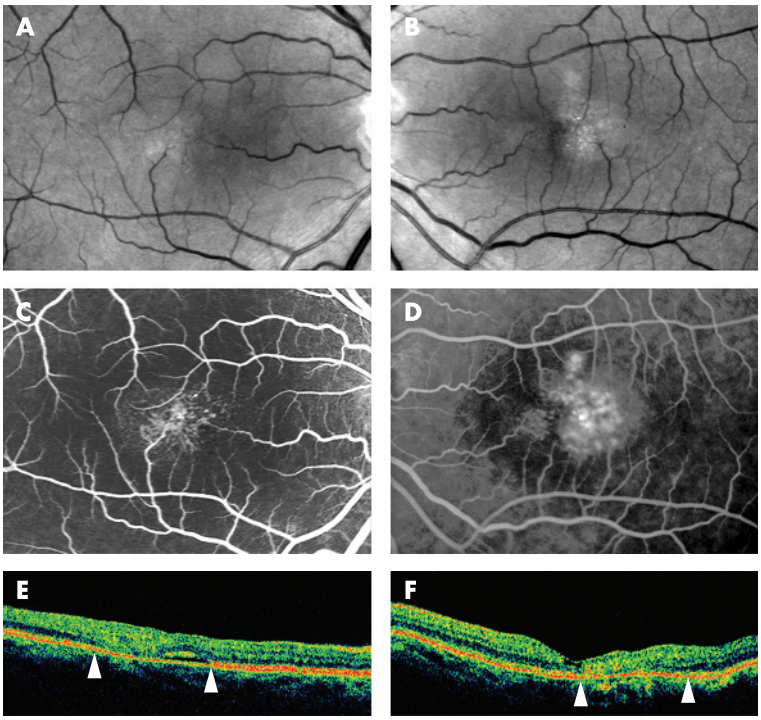

Figure 2 Case 2. A 59-year-old female with idiopathic parafoveolar telangiectasis and obliteration of the foveal avascular zone. Red-free photograph (A, right eye, B, left eye) demonstrated telangiectatic capillaries, intraretinal refractile deposits, right-angle venules and loss of macular transparency. Fluorescein angiography (C, right eye, D, left eye) revealed a deep layer of telangiectatic capillaries invading into the expected region of the foveal avascular zone. Optical coherence tomography, taken horizontally, demonstrated hyper-reflectivity of the outer nuclear layer in the macula and a break of the boundary between photoreceptor inner and outer segments bilaterally (E, F, between arrowheads), a loss of the foveal depression and subretinal fluid in the central fovea of the right eye (E) and an inner foveal cavitation in the left eye (F).

segments as a characteristic OCT finding in IPT.[8 9] Interestingly, experimental disruption of Muller cell metabolism induces photoreceptor dysmorphogenesis.[10] Although speculative, Muller cell abnormalities may secondarily affect photoreceptors in eyes with IPT, leading to the deep capillary proliferation.

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Expression of hypoxia-inducible factor 1α and 2α in choroidal neovascular membranes associated with age-related macular degeneration

Hypoxia-inducible factors (HIF-1α and HIF-2α) play pivotal roles in angiogenesis. However, their involvement in choroidal neovascular membranes (CNVMs) is still unknown. This study investigates the distribution of HIF-1α and HIF-2α proteins in six CNVMs associated with age-related macular degeneration (AMD). By means of immunohistochemical analysis, HIF-1α and HIF-2α were detected in 5 and 6 eyes, respectively. Endothelial cells and macrophages were immunostained by both HIF-1α and HIF-2α antibodies, whereas no staining was observed in retinal pigment epithelial (RPE) cells. Our study raises the possibility that HIF-1α and HIF-2α are involved in CNV formation.

