7). There were no peripheral abnormalities. B-scan echography disclosed no buried drusen of the optic nerveheads. A fluorescein angiogram disclosed prolonged arteriovenous transit time in the right eye (Fig. 8).

The patient' s symptoms were presumed to be due to intermittent CRVO OD. The vascular anomaly at the optic nervehead in the left eye was thought to be either a congenital malformation or an acquired manifestation of occult venous occlusive disease. The patient was continued on Timoptic and aspirin, which had been started by his general ophthalmologist (JH). The patient was seen by an internist, and the general medical examination was normal.

Over the next four weeks the vision declined, as the CRVO progressed on the right. By July 1996, the visual acuity was 20/160; pinhole, 20/50-1 OD and 20/20 OS. Amsler grid testing showed a central relative scotoma OD. The intraocular pressure was 15 mm Hg OD and 14 mm Hg OS. Slit lamp exam of the each eye was notable for the absence of rubeosis iridis. Funduscopic exam of the right eye disclosed increased intraretinal hemorrhage and the presence of macular edema (Fig. 9). Fundus exam of the left eye disclosed a few intraretinal hemorrhages in the temporal paramacular area (Fig. 9). The patient was diagnosed as having impending CRVO OS. The patient was referred to a hematologist (PG) for further evaluation (Tab. II).

A fluorescein angiogram transiting the right eye disclosed prolonged arm-eye circulation time OD, prolonged arteriovenous transit time OD, and no definite microvascular abnormalities OS (Fig. 10). A laser (argon blue-green) choroiretinal venous anastomosis was attempted in the right eye at this time (not shown).

At follow-up examination on July 26, the visual acuity was 5/160 OD and 20/20 OS. The intraocular pressure was 11 mm Hg OD and 18 mm Hg OS. Slit lamp

TABLE II - HEMATOLOGICAL EVALUATION OF THE FATHER

Test	Result	Normal range
CBC		
WBC	6.4 T/ul	4.5 - 11.0 T/ul
Hemoglobin	15.1 gm/dl	14.0 - 18.0 gm/dl
Hematocrit	43.9%	42.0 - 52.0%
Platelets	211 T/ul	130 - 400 T/ul
Chemistry		
Sodium	138 mEq/L	135 - 146 mEq/L
Potassium	4.5 mEq/L	3.5 - 5.3 mEq/L
Chloride	98 mEq/L	95 - 108 mEq/L
BUN	26 mg/dl	8 - 20 mg/dl
Creatinine	0.9 mg/dl	0.5 - 1.4 mg/dl
Glucose	96 mg/dl	60 - 120 mg/dl
Uric acid	8.9 mg/dl	2.6 - 7.2 mg/dl
SGOT	24 U/L	5 - 37 U/L
SGPT	12 U/L	0 - 48 U/L
LDH	124 U/L	100 - 190 U/L
Calcium	9.8 mg/dl	8.8 - 11.0 mg/dl
Phosphorus	2.7 mg/dl	2.5 - 4.0 mg/dl
PT	13.2 sec	10.0 - 14.0 sec
aPTT	32.6 sec	22.0 - 39.0 sec
Bleeding time	4.5 min	1.6 - 8.0 min
Cholesterol	178 mg/dl	<200 mg/dl
Triglycerides	102 mg/dl	<200 mg/dl
LDL	117 mg/dl	0 - 130 mg/dl
HDL	41 mg/dl	>34 mg/dl
Serum electrophoresis		
Protein, total	7.1 g/dl	6.0 - 8.5 g/dl
Albumin	4.0 g/dl	3.2 - 5.6 g/dl
Alpha-1-Globulin	0.3 g/dl	0.1 - 0.4 g/dl
Alpha-2-Globulin	0.8 g/dl	0.4- 1.2 g/dl
Beta Globulin	0.8 g/dl	0.6 - 1.3 g/dl
Gamma Globulin	1.0 g/dl	0.5 - 1.6 g/dl
Iron, total	103 mcg/dl	25 - 170 mcg/dl
Iron binding capacity	345 mcg/dl	200 - 450 mcg/dl
ESR	5 mm/hr	0 - 20 mm/hr
ANA	Negative	negative
Rheumatoid factor	Negative	negative
VDRL	non-reactive	non-reactive
Sickle cell screen	Negative	negative
Hemoglobin A	100%	100%
Protein S, total	76 mg/dl	56 - 124 mg/dl
activity	150%	65 - 140%
free	55%	56 - 124%

Test	Result	Normal range
Protein C antigen	98%	>70%
Protein C activity	124%	72 - 142%
Activated protein C resistance	3.61	2.49 - 4.49 ratio
Lupus anti-coagulant	Negative	negative
Cardiolipin antibody		
IgG	2 GPL units	0 - 12 GPL units
IgM	3 MPL units	0 - 6 MPL units
IgA	<10 SDU	<10 SDU
Antithrombin panel		
activity	137%	78 - 117%
antigen	23 mg/dl	25 - 33 mg/dl
Russell's viper venom	27.3 sec	21.4 - 36.2 sec
Plasminogen activity	110%	80 - 120%
Plasminogen activator inhibitory factor	20.0 UL/ml	2.5 - 27.5 UL/ml
Alpha-2 anti-plasmin	112%	80 - 120%
Fibrinogen	379 mg/dl	150 - 400 mg/dl
Factor V gene	no arg 506 to gln mutation	no arg 506 to gln mutation
Serum homocysteine	10.4 mcmol/L	5.1 - 13.9 mcmol/L
Platelet aggregation		
collagen	30 ohms	11 - 32 ohms
arachidonic acid	19 ohms	4 - 32 ohms
ristocetin	34 ohms	5 - 35 ohms
Platelet release		
thrombin	1.5 nmoles of ATP	>0.5 nmoles of ATP
collagen	0.8 nmoles of ATP	0.5 - 1.7 nmoles of ATP
arachidonic acid	0.4 nmoles of ATP	0.6 - 1.4 nmoles of ATP

exam of each eye was normal. Funduscopic exam of the right eye disclosed dilated, tortuous veins with retinal hemorrhage in all four quadrants and an increase in macular edema. Funduscopic exam of the left eye disclosed mildly increased intraretinal hemorrhage and three microaneurysms temporal to the fovea (Fig. 11). The venous loop at the optic nervehead was unchanged in appearance. Fluorescein angiography disclosed no evidence for a chorioretinal venous anastomosis, so laser photocoagulation was repeated superonasally (not shown).

