the distribution of the facial angioma. Tallman *et al*.[5] found that all patients who had glaucoma and/or CNS complications had facial angioma involving the eyelids. In 9% only the lower lid was involved, i.e. over the area of distribution of the mandibular branch of the trigeminal nerve (V2). In 91% of cases both the upper and lower lid were involved (V1 and V2 distribution, respectively).

Although studies of SWS suggest that glaucoma usually presents early in life, we believe that late onset glaucoma in association with isolated facial angioma may be more common than realised. An explanation may be bias in screening, as patients with SWS may be more likely to be screened for glaucoma. Furthermore, isolated facial angioma may represent a different clinical entity compared with SWS and therefore the age of presentation of glaucoma may also differ. However, to date there have been no studies looking at the age of presentation of glaucoma in isolated facial angioma. Since neither of our patients had any CNS symptoms, and in view of their age, we felt that neuroradiological investigations were not indicated. Classical SWS, although unlikely, cannot be excluded. Nevertheless we believe that all patients with isolated ipsilateral facial angioma, especially if involving the V1 or V2 dermatome, should be screened regularly for glaucoma. Since glaucoma may develop at any age, as reflected in both our cases, regular examination should be performed indefinitely. The diagnosis of SWS should also be considered and appropriate neurological investigations performed if necessary.

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Sir,

Expression of placenta growth factor (PIGF) in ischaemic retinal diseases

Intraocular angiogenesis in ischaemic retinal diseases after retinal vascular closure, which includes proliferative diabetic retinopathy (PDR), retinal vein occlusion and others, is caused by vascular endothelial growth factor (VEGF). VEGF is a homodimeric peptide growth factor, and is induced by retinal hypoxia as a result of retinal vascular closure.[1,2] Other growth factors have been shown to contribute to VEGF-induced angiogenesis.[3] Placenta growth factor (PIGF), a member of the VEGF family, forms homodimers, binds to flt-1 (a VEGF receptor) and stimulates angiogenesis.[4,5] PIGF stimulates proliferation and migration of vascular endothelial cells, and induces angiogenesis *in vivo*, which is very similar to the functions of VEGF.[4,5] However, PIGF homodimers are not so effective as VEGF in the induction of angiogenesis *in vivo*.[6] PIGF also forms heterodimers with VEGF which activate the other VEGF receptor (KDR/flk-1) and induce angiogenesis more effectively than PIGF homodimers.[6,7] The physiological functions *in vivo* of PIGF have not been clarified. Based on the results of *in vitro* and *in vivo* studies, PIGF is suggested to potentiate the action of VEGF at low concentrations.[4] PIGF has recently been reported to be expressed in eyes with PDR.[5] In this study, we observed the expression of PIGF in eyes with ischaemic retinal diseases and investigated the correlation between PIGF and retinal diseases.

Subjects and methods

We obtained 58 aqueous or vitreous samples from 56 eyes of 56 patients during cataract or vitreous surgery after securing permission from the patients, who were fully informed of the nature of the procedures performed during the surgery. The procedures were performed in accordance with the Helsinki Declaration of 1975, as revised in 1983. Aqueous humour was obtained from 3 eyes with PDR, 5 eyes with background diabetic retinopathy, 2 eyes with non-diabetic ischaemic retinopathy (branch retinal vein occlusion) and 26 eyes without retinal ischaemia (cataract, glaucoma). Vitreous specimens were obtained from 11 eyes with PDR, 2 eyes with non-diabetic ischaemic retinopathy (central retinal vein occlusion, acute retinal necrosis) and 7 eyes without retinal ischaemia. Retinal ischaemia was diagnosed as the status of retinal vascular closure by fluorescein angiography before and/or after the operations.

The concentrations of PIGF and VEGF were measured with ELISA kits (R&D System, MN, USA) according to the manufacturer's protocol.[8] The correlation among the concentration of PIGF, the concentration of VEGF, and clinical backgrounds (age, blood glucose control, nephropathy, grade of diabetic retinopathy, retinal photocoagulation, previous ocular surgery) was investigated statistically by multivariate regression

analysis using the logistic model. Selection of factors relevant to the concentration of PIGF was performed by the stepwise method.

