We thank Dr. Jansonius for his interest and thoughtful comments on our paper (Jung et al. 2013). We investigated the relationship between the tube length and intraocular pressure (IOP) from understanding the Poiseuille’s equation. As a result, the tube length was significantly correlated with final IOP in subgroups with two glaucoma medications. That finding has to be explained in many aspects including cellular and molecular response as well as physical equation. We agree that an increase in IOP per mm increase in tube length is not huge by computing the equation as you calculated. However, Poiseuille’s law definitely supports the direction of the relationship between the tube length and IOP in our study, even though the effect of it is not great. Postoperative IOP may be determined by aqueous flow both through tube and the bleb surrounding the endplate (Schwartz et al. 2006; Minckler et al. 2008). The tube made of silicone can cause cellular response and inflammation in anterior chamber or changes in the composition of the aqueous humour after glaucoma drainage valve implantation (Fiore et al. 1989; McDermott et al. 1993). Quantitatively, long tubes may develop more aggressive inflammatory cellular reaction in aqueous humour. That aqueous humour can flow to the endplate and induce severe fibrosis of bleb. That is, there is a possibility that the tube length affects the wound healing response of the bleb, although it is just an assumption. We suggest that the correlation between the tube length and IOP should be interpreted physically and biologically. Jansonius et al. mentioned that different tube lengths in eyes with various characteristics yielded our observation. We tried to find the confounding factor, but there was no significant association between tube length and diagnosis, age, axial length or preoperative IOP. We agree that surgeons should consider the tube retraction when trimming the tube. As we mentioned in our study, customization of the tube length for individual patient is definitely important for clinical application of glaucoma drainage valve. However, there is also a need to contemplate that too long tube is not unconditionally better to postoperative outcome physically and biologically. Further study will be needed to determine the effects of long tube on cellular events in anterior chamber and wound healing response of the bleb.
Editor,

Extensive phenotypic variability has been reported in ABCA4-related retinal disease since the discovery that mutations in the ABCA4 gene underlie Stargardt disease (STGD) (Al-likmet et al. 1997). This report describes four cases with fundus features of fine macular dots associated with STGD.

Four female cases from three families were recruited; two siblings were from one consanguineous family (case 1, 11 years and case 2, 9 years) and two cases from two additional families (case 3, 11 years and case 4, 11 years). After informed consent was obtained, blood samples were taken from probands of 2/3 families for ABCA4 screening. A full medical history was obtained, and a full ophthalmologic examination was performed in all cases.

The age of disease onset in cases 1–4, defined as either the age at which visual loss was first noted by the subject or in the asymptomatic subjects when abnormal retinal appearance was first detected, was 5, 7, 8 and 6 years old, respectively. LogMAR visual acuity for the right and left eye of cases 1–4 was 0.3 and 0.2, 0.1 and 0.1, 0.5 and 0.4, and 0.3 and 0.4, respectively. Fundus photography identified symmetrical yellowish-white fine dots at the central macula in all cases; in three (cases 1, 2 and 3), there were also numerous peripheral yellowish-white flecks (Fig. 1). Autofluorescence (AF) imaging showed well-defined dots of high AF signal corresponding to the macular dots seen clinically in all cases (Fig. 1). Additional foci of high or low signal extending to the peripheral retina were observed in cases 1, 2 and 3. In addition, case 1 had a ring of increased AF signal at the macula surrounding the area with the dots.