The patient was referred to the Wilmer Ophthalmological Institute (MFG) on July 29, 1997 for further evaluation and management. His visual acuity was 1/200 OD and 20/16 OS. The intraocular pressure was 15 mm Hg OD and 16 mm Hg OS. Fundus exam of the right eye disclosed dilated, tortuous veins with flame-shaped moderate intraretinal hemorrhages in all four quadrants and marked cystoid macular edema. An area of choroido-vitreal neovascularization was evident at the site of the chorioretinal anastomosis inferonasal to the optic disc. Funduscopic examination of the left eye disclosed a new finding of some scattered dot and blot hemorrhages in the inferior periphery temporally and nasally, posterior to the equator. Extensive hematological studies were done at the Johns Hopkins Hospital (WB). The evaluation was within normal limits except for mildly elevated antithrombin and protein S activity. These abnormalities were not felt to be clinically significant.

On the patient's return visit to the New Jersey Medical School on August 2, the vision was 5/200 OD

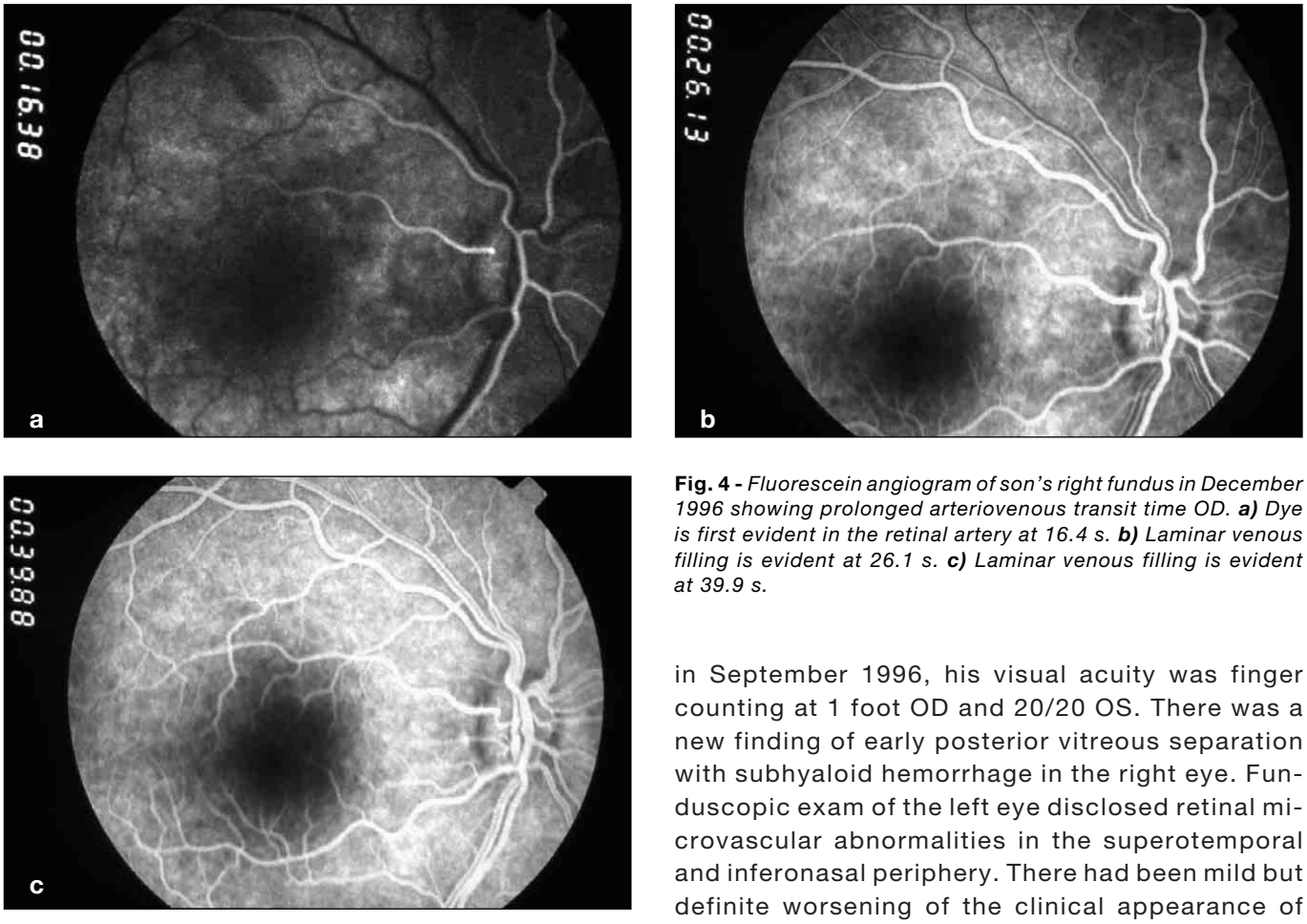


Fig. 4 - *Fluorescein angiogram of son's right fundus in December 1996 showing prolonged arteriovenous transit time OD.* ***a)*** *Dye is first evident in the retinal artery at 16.4 s.* ***b)*** *Laminar venous filling is evident at 26.1 s.* ***c)*** *Laminar venous filling is evident at 39.9 s.*

and 20/20 OS. Funduscopic exam showed CRVO and an inferonasal choroido-vitreal neovascular membrane at the site of previous laser photocoagulation (Fig. 12). Fluorescein angiography revealed a choroido-vitreal neovascular membrane approximately 1 1/2 disc areas in size at the anastomosis site (Fig. 12). Using Krypton red laser, the choroido-vitreal neovascular membrane was treated with confluent white laser burns. Fluorescein angiography on August 6, 1996 showed prolonged arm-eye and arteriovenous transit times of the left eye, for the first time (Fig. 13).

The patient went to Portugal for further medical evaluation. During the evaluation, a heart murmur was noted, and echocardiography revealed an extensive thrombus emanating from the mitral valve. Coumadin therapy was instituted such that INR was between 1.5-2.0.

