- 7 Kline L, Margulies SL, Oh SJ. Optic neuritis and myelitis following rubella vaccination. *Arch Neurol* 1982;39:443-4.
- 8 Riikonen R. The role of infection and vaccination in the genesis of optic neuritis and multiple sclerosis in children. *Acta Neurol Scand* 1989;80:425-31.
- 9 Kriss A, Francis DA, Cuendet F, Halliday AM, Taylor DSL, Wilson J, et al. Recovery after optic neuritis in children. *J Neurol Neurosurg Psychiatry* 1988;51:1253-8.
- 10 Parkin PJ, Hierons R, McDonald WI. Bilateral optic neuritis. A long term follow up. *Brain* 1984;107:951-64.
- 11 Riordan-Eva P, Sanders MD, Govan GG, Sweeney MG, Da Costa J, Harding AE. The clinical features of Leber's hereditary optic neuropathy defined by the presence of a pathogenic mitochondrial DNA mutation. *Brain* 1995; (Pt 2):319-37.
- 12 Stratton KR, Howe CJ, Johnston Jr RB. Adverse events associated with childhood vaccines. Evidence bearing on causality. Vaccine safety committee. Washington DC: Institute of Medicine, National Academy Press, 1994.

Retinal arterial occlusion associated with resistance to activated protein C

EDITOR.—Resistance to activated protein C (APC) was described in 1994 as a thrombophilic factor responsible for deep venous thrombosis and pulmonary embolism.^{1,2} It represents the major cause of thrombophilic disorder in the normal population (5%). APC is an important component of the physiological anticoagulant system that inhibits factors Va and VIIIa. The resistance to APC is related to a single mutation in the factor V gene which causes the switch from arginine to glutamine at position 506. This mutation of factor V blocks the site of cleavage by APC.³ Reported thrombophilic manifestations include venous thrombosis and a case of central retinal vein thrombosis.⁴ Arterial occlusion is not clearly associated with resistance to APC. Ischaemic stroke was recently reported in three patients with resistance to APC.⁵ We described a case of branched retinal artery occlusion associated with resistance to APC.

CASE REPORT

A 35-year-old non-smoking man was referred for a sudden decrease of visual acuity in the left eye. He had no familial or personal history of thrombophilic disorders. At examination, his best corrected visual acuity was 20/20 in the right eye and 20/30 in the left. A superotemporal branched retinal artery occlusion was noted in the left eye with an oedematous, whitish, retinal infarction in the affected vessel. A fluorescein angiogram confirmed the branched retinal artery occlusion (Fig 1). After 2 months, visual acuity improved to 20/25 in the left eye. He had a permanent visual field defect in the area of damaged retina confirmed by Goldmann perimetry. Cardiac rhythm was regular; transthoracic echocardiography, and carotid Doppler studies showed no abnormalities. Red blood cell, white cell, platelet counts, and erythrocyte sedimentation rate were all normal. Platelet aggregation was normal. A search for antinuclear and anticardiolipin antibodies was negative. Prothrombin time and activated partial thromboplastin time (APTT) were normal. Plasma levels of protein C, S, antithrombin III, fibrinogen, plasminogen, plasminogen activator inhibitor were within normal ranges. APC resistance was determined by evaluating the anticoagulant response of plasma samples to APC with an APTT based assay. Results were expressed as the following APC sensitivity ratio (APTT + APC)/(APTT - APC). The cut off value was 2.2. In our patient, the APC

Figure 1 Superotemporal branched retinal artery occlusion.

sensitivity ratio was 2.1. Heterozygous factor V Leiden mutation was disclosed by molecular analysis.

COMMENT

Occlusion of the retinal artery is more rarely encountered in younger than in older patients.⁶ Multiple causes of arterial occlusion in the retina were described. In a recent report, the causes of retinal arterial occlusions in 21 young adults were analysed.⁷ Emboli were identified in 33% of the patients. Cardiac valvular disease, including atrial myxoma, bacterial endocarditis, and mitral valve vegetation due to lupus anticoagulant, was the mainly recognised condition and was present in 19% of the patients. Other associated risk factors for cerebrovascular occlusion such as cigarette smoking, oral contraceptive use, obesity, pregnancy, and Behçet's disease were found in 91% of the patients. Antithrombin III, protein S, or protein C deficiencies are hypercoagulable conditions that can lead to recurrent venous or arterial thrombotic events.⁸ Protein S deficiency was associated with a case of bilateral branch retinal artery occlusion.⁹ This biological abnormality was detected in only one young woman with diabetes mellitus and pregnancy in the series of Greven *et al.*⁷ Antiphospholipid antibody syndromes are thrombophilic factors that occur in patients with either lupus anticoagulants or antibodies to anticardiolipin or dissociated syphilis serology. Antiphospholipid antibodies can lead to recurrent arterial and/or venous thrombosis.¹⁰