Fig. 1. Fundus photographs, autofluorescence images and disruption in retinal lamination of cases with fine central macular dots associated with childhood-onset Stargardt Disease. Subtle white-yellowish fine dots at the macula and numerous white-yellowish flecks extending anterior to the arcade are shown in the colour fundus photograph of case 1. Autofluorescence (AF) imaging of case 1 detected well-defined dots with high signal at the central macula surrounded by a ring of increased signal and numerous foci with high or low signal extending to the peripheral retina. Case 2 also had subtle white-yellowish fine dots at the central macula and numerous white-yellowish flecks extending anterior to the arcade, both associated with high signal on AF imaging. Case 3 had white-yellowish fine dots at the macula and numerous white-yellowish flecks extending to the periphery, both of which had high or low signal on AF imaging. Case 4 showed subtle fine macular dots mainly in a para-foveal location which are well-defined on AF imaging. Spectral domain optical coherence tomography (SD-OCT) B-scans from a 26-year-old unaffected female, case 2 and case 4 are shown on the right. Gross disruption of the outer retinal layers is visible in both cases, including a thinning of the outer nuclear layer (ONL). A longitudinal reflectivity profile (LRP) taken through the foveal centre of each scan is also demonstrated. These plots show intensity as a function of depth and allow easier localization of specific layers appearing as peaks or troughs. The prominent inner limiting membrane (ILM) and retinal pigment epithelium (RPE) peaks are visible in each case. Normally, the external limiting membrane (ELM) appears as a narrow peak just anterior to the inner segment ellipsoid band (ISE). However, in cases 2 and 4, the presumed ELM peak is broader and the ISE band is missing or severely diminished at the fovea. The diffuse nature of the ELM can also be appreciated in the individual B-scans.
Diffuse large B-cell lymphoma in immunoprivileged sites: association of vitreoretinal, testicular and central nervous system lymphoma

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References


Editor,

Primary vitreoretinal lymphoma (PVR) is highly associated with central nervous system lymphoma (CNSL; Coupland Damato 2008). So far it is not certain whether PVR and PCNSL represent multiple manifestations of one entity or whether they are distinct disorders, one originating in the eye(s) and the other in the brain. The central nervous system (CNS), eyes and testes are immune-privileged sites and have been considered to represent sites where lymphoma cells might escape from lymphocyte-mediated immunosurveillance and where chemotherapy might have reduced efficacy (Riemersma et al. 2000).

We report on nine patients diagnosed with a combination of testicular and vitreoretinal diffuse large B-cell lymphoma (DLBCL) of whom seven with concurrent CNS manifestations (Table 1). Diagnosis was based on tumour biopsy from the testes and on vitreous fluid obtained by vitrectomy from the eye. CNS localization was based on combination of neuroimaging (MRI), biopsy and/or cytological analyses of cerebrospinal fluid. The histological type of non-Hodgkin lymphoma (NHL) was DLBCL in all patients. The mean age at the moment of first diagnosis lymphoma was 66 years. Although only one patient had PVR at onset, eight patients developed VRL after a median interval of 52 (range 12–120) months. The mean interval between onset of symptoms and diagnosis of VRL was 12 (SD 24) months. CNS involvement developed in seven of nine patients, in two patients at onset and five additional patients developed CNS manifestation after a median interval of 50 (range 3–119) months (Table 1). Treatment regimes are displayed in Table 1. Ocular involvement (4 unilateral, 5 bilateral) in all patients was first diagnosed as uveitis. During the follow-up, 6/9 (67%) patients died with a median survival of 76 months (range 25–205 months).

Only occasional cases of concurrent vitreoretinal and testicular lymphoma have been reported previously (Pe’er et al. 2010). It was hypothesized that in immune privileged sites, the malignant cells can escape the immunosurveillance and thereby the destruction initiated by the immune system as well as from chemotherapy (Riemersma et al. 2000). The crucial issue that remains to be elucidated is whether the DBLC located in immunoprivileged sites is of multifocal origin and originates independently or whether this type of lymphoma has one site of origin and spreads subsequently. Controversial reports on this topic were reported. Booman et al. (2008) describe that both shared and site-specific genomic aberrations are present in testicular and CNS lymphoma, which suggests that these are not a homogeneous entity, while others demonstrate that one single B-cell clone was responsible for the manifestation of bilateral ocular lymphoma and CNSL (Coupland et al. 2005). Different IgH gene rearrangement