When the patient returned to the United States in September 1996, his visual acuity was finger counting at 1 foot OD and 20/20 OS. There was a new finding of early posterior vitreous separation with subhyaloid hemorrhage in the right eye. Funduscopic exam of the left eye disclosed retinal microvascular abnormalities in the superotemporal and inferonasal periphery. There had been mild but definite worsening of the clinical appearance of the left fundus. A repeat fluorescein angiogram revealed that the arm-eye circulation time had normalized, and the arteriovenous transit time had improved substantially following the initiation of coumadin therapy in Portugal (Fig. 14).

At follow-up in November 1996, the visual acuity was bare light perception OD and 20/20 OS. Slit lamp exam of both eyes was within normal limits. The intraocular pressure was 15 mm Hg OU. Funduscopic exam OD showed a dull orange reflex. Funduscopic exam OS revealed clear media and a few microaneurysms in the macula and within the superotemporal arcade. The veins were slightly dilated. Combined A and B scan echography of the right eye revealed dispersed blood in the vitreous cavity, subhyaloid hemorrhage, and tractional retinal elevation involving the macula. Repeat blood testing revealed that the patient was excessively anticoagulated. The prothrombin time was 21.7 seconds with an INR of 3.31. The coumadin dose was

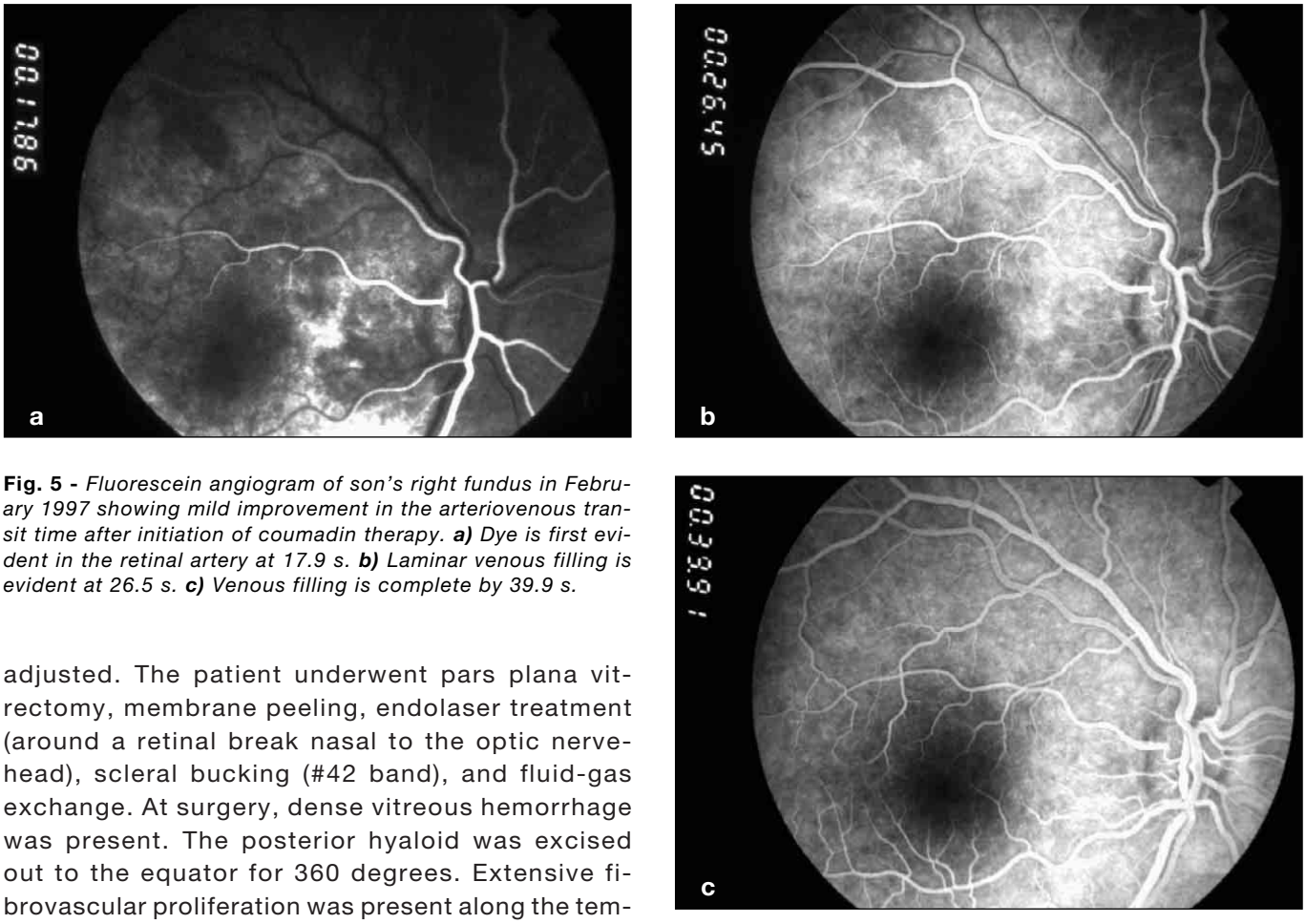


Fig. 5 - *Fluorescein angiogram of son's right fundus in February 1997 showing mild improvement in the arteriovenous transit time after initiation of coumadin therapy.* ***a)*** *Dye is first evident in the retinal artery at 17.9 s.* ***b)*** *Laminar venous filling is evident at 26.5 s.* ***c)*** *Venous filling is complete by 39.9 s.*

adjusted. The patient underwent pars plana vitrectomy, membrane peeling, endolaser treatment (around a retinal break nasal to the optic nervehead), scleral bucking (#42 band), and fluid-gas exchange. At surgery, dense vitreous hemorrhage was present. The posterior hyaloid was excised out to the equator for 360 degrees. Extensive fibrovascular proliferation was present along the temporal arcades, over the optic nervehead, and in the nasal mid-periphery, and appeared to have emanated from the retino-choroidal anastomosis. In addition, the vascular caliber at the optic nerve-head was markedly attenuated. There was mild pallor of the optic nervehead, and the retina appeared ischemic. Postoperatively, the patient lost light perception despite complete retinal reattachment and normal perioperative intraocular pressure.