APC resistance is clearly related to venous thromboembolism.² A recent report suggests the possible role of APC resistance in arterial thrombosis.⁵ APC resistance was not searched for as a thrombophilic factor in retinal arterial occlusions in young adults. In our case, the cause of retinal arterial occlusion could be attributed to the heterozygous mutation of factor V. Owing to the severity of retinal arterial occlusion, long term oral anticoagulant treatment was proposed in our patient for secondary prevention of thrombosis. APC resistance should be considered in patients with retinal arterial occlusion when the usual embolic or thrombotic diseases are ruled out.

STÉPHANE VIGNES
BERTRAND WECHSLER

Service de Médecine Interne,
Hôpital de la Pitié-Salpêtrière,
47-83 Boulevard de l'Hôpital, 75651 Paris Cedex 13

CLAUDE ELMALEH
Service d'Ophthalmologie, Hôpital Hôtel-Dieu,
1 place du Parvis de Notre Dame,
75181 Paris Cedex 04

NATHALIE CASSOUX
Service d'Ophthalmologie,
Hôpital de la Pitié-Salpêtrière,
47-83 Boulevard de l'Hôpital, 75651 Paris Cedex 13

MARIE HÉLÈNE HORELLOU
Laboratoire Central d'Hématologie,
Hôpital Hôtel-Dieu,
1 Place du Parvis de Notre Dame,
75181 Paris Cedex 04

PIERRE GODEAU
Service de Médecine Interne,
Hôpital de la Pitié-Salpêtrière,
47-83 Boulevard de l'Hôpital, 75651 Paris Cedex 13

Correspondence to: B Wechsler, Service de Médecine Interne, Hôpital de la Pitié-Salpêtrière, 47-83 Boulevard de l'Hôpital, 75651 Paris Cedex 13, France.

Accepted for publication 13 September 1996

- 1 Dahlbäck B. Physiological anticoagulation: resistance to activated protein C and venous thromboembolism. *J Clin Invest* 1994;94:923-7.
- 2 Svensson PJ, Dahlbäck B. Resistance to activated protein C as basis for venous thrombosis. *N Engl J Med* 1994;330:517-22.
- 3 Zöller B, Dahlbäck B. Linkage between inherited resistance to activated protein C and factor V mutation in venous thrombosis. *Lancet* 1994; 343:1536-83.
- 4 Dhôte R, Bachmeyer C, Horellou MH, Toulon P, Christoforov B. Central retinal vein thrombosis associated with resistance to activated protein C. *Am J Ophthalmol* 1995;120:388-9.
- 5 Simioni P, de Ronde H, Prandoni P, Saladini M, Bertina RM, Girolami A. Ischemic stroke in young patients with activated protein C resistance. *Stroke* 1995;26:885-90.
- 6 Brown GC, Magargal LE, Shields JA, Goldberg RE, Walsh PN. Retinal arterial obstruction in children and young adults. *Ophthalmology* 1981; 88:18-25.
- 7 Greven CM, Slusher MM, Weaver RG. Retinal arterial occlusions in young adults. *Am J Ophthalmol* 1995;120:776-83.
- 8 Israel SJ, Seshia SS. Childhood stroke associated with protein C or S deficiency. *J Pediatr* 1987;111:562-4.
- 9 Greven CM, Weaver RG, Owen J, Slusher MM. Protein S deficiency and bilateral branch retinal artery occlusion. *Ophthalmology* 1991;98:33-4.
- 10 Love PE, Santoro SA. Antiphospholipid antibodies: anticardiolipin and the lupus anticoagulant in systemic lupus erythematosus (SLE) and in non-SLE disorders. Prevalence and clinical significance. *Ann Intern Med* 1990;112:682-98.

Recurrent septic retinal emboli following dental surgery

EDITOR.—Metastatic bacterial endophthalmitis following head and neck surgery is rare.¹⁻³ To our knowledge, no case of recurrent septic retinal emboli with a presumed dental source has been described before.

CASE REPORT

A healthy 36-year-old white man presented to a dental surgeon with a localised periapical abscess at his right upper first molar, which was confirmed by dental x ray. A volume of 0.2 ml of pus was drained after local periapical infiltration with 2% lignocaine 1 ml with adrenaline 1:80 000 and postoperative irrigation with 0.01% dexamethasone solution. He was prescribed oral amoxycillin/clavulanic acid 375 mg three times daily but did not start antibiotics until 12 hours after the procedure. Three days later, the patient noted sudden blurring of vision and floaters in his right eye but was systemically well.