HIF-1α and HIF-2α are transcription factors that transactivate the expression of pro-angiogenic genes in response to hypoxic conditions, and play important roles in vasculogenesis and angiogenesis.[1 2] HIF-1α is increased in ischaemic retina, subsequently upregulating the expression of vascular endothelial growth factor (VEGF).[3] HIF-2α exerts pro-angiogenic functions in retinopathy of prematurity, presumably by upregulating the expression of a potent angiogenic factor, erythropoietin.[4] However, to the best of our knowledge, there has been no study investigating the expression of HIF proteins in human CNVMs. In this study, we performed immunohistochemical analysis to investigate the distribution of HIF proteins in CNVMs.

Specimens were obtained from 6 eyes of 6 AMD patients (aged 65–86 years). Informed consent for the use of excised tissue was obtained from all patients. All procedures followed the tenets of the Declaration of Helsinki, and Institutional Review Board approval was obtained for the study. Between January 2003 and September 2004, submacular surgery was performed according to the technique described previously.[5] Fluorescein angiography was used to classify the CNV type.[6] Clinical characteristics of all patients are presented in table 1.

Table 1 Clinical characteristics

Eye	Age	Sex	Affected eye	CNV type[6] classification	CNVM size*
1	80	M	R	Classic	1.5
2	79	F	L	Predominantly classic	0.8
3	79	F	L	Classic	1.5
4	65	M	L	Classic	1.0
5	86	M	R	Classic	1.3
6	83	F	L	Classic	1.0

M, Male; F, Female; R, right; L, left
CNV, choroidal neovascularization; CNVM, choroidal neovascular membrane
*in disc diameter

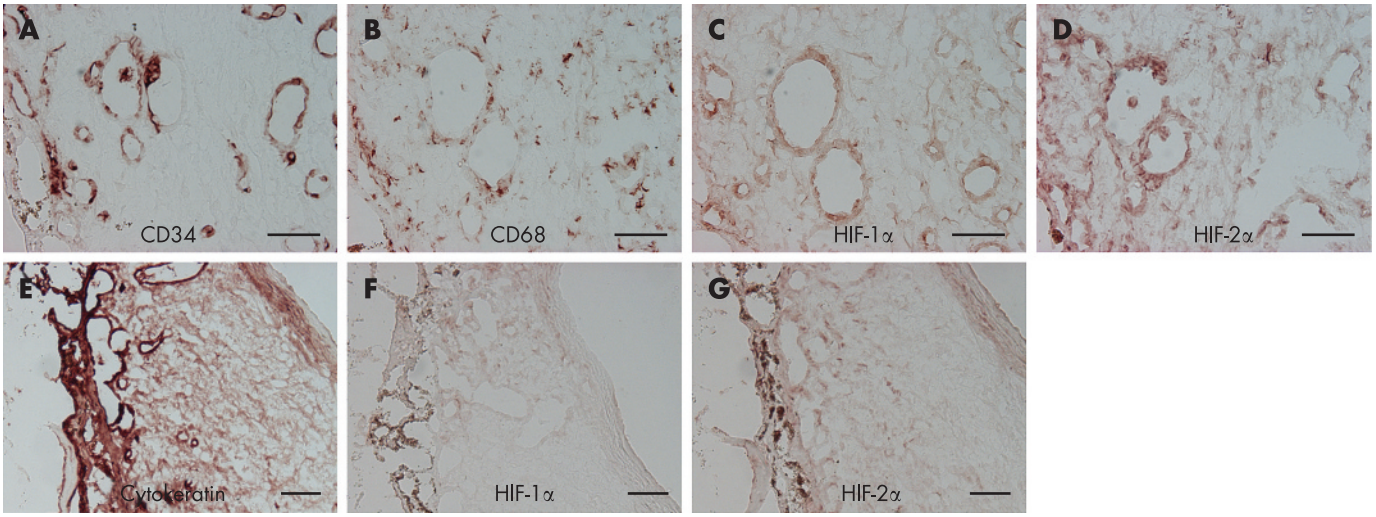

Figure 1 Immunostaining of CNVMs by cell-specific marker and HIF. Immunostaining was performed to confirm the cellular source of expression for HIF-1α and HIF-2α. (A–D) Serial sections were immunostained by CD34, CD68, HIF-1α and HIF-2α. The vascular endothelium cells were stained by CD34 (A), and some of the endothelial cells were stained by HIF-1α and similarly by HIF-2α. (C and D) Macrophages, identified by immunostaining of CD68 (B), were detected abundantly in all CNVMs and were located uniformly in stroma. Most of the macrophages that were immunostained were immunoreactive to HIF-1α and HIF-2α (C and D). A partially intact monolayer of retinal pigment epithelium (RPE) cells located on one side of the CNVMs was immunostained by pancytokeratin (E). However, no overlap was observed with HIFs staining (F and G) and RPE cells. Scale bars, 50 μm.