In January 1997, the visual acuity was no light perception OD and 20/20 OS. The intraocular pressure was 6 mm Hg OD and 15 mm Hg OS. Slit lamp exam was unremarkable OU. Funduscopic exam of the right eye disclosed clear media and a flat retina with a moderate encircling scleral buckle. Regressed neovascular tissue was present nasal to the optic nervehead, which was pale temporally. Funduscopic exam of the left eye appeared stable and disclosed a number of microaneurysms in the inferonasal and superotemporal periphery. A repeat fluorescein angiogram showed definite improvement in the arteriovenous transit time in the left eye as well as in the arm eye circulation time compared to the studies of November 1996. A repeat examination in November 1997 also disclosed a stable funduscopic examination with nearly normal arteriovenous transit time in the left eye (Fig. 15). Thus, the father' s arm-eye circulation time and arteriovenous transit time in the left eye improved substantially following the initiation of coumadin therapy.

In view of the bilateral nature of the vascular anomalies and the prolonged arm-eye circulation time, the possibility of aortic arch disease (e.g., Takayasu disease or a disease with similar anatomic consequences) was considered. A magnetic resonance angiogram (including visualization of the carotid system) was done in both the father and the son, and no major congenital structural abnormalities were detected in either patient.

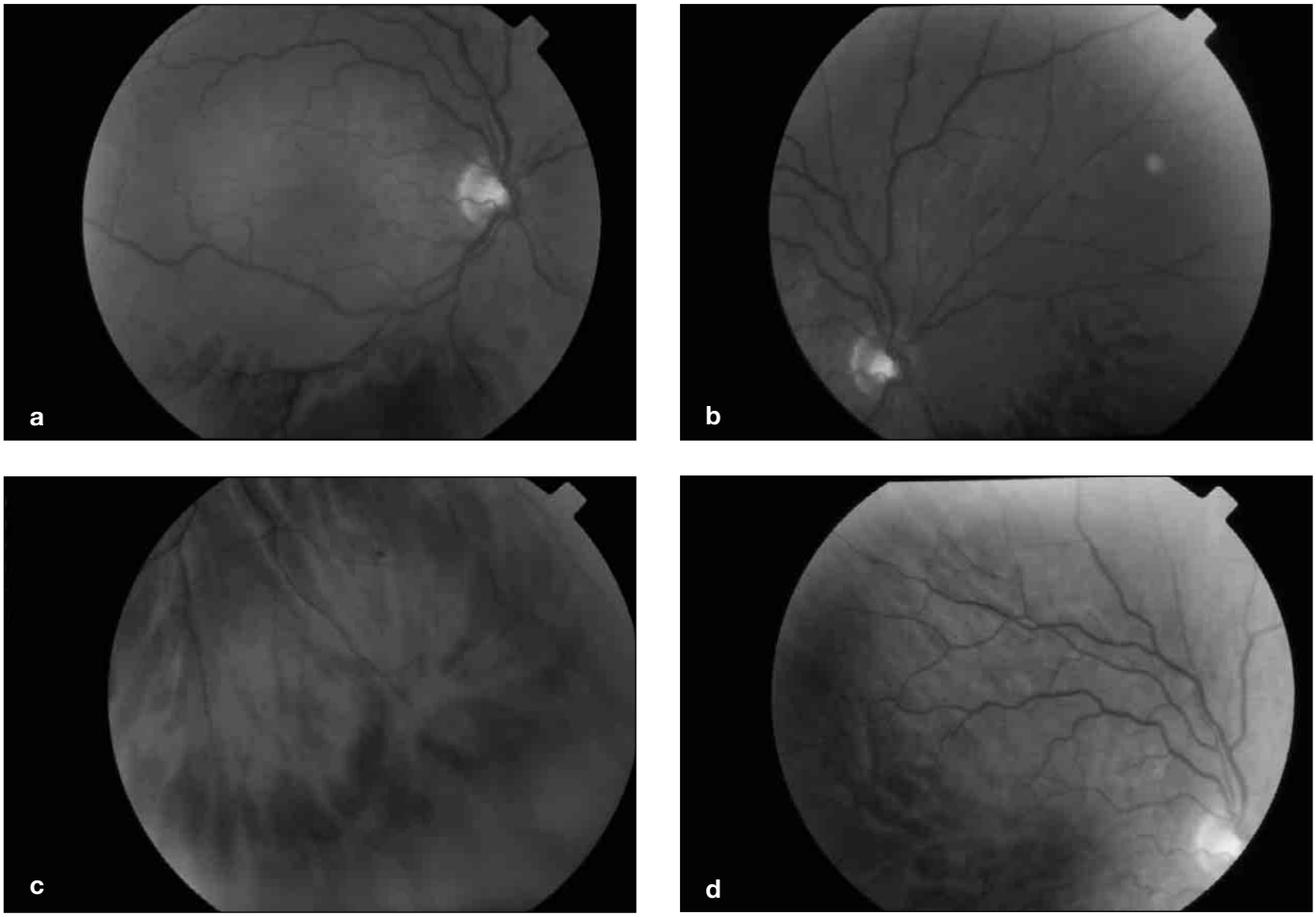


Fig. 6 - ***a)*** *Appearance of father' s right fundus on presentation (5/96). The nerve and macula appear normal although the veins are somewhat engorged.* ***b)*** *Superonasal periphery of photo in* ***a*** *showing intraretinal hemorrhages along the superotemporal arcade and in the nasal periphery.* ***c)*** *Inferonasal periphery showing intraretinal hemorrhage.* ***d)*** *Intraretinal hemorrhage near superotemporal arcade. The hemorrhage is slightly out of focus.*

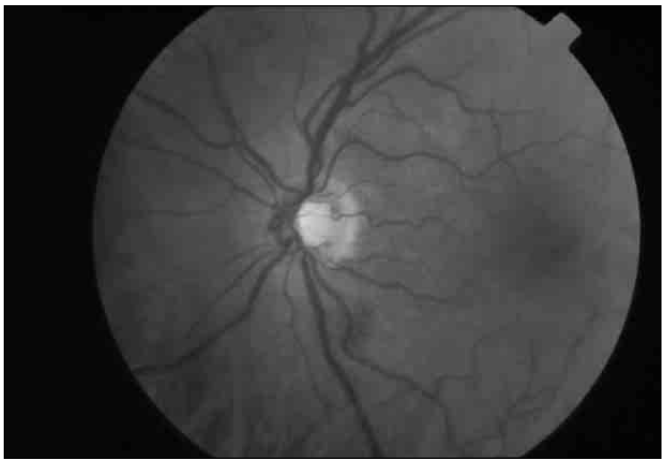


Fig. 7 - *Appearance of father's left fundus on presentation (5/96). Note venous shunt vessels on the optic disc nasally in addition to the choroidal nevus inferior to the disc.*

DISCUSSION

CRVO in young adults is uncommon: 10-15% of patients with CRVO are under 40 years of age (2-4). Although CRVO is occasionally associated with a systemic disease, the cause is unknown in the majority of cases. Bilateral CRVO has been reported in a patient with scleroderma who also had pulmonary fibrosis, cor pulmonale, cardiac decompensation, and secondary polycythemia (5). This patient also had delayed retinal arterial filling on fluorescein angiography. Our patients did not have evidence of scleroderma.