There was no previous ocular history and the medical history was negative for intravenous drug use, rheumatic fever, or other cardiac disease. He had no risk factors to suggest systemic immunosuppression. General examination was unremarkable and, significantly, he was afebrile with no cardiac signs or peripheral stigmata of infective endocarditis. Uncorrected visual acuity was 6/5 in both eyes and there was no relative afferent

pupillary defect. Anterior segment examination was normal. Funduscopy revealed multiple white emboli in branches of the right inferotemporal retinal artery with superficial retinal haemorrhage and macular oedema (Fig 1). There were also smaller emboli in the left inferonasal, inferotemporal, and superonasal retinal arteries (Fig 2). Vitreous cells 1+ were noted in both eyes. This appearance was consistent with bilateral septic retinal emboli.

Fluorescein angiography showed hypofluorescence at and distal to the right intra-arterial emboli with normal choroidal fluorescence and a normal angiogram appearance in the left eye. The white blood cell count was 10.3 with a normal differential and his erythrocyte sedimentation rate was 2 mm in the first hour. Serial blood cultures produced no growth and a gingival swab produced normal flora.

Electrocardiography, transthoracic echocardiography, and a carotid duplex scan were normal. Fasting total cholesterol and triglycerides were mildly elevated at 6.1 and 2.89 mmol/l (upper limits of normal 5.8 and 1.8 mmol/l) respectively. Coagulation studies and plasma viscosity were normal. Values for anti-nuclear antibody, anticardiolipin antibodies, activated protein C resistance, antithrombin III, protein C, and protein S were all normal. No other infective source was found and he was started empirically on cefuroxime 750 mg intravenously three times daily, metronidazole 500 mg intravenously three times daily, hydrocortisone 100 mg intravenously four times daily, and aspirin 300 mg orally daily. There was little change in the fundal appearance over the next few days but visual acuity remained good at 6/5 in both eyes.

On discharge, on the fourth day, he was converted to oral antibiotics and steroids for a further 2 weeks. At a 1 week follow up visit, there was reduced vitreous activity which

resolved at 2 weeks and the emboli appeared a little smaller. Two months later, he underwent extraction of his previously abscessed tooth under periapical local anaesthetic having started oral amoxycillin/clavulanic acid and metronidazole 3 days earlier for 1 week.

Three weeks afterwards, he presented with fresh bilateral white intra-arterial septic retinal emboli and bilateral vitreous cells 2+. Blood cultures were negative and there was no clinical evidence of infective endocarditis. Repeat haematological investigations were normal. CD4 count was normal and cytomegalovirus titres were negative. His symptoms settled and the emboli reduced in size after 5 days of cefuroxime 750 mg intravenously three times daily and metronidazole 500 mg intravenously three times daily, which was continued orally for a further 2 weeks. Oral aspirin therapy was commenced. He presented 1 month later, while on aspirin, with renewed vitreous activity and right inferotemporal and superotemporal retinal arterial emboli. He was given intravenous cefuroxime and metronidazole for 7 days converting to oral therapy for a further 2 weeks. Oral anticoagulants were started and he had no further episodes. Seven months later, visual acuity remains at 6/5 in both eyes but small white intra-arterial emboli persist with distal luminal narrowing and pallor.

COMMENT

Focal metastatic endophthalmitis with discrete retinal septic emboli is a very rare complication of dental surgery.^{1,2} The clinical appearance in this patient and subsequent partial resolution following intravenous antibiotics implicate infective emboli. The dental origin of sepsis in this patient was presumed as each episode occurred within 1, 3, and 7 weeks of dental surgery on an infected tooth and no other focus was found. The initial episode may have been due to an initial transient bacteraemia or possibly paradoxical embolism but the subsequent delayed episodes may have been of cardiac origin. A normal transthoracic echocardiogram cannot completely rule out the possibility of an intracardiac communication allowing right to left shunting and paradoxical embolism.⁴

The third episode of acute septic emboli occurred 7 weeks after dental extraction and may be due to subclinical infective endocarditis despite negative investigations. Each episode was treated with 1 week or less of intravenous antibiotics which may have been insufficient. Transient bacteraemia following dental surgery has been reported to occur in 15–55% of cases,⁵ the most common organism being viridans streptococci.⁶ Amoxycillin is regarded as the most appropriate antibiotic prophylaxis for patients at risk for infective endocarditis after dental surgery.⁷ However, prophylactic administration of amoxycillin does not reduce the incidence of postextraction bacteraemia⁸ and may not affect bacterial cardiac adherence.

