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At 34 years of age, her best-corrected visual acuity remained 20/30, but visual fields had decreased to only a central island. OCT was performed using topographical mapping and longitudinal reflectivity profile (LRP) analyses. Retinal thickness topography in the patient differed dramatically from normal (fig 1A). Especially notable was the abnormally thickened retina along the arcades (fig 1B). A difference map highlights parafocal thinning and patches of thickened superior and inferior retina (fig 1B, inset). Laminar architecture was explored using LRP’s overlaid on cross-sectional images from the fovea into the superior retina (fig 1C,D). The patient had laminated but thinned retina in the parafovea, and, with increasing eccentricity, there was a coarsely laminated and thickened region. At further superior loci, the retina had normal thickness but was delaminated. A more detailed comparison was made of LRP’s at three eccentricities (fig 1E). At the parafoveal locus, thinning could be accounted for by missing retinal layers, specifically loss of photoreceptor wave- form components. At the more superior loci, whether increased in thickness or not, the patient’s retina had no comparable lamination with normal retina.

Comment

The OCT results in this patient with retinitis pigmentosa and PDE6B mutations are complex but interpretable. Parafocal thinning is attributable to rod (and cone) photoreceptor layer losses. The remarkable thickening and loss of normal laminar pattern at further eccentricities is probably an OCT marker for retinal disorganization. Thickened and dysplastic-appearing retina on OCT scans has been previously reported in two early-onset retinal degenerations with a developmental component: one, a form of Leber congenital amaurosis caused by CRB1 mutations, and the other, enhanced S cone syndrome due to NUB2 mutations. The present observations are the first in a form of retinitis pigmentosa. We propose that the results represent in vivo evidence for retinal remodelling, a process involving neuronal loss and migration, glial hypertrophy and abnormal circuitry occurring in reaction to photoreceptor death. Retinal remodelling has been demonstrated using histopathology in postmortem human retinas and in animals with retinal degeneration, including those with PDE6B mutations. Identifying retinal remodelling in human retinal degenerations will be valuable in future clinical trials as a structural criterion to determine the potential for therapeutic benefit.

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Changes in the retinal inner limiting membrane associated with Valsalva retinopathy

Valsalva retinopathy was first described in 1972 by Thomas Duane as “a particular form of retinopathy, pre-retinal and haemorrhagic in nature, secondary to a sudden increase in intraocular pressure.” Incompetent or no valves in the venous system of head and neck allow direct transmission of intraocular or intra-abdominal pressure into the head and neck. Sudden elevation of venous pressure may cause a decompression in the retinal capillary bed, with subinternal limiting membrane haemorrhages (Hg) that rarely may break through and become subhyaloid or intraretinal. We report histopathological findings of internal limiting membrane (ILM) peel in a case of Valsalva retinopathy.

Case report

A 41-year-old Caucasian male was referred to the vitreoretinal services with a spontaneous and sudden loss of vision in left eye for 3 weeks. There was no history of trauma or violent exertion but the patient had hay fever and had frequent episodes of sneezing. On examination his vision was 6/6 and hand movements in right and left eyes, respectively. Anterior segment examination segment exam showed normal media. Dilated fundoscopy revealed a dense vitreous haemorrhage in the left eye and normal fundus appearance in the right eye. Ultrasound echography revealed a posterior vitreous detachment, vitreous haemorrhage and a macular elevation in the left eye. Systemic examination was normal. Laboratory investigations showed normal complete blood count, prothrombin time and activated partial thromboplastin time. Blood pressure and urine analysis were normal. After discussions with the patient, a decision was made to perform a 20-gauge three-port pars plana vitrectomy. Intraoperatively, after core vitrectomy and removal of the vitreous haemorrhage, a sub-ILM haemorrhage typical of Valsalva retinopathy was noted. ILM peel was performed without the assistance of dye, and the excised tissue was processed for histopathological assessment. Postoperatively, 3 months after surgery, the patient’s vision remained stable (6/6 unaided, with no secondary complications).

Histological examination of the excised tissue (fig 1A) revealed that it contained convoluted ILM. The vitreous (smooth) surface of the ILM was free of cellular and a cellular component in the specimen, and this component was on the retinal side (undulated surface) of the ILM (fig 1B). The cellular component included a prominent multilayer aggregate of cells that was immunoreactive for cytoketerin 7 (fig 1C), which is a marker of transdifferentiated retinal pigment epithelial (RPE) cells 4. These cells were negative for glial and neural markers. Nevertheless, glial and neural elements were present elsewhere in the specimen, again on the retinal rather than the vitreous surface of the ILM (fig 1D,E). CD68pg-positive macrophages were scattered throughout the specimen and there was also scattered pigment that was partly intracellular and partly extracellular. Perl’s (Prussian blue) staining confirmed that the pigment was a mix of melanin and haemosiderin (fig 1F).

Discussion

The plane of retinal Hg in Valsalva retinopathy is sometimes difficult to determine, especially in the absence of PVD. Ocular coherence tomography (OCT) has been used to determine the exact location when the vitreous medium is clear and it is generally agreed that it is sub-ILM in location. Following core and posterior vitrectomy, we could confirm that a sub-ILM haemorrhage was present. The Hg was possibly a consequence of the patient’s hay fever-related sneezing that is thought to occur from a sudden rise in the intraocular pressure caused by a forceful exhalation against a closed glottis.