Heritable conditions that might conceivably lead to familial CRVO include hypercoagulable states such as protein C deficiency, protein S deficiency, activated protein C resistance, antithrombin deficiency, hyper-

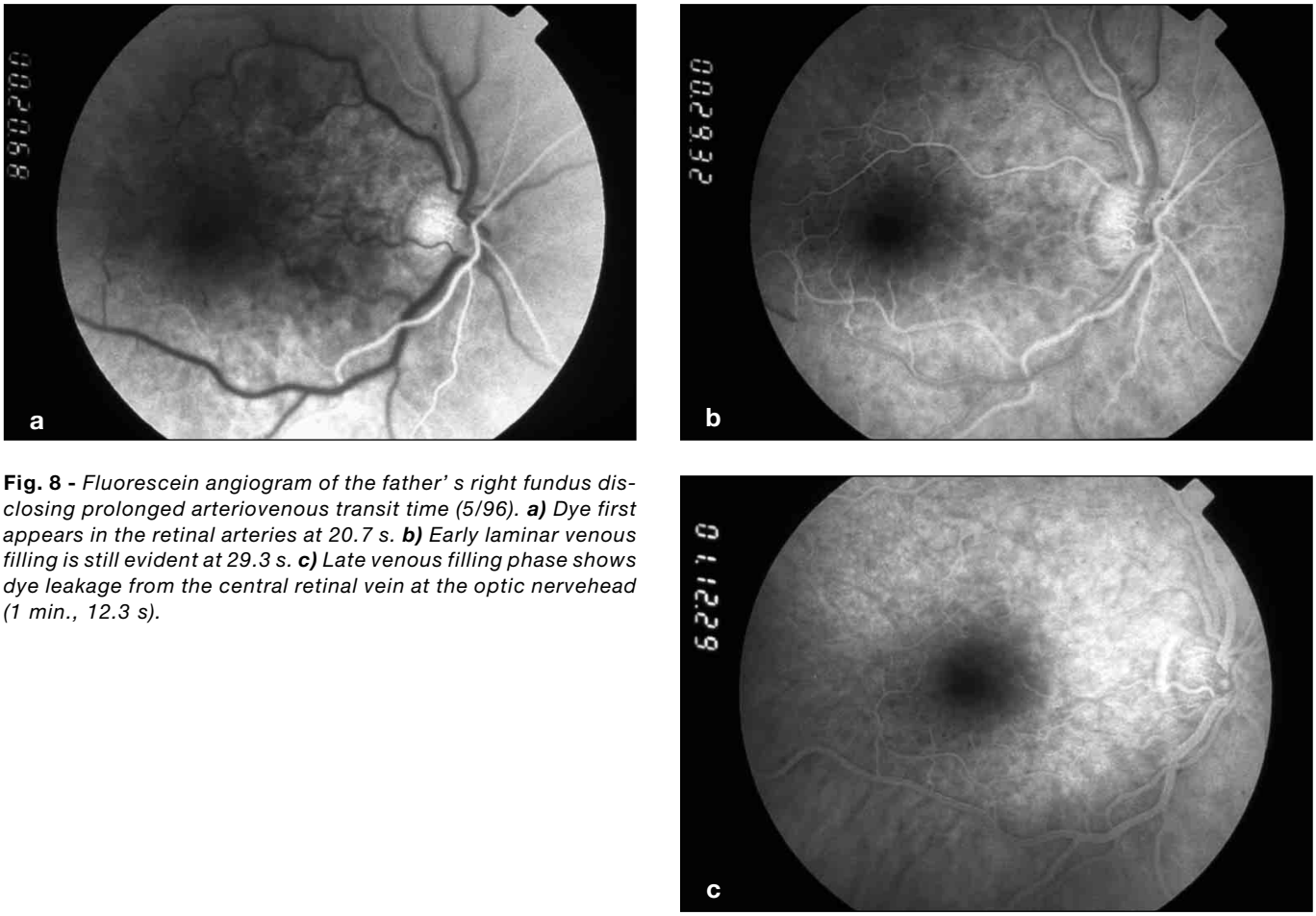


Fig. 8 - *Fluorescein angiogram of the father' s right fundus disclosing prolonged arteriovenous transit time (5/96).* ***a)*** *Dye first appears in the retinal arteries at 20.7 s.* ***b)*** *Early laminar venous filling is still evident at 29.3 s.* ***c)*** *Late venous filling phase shows dye leakage from the central retinal vein at the optic nervehead (1 min., 12.3 s).*