Despite amoxycillin prophylaxis in this otherwise healthy patient, septic retinal emboli developed 3 weeks after the dental procedure. Focal metastatic endophthalmitis, if treated with appropriate antibiotics, has an excellent prognosis with minor permanent ocular changes.⁹ Our patient maintained an excellent visual acuity of 6/5 in both eyes but scotomata persisted corresponding to ischaemic retina distal to the arterial emboli despite appropriate antibiotic therapy. Despite the lack of supporting evidence, the possibility of subclinical infective endocarditis cannot be excluded to

account for recurrent septic retinal emboli following dental surgery in this patient.

D J KILMARTIN
P BARRY

Research Foundation, Royal Victoria Eye and Ear Hospital, Dublin, Ireland

Correspondence to: Mr D J Kilmartin, Department of Ophthalmology, Aberdeen Royal Infirmary, Foresterhill, Aberdeen AB9 2ZD.

Accepted for publication 27 August 1996

- 1 May DR, Peyman GA, Raichand M, Friedman E. Metastatic endophthalmitis after a dental procedure. *Am J Ophthalmol* 1978;85:662–5.
- 2 King LP, Libby C, Coats DK, Lee WH 3d. Presumed septic emboli following dental extraction. *Graefes Arch Clin Exp Ophthalmol* 1993; 231:667–8.
- 3 Weinberg RS, Dorfman MS. Vitritis as the initial presentation of bacterial endocarditis. In: Der-nouchamps JP, Verougstraete C, Caspers-Velu L, Tassinon MJ, eds. *Recent advances in uveitis*. Amsterdam: Kugler Publications, 1993:29–30.
- 4 Konstadt SN, Louie EK. Echocardiographic diagnosis of paradoxical embolism and the potential for right to left shunting. *Am J Cardiac Imaging* 1994;8:28–38.
- 5 Bayliss R, Clarke C, Oakley C, Sommerville W, Whitfield AG. The teeth and endocarditis. *Br Heart J* 1983;50:506–12.
- 6 Knox KW, Hunter N. The role of oral bacteria in the pathogenesis of infective endocarditis. *Aust Dent J* 1991;36:286–92.
- 7 Leport C, Horstkotte D, Burckhardt D. Antibiotic prophylaxis for infective endocarditis from an international group of experts towards a European consensus. Group of Experts of the International Society for Chemotherapy. *Eur Heart J* 1995;16 (Suppl B):126–31.
- 8 Hall G, Hedstrom SA, Heimdahl A, Nord CE. Prophylactic administration of penicillins for endocarditis does not reduce the incidence of postextraction bacteremia. *Clin Infect Dis* 1993; 17:188–94.
- 9 Greenwald MJ, Whol LG, Sell CH. Metastatic bacterial endophthalmitis: a contemporary appraisal. *Surv Ophthalmol* 1986;31:81–101.

An unusual corneal injury

EDITOR.—Most thermal injuries to the cornea are superficial and tend to heal rapidly^{1,2} but deeper sight threatening burns may occur when extended contact between the heat source and the cornea occurs.³ New methods of demolition using an exothermic chemical reaction to crack stone and reinforced concrete are becoming increasingly popular. We present a man who sustained severe bilateral thermal corneal burns following exposure to such a chemical.

CASE PRESENTATION

Mr JP presented with bilateral corneal injuries and hand movement vision in both eyes. One hour earlier a tube of 'Betonamit' had exploded into his face.

Betonamit, a 'non-explosive' cracking agent is a mixture of calcium oxide, silicon oxide, aluminium oxide, and magnesium oxide, which when hydrated forms calcium hydroxide in an exothermic reaction. During normal use it is mixed with water and poured into drill holes of specific depth and diameter. The substance then expands and pressures of up to 9000 tonnes/m² develop, fracturing the surrounding concrete/stone.

The patient had dense white corneal opacities in both eyes with lacunae of transparent healthy cornea (Fig 1). Similarly, there were multiple patches of pale conjunctiva. The face and lids were unharmed. He immediately underwent ocular irrigation and particulate material was removed from the fornices. The pH was not lowered; nevertheless, the initial clinical impression was of severe bilateral

Figure 1 White emboli in branches of the right inferotemporal retinal artery with macular oedema and superficial retinal haemorrhage at first presentation.

Figure 2 Close inspection revealed small white emboli in branches of the left inferonasal, inferotemporal, and superonasal retinal arteries at initial presentation.