Each CNVM specimen was immediately embedded in OCT compound (O.C.T. Compound; Sakura Finetek Co., Ltd., Tokyo, Japan), rapidly frozen and prepared for avidin-Biotin complex immunohistochemistry (VECTASTAIN ABC kit, Vector Laboratories, Burlingane, CA).

HIF-1α and HIF-2α were detected in 5 and 6 eyes of 6 eyes, respectively, as revealed by immunolabelling with anti-HIF-1α and anti-HIF-2α antibody (Novus Biologicals, Littleton, CO). Neovascular vessels immunostained by CD34 (Biomeda, Foaster, CA) were detected in all CNVMs and located in stroma, and half of the endothelial cells were immunostained by both HIF proteins (fig 1A-B). CD68-positive (Ylem, Roma, Italy) macrophages were located uniformly in stroma in all CNVMs and almost all macrophages were stained with both HIF antibodies (fig 1C-D). All specimens contained a partially intact monolayer of RPE cells located on one side of the CNVMs and immunostained by pancytokeratin (Sigma, St. Louis, MO) (fig 1E-F). No overlap was observed with HIF proteins and RPE cells (fig 1E-F). The distribution pattern of HIF-1α and HIF-2α in the CNVMs was similar in all specimens.

In summary, HIF-1α and HIF-2α are detected in the endothelium and macrophages. The HIF transcription factors activate the expression of the *VEGF* gene in response to hypoxic conditions. VEGF, in turn, induces angiogenesis.[7 8] RPE cells, endothelial cells and macrophages are VEGF-positive in CNVMs from AMD patients,[9 10] suggesting that VEGF is involved in CNVM formation.[10] Our results, together with previous results, may indicate that HIFs in endothelial cells induce VEGF, thereby contributing to the development of CNVM. In the current study, however, expression of HIF proteins was not detectable in RPE cells, raising the possibility that other mechanisms are involved in the production of VEGF in these cells. Further studies are needed to explore the possible causal relationship between hypoxia and the expressions of HIF proteins.

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'Ab interno' intravitreal suturing of a large traumatic scleral perforation at the posterior pole

Closure of scleral perforations after trauma is frequently achieved by external suturing. Enlarged perforations towards the equator may require temporary removal of the external ocular muscle to visualise and fix the scleral wound.[1] *Nakashizuka et al.* attached 'ab interno' a dislocated intraocular lens by introducing a 10–0 polypropylen loop, held by an intraocular forceps, into the vitreous cavity through a sclerotomy.[2] Here, we describe the 'ab interno' intravitreal suturing of a large traumatic posterior scleral perforation at the posterior pole.

A 34-year-old patient presented with a paracentral corneal perforation, collapse of the anterior chamber and severe vitreous haemorrhage OD. The patient's visual acuity was light perception. The patient was treated in a two-step fashion according to Kuhn *et al.*[3] A primary corneal wound closure and placement of a mild scleral buckle was immediately performed, with the application of topical and systemic corticosteroids. The following day, a computed tomography scan was ordered, which showed a 25-mm-length splinter at the posterior pole (fig 1). On day four, we performed a comprehensive reconstruction under general anaesthesia, including a lensectomy and removal of the vitreous haemorrhage by complete three-port vitrectomy. When the pars plana vitrectomy removed the crystalline lens and vitreous haemorrhage, a large metal foreign body, sticking in the posterior bulbus with a consecutive incarceration of the adjacent retina, became evident. After the splinter was removed from the sclera, a