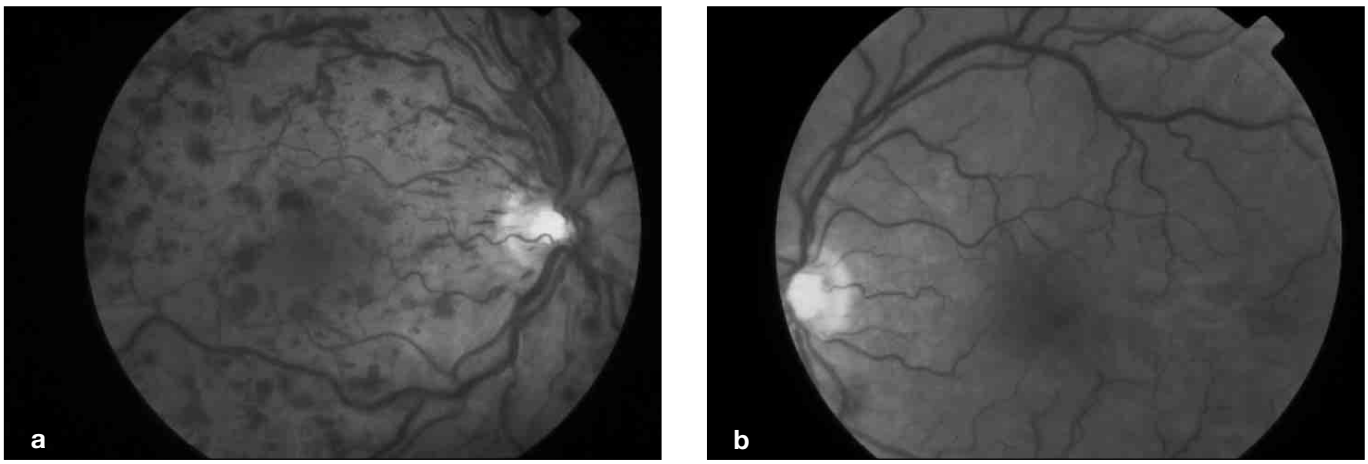
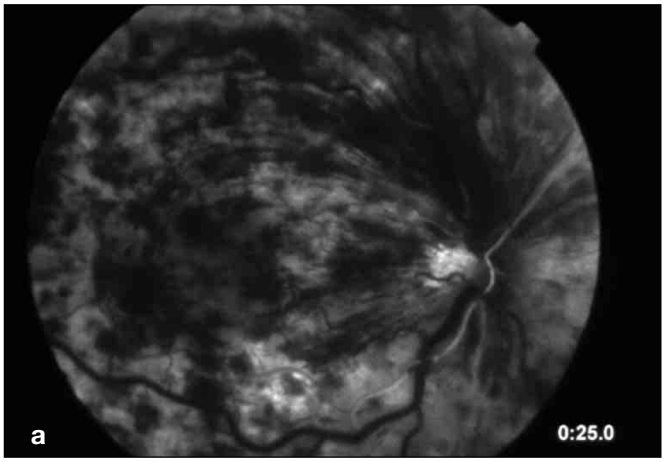
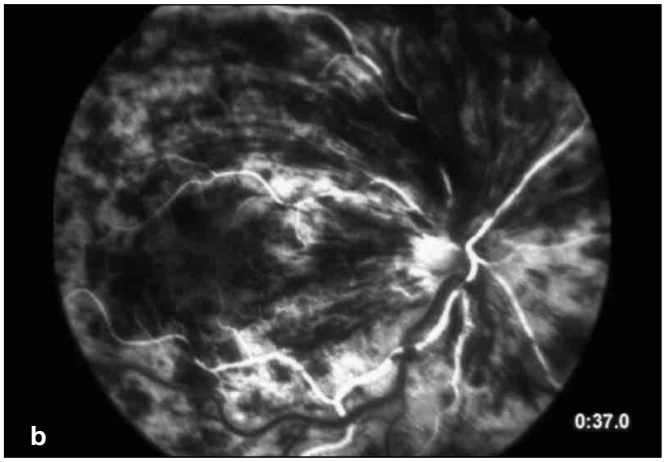


Fig. 9 - ***a)*** *Appearance of father's right fundus in June 1996. CRVO was present.* ***b)*** *Appearance of father's left fundus in June 1996. A few retinal microaneurysms are present temporal to the fovea in the 3:45 o'clock meridian.*





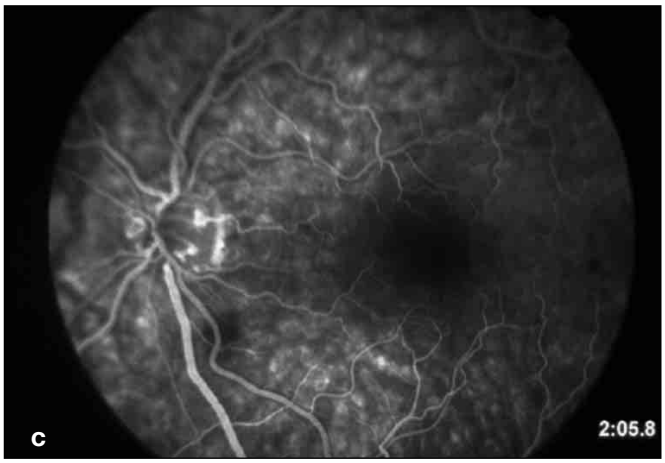
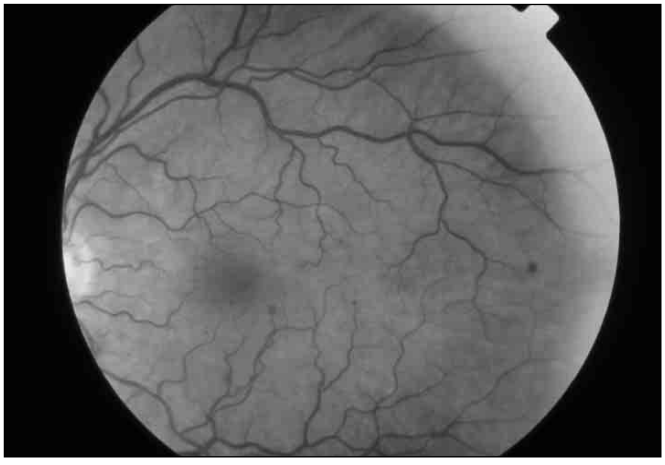


Fig. 10 - *Fundus fluorescein angiogram of father in July 1996.* ***a)*** *Dye first appears in the retinal arteries at 25.0 s.* ***b)*** *Laminar venous filling is evident at 37.0 s.* ***c)*** *Area of intraretinal hemorrhage temporal to the left macula blocks fluorescence.*

