Positive correlation between vitreous levels of advanced glycation end products and vascular endothelial growth factor in patients with diabetic retinopathy sufficiently treated with photocoagulation

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We investigated whether vitreous levels of advanced glycation end products (AGEs) were positively correlated with vascular endothelial growth factor (VEGF) in patients with diabetic retinopathy sufficiently treated with photocoagulation. Vitreous AGE and VEGF levels were significantly higher in patients with diabetes than in controls. Positive correlation between AGE and VEGF was found in patients with diabetic retinopathy sufficiently treated with photocoagulation (r = 0.44, p < 0.05), but not in those who were insufficiently treated (r = 0.26, p = 0.18). The present observations suggest that AGE may induce VEGF expression in an ischaemia-independent mechanism. AGE could be one of the important determinants of VEGF in diabetic retinopathy without obvious ischaemic regions.

References

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Background
Vascular endothelial growth factor (VEGF) elicits retinal vascular hyperpermeability, thrombosis and angiogenesis, having a central role in the pathogenesis of diabetic retinopathy. Furthermore, vitreous VEGF levels are increased in proliferative diabetic retinopathy, whereas the levels are decreased after treatment with panretinal photocoagulation (PRP). These observations suggest that retinal ischaemia and resultant hypoxia could mainly contribute to VEGF induction in diabetic retinopathy.

Advanced glycation end products (AGEs), senescent macroprotein derivatives formed at an accelerated rate under diabetes, also stimulate VEGF expression in cell cultures and animal models. In addition, vitreous AGE levels are positively correlated with VEGF in patients with diabetic retinopathy, suggesting that AGEs may be a stimulant of VEGF in vivo. However, as AGEs predispose the retinal vessels to thrombogenesis, whether AGEs could induce VEGF expression in an ischaemia-independent manner remains unknown.

Therefore, in this study, we determined the relationship between vitreous levels of AGEs and VEGF in patients with diabetic retinopathy who were sufficiently treated with PRP for controlling retinal ischaemia.
positive correlation between vitreous AGEs and VEGF levels disappeared when retinal ischaemia was not sufficiently controlled. Therefore, with the progress of diabetic retinopathy, retinal ischaemia and subsequent hypoxia may become a major determinant of VEGF.

Our findings suggest that inhibition of AGE may become a major determinant of VEGF.

References


Postoperative subconjunctival 5-fluorouracil in the management of recurring pterygium

The treatment of choice for pterygium is surgical excision. Recurrence is the most common undesirable treatment outcome. Surgery and other modalities of treatment including β-irradiation, topical thiotepa, intraoperative and postoperative use of mitomycin C, 5-fluorouracil (5-FU) and daunorubicin, have been described to reduce recurrence. Multiple surgery is itself a risk factor for recurrence. We present a case in which the fourth surgery for recurrent pterygium resulted in further recurrence, which was thwarted by multiple intralesional injections of 5-FU.

Case report

A 34-year-old Afro-Caribbean woman was referred to us in October 2004 for the management of recurrent pterygium in the right eye. She had two previous surgeries, the first in 2002 with conjunctival autograft and the second in 2003 leaving behind bare sclera. A third attempt at removal in 2004 was aborted owing to excessive intraoperative bleeding. Her unaided visual acuity was 6/9 right eye and 6/6 left eye. The right eye showed a highly vascularised, fleshy nasal pterygium measuring 8 mm × 8 mm. It had encroached 2.5 mm into the cornea. At this point, subconjunctival injection of 5-FU even at large doses seems to be safe, effective and well tolerated by the eye. Such an intervention should be considered as an option in the management of difficult cases of recurrent pterygium.

Comment

Pterygium recurrence is thought to be due to fibroblast proliferation and migration and hence use of 5FU, which inhibits fibroblastic activity, is believed to reduce recurrence rates. 5-FU is toxic only to proliferating cells and is considered to be safer than other agents. Postoperative use of 5-FU to halt the progression of recurrence has been described before, but involved a maximum of four injections with a maximum dose of 3 mg. Our patient received 10 injections totalling 50 mg of 5-FU with no complications.

In cases with a high risk of recurrence, such as the one described, intralesional subconjunctival injection of 5-FU even at large doses seems to be safe, effective and well tolerated by the eye. Such an intervention should be considered as an option in the management of difficult cases of recurrent pterygium.

Figure 1 (A) Anterior segment photograph showing the fleshy recurrent pterygium before the third excision. (B) Photograph showing conjunctival recurrence of the pterygium 2 months after the third excision with intraoperative mitomycin C and amniotic membrane. (C) Photograph showing progression of recurrence and encroachment into the cornea. (D) Photograph showing appearance of the pterygium 8 months after the tenth 5-fluorouracil injection. Informed consent was obtained for publication of this figure.