Results

Among 36 aqueous samples, PIGF was detected in only one sample of the eye with severe PDR at a very high concentration (2270 pg/ml). PIGF was not detectable in any other aqueous samples. The mean concentration of PIGF in 13 vitreous samples from 11 eyes with PDR was 360 ± 272 (standard error of the mean, SEM) pg/ml. (Two samples were obtained from each of 2 eyes in the repeated operations.) The concentration of PIGF was also high in the 2 eyes with non-diabetic ischaemic retinopathy (224 pg/ml and 691 pg/ml), with a mean concentration of 458 pg/ml. PIGF was not detected in the eyes without ischaemia. The concentration of PIGF was significantly correlated with that of VEGF (n = 19, R = 0.526, p = 0.019) (Fig. 1). Multivariate regression analysis revealed that the concentration of PIGF was significantly correlated with the concentration of VEGF (standard partial regression coefficient = 0.48), age (−0.55) and photocoagulation (0.43) (R = 0.76, p = 0.0037). In summary, PIGF was detected in eyes with ischaemic retinal diseases, including PDR, retinal vein occlusion and acute retinal necrosis. In addition, the concentration of PIGF was significantly correlated with the concentration of VEGF in these samples.

Comments

The results of the present study show that PIGF in the vitreous humour is correlated with retinal hypoxia, which also induces VEGF. The concentration of PIGF in the aqueous humour was very low, but that in the vitreous humour was high enough to be detected. This observation corresponds to the report that the concentration of VEGF in the vitreous humour was higher than that in the aqueous humour, and suggests that PIGF was produced mainly from retina and diffused from vitreous to anterior chamber.[9] These speculations remain to be confirmed because we did not measure the concentrations of PIGF in the aqueous and vitreous humour from the same patients simultaneously. PIGF is reported to be less effective than VEGF in inducing the mitogenic activity of vascular endothelial cells and in the induction of an increase in vascular permeability.[4] The present study did not support the possibility that the homodimer of PIGF is one of the *bona fide* angiogenic factors in diabetic retinopathy or other ischaemic retinopathies because its concentration was low. According to previous reports, we can propose three possibilities concerning the functions of PIGF in the pathogenesis of ocular angiogenesis: (1) PIGF potentiates the functions of VEGF at low concentration,[4] so angiogenic activity is accelerated by the simultaneous expression of PIGF and VEGF. (2) If heterodimers of PIGF and VEGF are formed in eyes with ischaemic retinal diseases, the heterodimers may accelerate angiogenesis.[6] (3) PIGF may function through flt-1 receptors to recruit macrophages in the pathogenesis of proliferative vitreoretinopathy.[10,11] Further studies are necessary to clarify the clinical significance of PIGF.

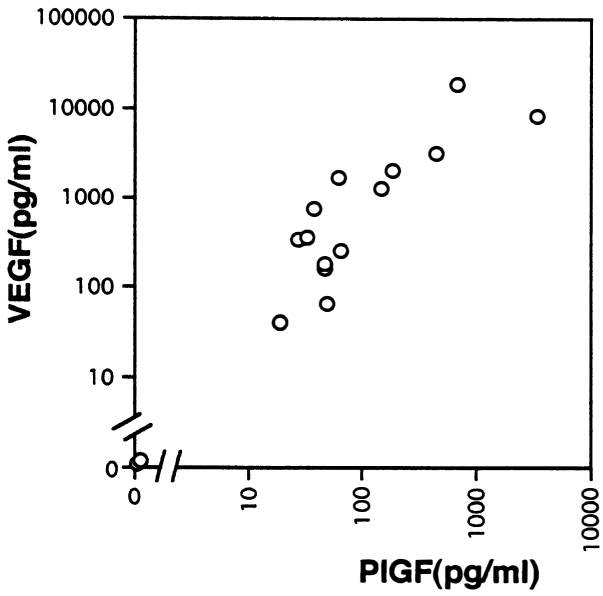

Fig. 1. *Correlation between concentrations of PIGF and VEGF. The zero level of PIGF and VEGF shows the level below detection.* (n = *19, correlation coefficient = 0.526,* p = *0.019.)*

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Sir,

Central retinal artery occlusion and bilateral choroidal infarcts in Wegener's granulomatosis

Up to 77% of patients with Wegener's granulomatosis (WG) develop ocular manifestations during the course of their disease. However, clinically identifiable retinal involvement is rare and only three cases of central retinal artery occlusion (CRAO) occurring in patients with WG have been reported. We describe the case of a patient with WG who developed unilateral CRAO associated with bilateral choroidal infarcts.