Fig. 11 - *Fundus photograph of father's left eye in July 1996. Note increased intraretinal hemorrhage temporal to the fovea compared to Figure 9b.*



lipoproteinemia (a), hyperhomocysteinemia, and increased plasminogen activator inhibitor activity (1, 6-18). Familial CRVO has been reported by Castella and Othenin-Girard (19). Three members of a family with type II hyperlipoproteinemia, two of whom were less than 40 years of age, presented with CRVO. Our patients did not have these predisposing conditions. The family history in the cases reported here suggests the possibility of an autosomal dominant gene predisposing to vascular occlusion. The father might be the first person in his family to carry this putative gene, or there may be other asymptomatic carriers due to variable penetrance. The only abnormality present in both the father and son appears to be a reduced release of ATP with arachidonic acid as a challenger. The isolated finding of reduced aggregation to arachidonic acid does not fit any of the known platelet defects. This abnormality is seen in Glanzmann's thrombasthenia and storage-pool deficiency or in aspirin effect (20). If any of the three conditions were present, there would have been other abnormalities besides reduced response to arachidonic acid. In the case of heterozygotes, one also can expect abnormalities in platelet function, but in more than one parameter. In summary, we find no logical explanation for this *in vitro* result of reduced ATP release in response to arachidonic acid challenge, especially as a unique feature. In any case, any of the three conditions mentioned above would predispose the patient towards bleeding, quite the opposite of what we observed in this father and son.

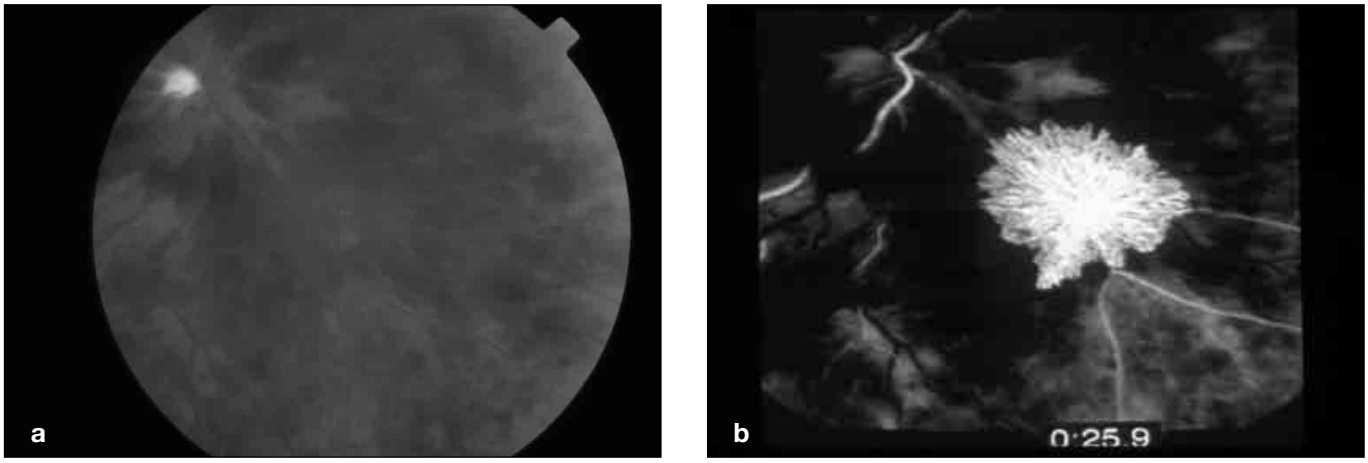
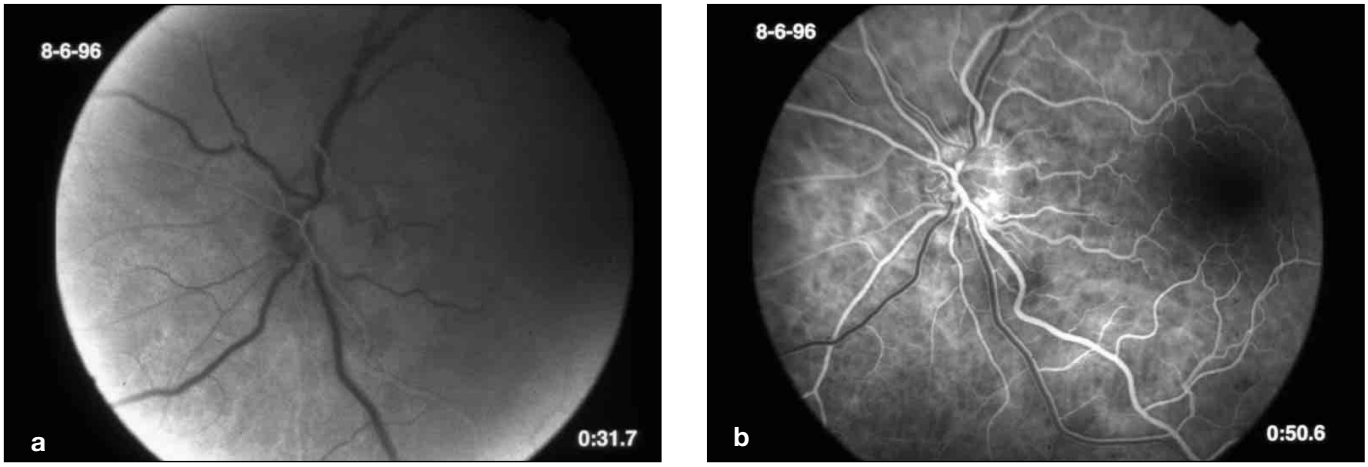


Fig. 12 - a) *Fundus photograph of father's right eye in August 1996 showing choroido-vitreal neovascularization at the site of previous laser photocoagulation.* ***b)*** *Fluorescein angiogram of the area shown in* ***a****.*



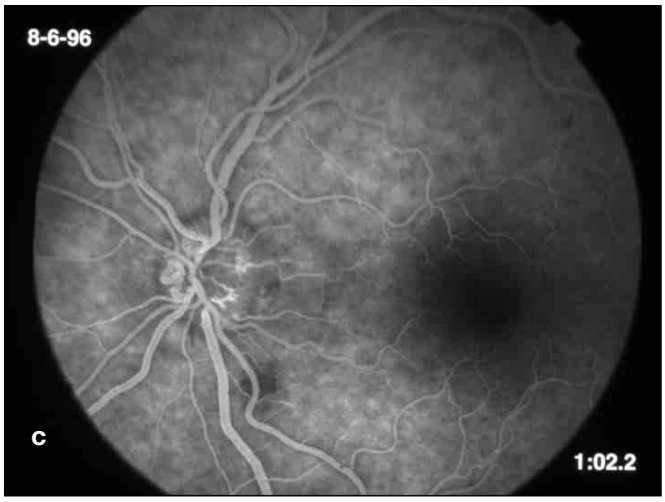


Fig. 13 - *Fundus fluorescein angiogram of the father's left eye showing prolonged arm-eye and arteriovenous transit times (8/6/96).* ***a)*** *Retinal arterial filling is first evident at 31.7 s.* ***b)*** *Early laminar venous filling is evident at 50.6 s.* ***c)*** *Venous filling is complete at 1 min., 2.2 s.*