Therapeutic options in Valsalva retinopathy include conservative management, surgery (vitrectomy) and laser membraneotomy. Epiretinal membrane (ERM) formation with ILM wrinkling has been reported 10 months after Nd-YAG membraneotomy of Valsalva Hg. Histological examination of surgically removed ILM revealed the presence of haemosiderin within macrophages on the retinal side of the ILM and a fine glial ERM, resembling possible proliferations on the vitreous surface of the ILM. Our case also revealed haemosiderin on the retinal surface of the ILM, again confirming the sub-ILM location of the haemorrhage, but

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Sections through the excised internal limiting membrane (ILM). (A) Staining with periodic acid Schiff reagent and haematoxylin reveals convoluted ILM with adjacent cells. (B) High-power view of section in (A) to show that the cells are on the undulated (retinal) surface of the ILM (arrows) whereas no cells are seen on the smooth (vitreous) surface (arrowheads). (C) Stained with the immunoperoxidase technique for cytokeratin 7 (red-brown chromogen) and counterstained with haematoxylin; layers of transdifferentiated retinal pigment epithelial (RPE) cells are observed (arrows). Inset: higher magnification demonstrates that the RPE cells are adjacent to the undulated (retinal) surface of the ILM (arrow). (D, E) Sections stained with the immunoperoxidase technique (red-brown chromogen) for the glial marker glial fibrillary acidic protein (D) and the macrophage marker CD68 ppq (E), respectively, and counterstained with haematoxylin. (D) Gial cells are abundant in the tissue but have a distribution different from that of RPE cells (compare with C). (E) Macrophages are more scattered throughout the tissue. (F) A section stained with Perls method reveals iron of presumed blood origin (blue deposit; arrow) as well as melanin pigment (arrowhead).

Instead of an ERM there was a mixed-cell-type proliferation on the retinal surface of the ILM. The sub-ILM cells included trans-differentiated RPE cells, and hence the proliferation had the histological appearances of a proliferative vitreoretinopathy (PVR)-type membrane “beneath” the ILM. Presumably, the RPE cells had been attracted to this location by the sub-ILM blood, since it is well established that RPE cells migrate to various blood components and can move through intact retina.

Intraretinal pathology in PVR is a well-recognised pathological event, but usually the retinal changes resemble gliosis. Our case suggests that focal RPE proliferation, similar to that seen in PVR epiretinal membranes, can occur within the neuroretina, and specifically in a sub-ILM location, by transmigrated RPE cells as a response to intraretinal haemorrhage. Such proliferation might prevent complete visual recovery after reabsorption of the retinal haemorrhage and justify early surgical intervention instead of routine observation or laser membranotomy.

References

Lemon juice and Candida endophthalmitis in crack-cocaine misuse

The Centers for Disease Control and Prevention recently reported that a substantial number of drug misusers in the US are injecting crack cocaine instead of smoking it, owing to the decreased availability and increased cost of powdered cocaine. The use of lemon juice to dissolve crack-cocaine has been shown to cause abscesses, permanent vein damage and infections. Furthermore, heroin dissolved in preserved lemon juice was documented to be a source of Candida albicans in multiple, small epidemics of fungal endophthalmitis in the 1980s in the UK and Australia. We report here two recent cases of fungal endophthalmitis in crack users who similarly disclose dissolving crack-cocaine in lemon juice injection.

Case 1
A 34-year-old male intravenous drug user presented to his primary care physician with high fever and bilateral blurry vision for the past 20 days. Blood cultures and ECG were negative. The patient reported dissolving crack in preserved lemon juice.

His visual acuity was 20/40 OD and 20/70 OS. Dilated fundus examination revealed multiple condensations in the vitreous with choroidal and retinal foci in both eyes. A pars plana vitrectomy was performed OD with intravitreal injections of vancomycin (1 mg/0.1 ml), ceftazidime (2 mg/0.1 ml) and amphotericin B (7.5 μg/0.1 ml). Viscous cultures grew Candida albicans, and the patient was treated with oral diflucan (200 mg daily). The patient received five intravitreal injections of amphotericin B (5 μg/0.1 ml) in the vitrectomised right eye and three in the non-vitrectomised left eye over 3 weeks for persistent active lesions. At the most recent examination, 12 weeks after presentation, the patient’s vision was 20/20 OD and 20/30 OS.

Case 2
A 37-year-old homeless male intravenous drug user reported a 3-month history of decreased vision, eye pain and floaters in his right eye. His medical history was significant for HIV (recent CD4 count of 799 cells/mm³) and hepatitis C. The patient reported the use of preserved lemon juice to dissolve crack-cocaine for injection.

His visual acuity was hand motions OD and 20/20 OS. Dilated fundus examination of the right eye was obscured by 3+ vitritis, but there appeared to be a large infiltrate in the macula. A vitreous aspiration was performed, with intravitreal injections of ceftazidime (2 mg/0.1 ml) and vancomycin (1 mg/0.1 ml) in the right eye. The vitreous aspirate grew C albicans.
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