Case report

A 58-year-old Caucasian man presented to a respiratory clinic with a 10 month history of productive cough with dyspnoea on exertion. He had general malaise with poor appetite and weight loss, night sweats and arthralgia. He had been attending an ENT clinic with symptoms of stuffy nose, postnasal drip and decreased hearing in his left ear. He had a strong family history of lung cancer and also had contracted tuberculosis as a child.

General examination was normal. Investigations revealed a leucocytosis, ESR 94 mm/h and a high CRP (464 mg/l). Chest radiograph showed a prominent right hilum and small right pleural effusion. A differential diagnosis of bronchial carcinoma and tuberculosis was considered. Sputum samples for AFB were negative. A week later he was admitted to hospital with a 3 day history of forgetfulness, disorientation, slurred speech and painless loss of vision in the left eye. Apart from slight ataxia there were no abnormal neurological signs. No focal endobronchial lesion was evident on bronchoscopy but the mucosa was congested and the biopsy revealed ulceration with non-specific granulomatous inflammation with no suggestion of malignancy.

Vision was 6/9 in the right eye, and hand movements in the left eye. A left relative afferent pupillary defect was present. Orbits and anterior segments were normal with clear vitreous in both eyes. Fundoscopy of the left eye showed attenuated arterioles, a pale oedematous retina, and a cherry-red spot at the fovea. In the right eye multiple, discrete, round, yellow-white, choroidal lesions were scattered around the posterior pole. The lesions in the left eye showed gradual resolution of the retinal oedema to reveal discrete lesions similar to those present in the right eye (Fig. 1). The fundus lesions regressed to leave atrophic pigmented areas, with the vision remaining unchanged during follow-up. Fundus fluorescein angiography showed blocking of choroidal fluorescence during the early phase, with little filling even in the mid- or late phase. As the disease resolved, angiography demonstrated staining of these lesions with alteration in background fluorescence due to changes in the pigment epithelium (Fig. 2). These findings were consistent with a left CRAO and bilateral choroidal infarcts.

Considering the ocular and bronchoscopic findings with repeatedly negative sputum samples, tuberculosis and bronchial carcinoma were unlikely. Serology for cANCA was positive to a 1:80 dilution and blood urea was 11.2 mmol/l with normal serum electrolytes. A CT scan of the chest demonstrated multiple cavitating nodules in both lungs, a right pleural effusion and right

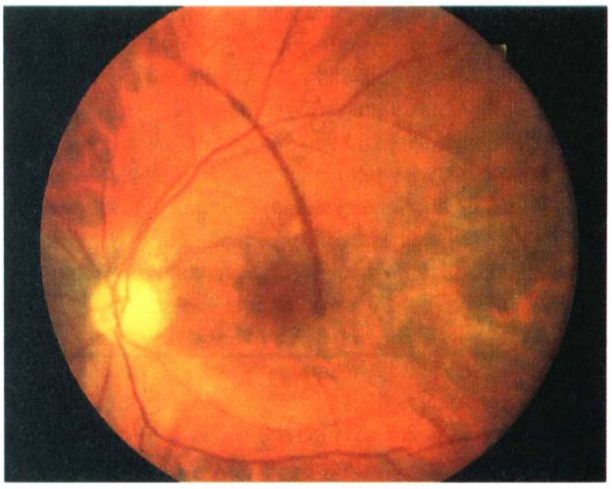

Fig. 1. *The left eye showing the pale optic disc and discrete choroidal lesions with alteration in the retinal pigment epithelium at the posterior pole.*