The presence of CRVO in the father and son represents an interesting and infrequently reported finding. The heritable causes of CRVO mentioned above were ruled out in these two patients. The father had signs of impending CRVO in the other healthy eye, the progress of which halted following the initiation of the anticoagulant therapy, coumadin. The prolonged arm-eye circulation time and arteriovenous transit time improved after a few weeks of therapy. The son had prolonged reti-

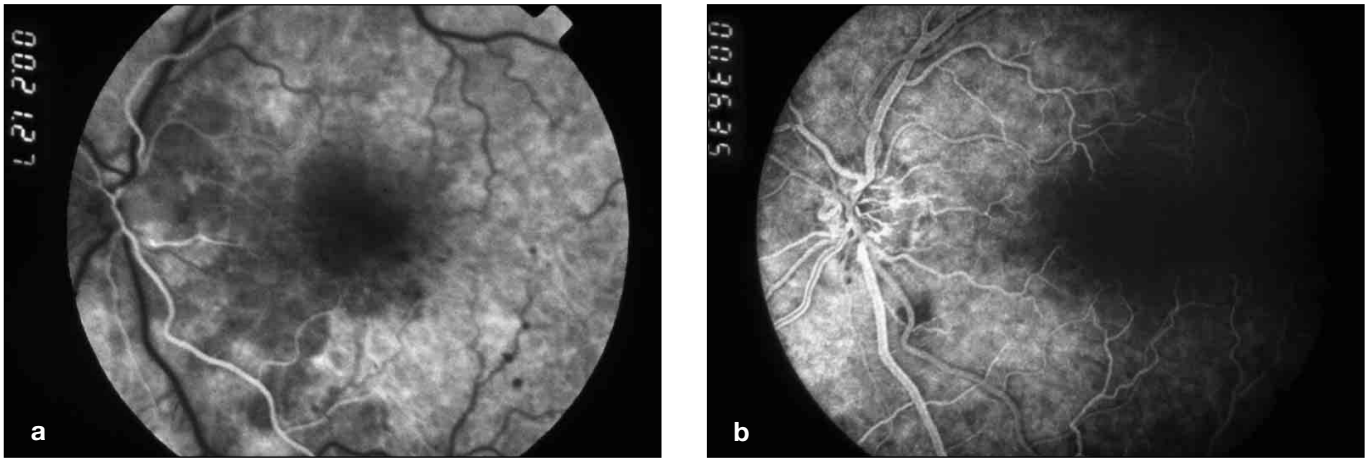


Fig. 14 - *Fundus fluorescein angiogram of the father's left eye showing improved arm-eye and arteriovenous transit times after initiation of coumadin therapy (9/13/96).* ***a)*** *Dye first appears in the retinal arteries at 21.3 s.* ***b)*** *Venous filling is nearly complete by 36.4 s.*

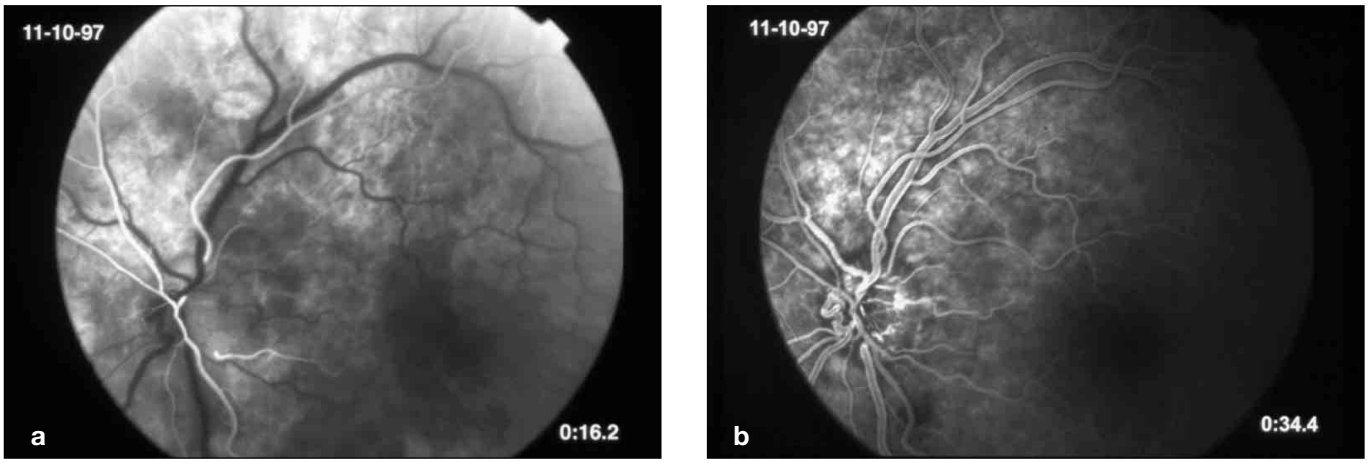


Fig. 15 - *Fundus fluorescein angiogram of father's left eye in November 1997. Note the sustained improvement in the arm-eye and arteriovenous transit times.* ***a)*** *Dye first appears in the retinal arteries at 16.2 s.* ***b)*** *Venous filling is nearly complete by 34.4 s.*

nal arteriovenous filling in the fellow eye, but no intraretinal hemorrhage or microvascular abnormalities. The retinal arteriovenous filling time improved following coumadin therapy. Anticoagulants have been used to treat some patients with retinal vascular occlusion (1). Anticoagulation with coumadin may cause increased intraretinal and intravitreal hemorrhage in some patients. The significance of the response to coumadin regarding the pathogenesis of the condition in these two patients is unknown.

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