proliferative index (< 5% of all cells) (Fig. 1E). Using FISH analysis, we found no 13q14 deletion (site of the retinoblastoma gene) in the atypical cells. However, lacked 13q14 deletion does not exclude retinoblastoma, as only 5–10% of hereditary retinoblastomas reveal deletion in the 13q14 RB1 locus (Kivelä et al. 2003).

The low proliferation rate (Kim et al. 1999; Schwimer & Prayson 2001), the GFAP-positivity of the cells (He et al. 1992), and the negative FISH analysis of 13q14 did not support a retinoblastoma diagnosis but pointed towards retinal dysplasia like Norrie's disease.

DNA analysis of the child and his mother was performed in regard to the NDP gene, which upon mutation is responsible for Norrie's disease, ROP, or X-linked familial exudative vitreoretinopathy (Berger et al. 1992; Wu et al. 2007). The NDP gene was evaluated for mutations by PCR amplification of all three exons and all four exon–intron boundaries followed by direct sequencing. The DNA analysis revealed a mutation in the first codon of the Norrin gene (c.1A > G and p.M1V genes) which because of the localization of the NDP gene on the X chromosome caused hemizygous situation in the child. Further DNA analysis confirmed the mother to be a carrier of the same sequence variant c.1A > G (p.M1V). Thus, all results taken together were consistent with X-linked Norrie's disease.

In conclusion, based on our results, in cases of dysplastic retinas with bilateral multiple unclear pseudotumourous lesions, cytology seems to be a useful tool to differentiate in a very short term patients with Norrie's syndrome from those with retinoblastoma or lymphoma. However, retinoblastomas frequently harbour infiltrated retinal elements that may cause confusion or misdiagnosis if only small tumour portions are available for assessment. Also, an eye with suspected retinoblastoma should not be vitrectomized or biopsied, so as not to spread tumour cells extrasclerally.

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Three versus one intravitreal bevacizumab injections as initial protocol to treat myopic choroidal neovascularization

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Editor,

Bevacizumab has been used off-label to treat subfoveal choroidal neovascularization (CNV) secondary to high myopia with good results following an initial therapeutic protocol consisting of three monthly consecutive injections (Gharbiya et al. 2009) or one single injection (Ikuno et al. 2009a,b).

A retrospective, non-randomized, multicentre, consecutive, interventional case series study was performed on 139 eyes from 139 highly myopic patients with active subfoveal or juxtafoveal classic CNV from six different centres. Group 1 comprised 107 eyes treated by one single intravitreal injection (IVB). Group 2 comprised 32 eyes treated by three consecutive monthly IVB. Follow-up was at least 1 year in all of them. The study was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki.

A complete ocular examination including determination of LogMAR best-corrected visual acuity (BCVA) and macular examination by Stratus optical coherence tomography (OCT) was performed at the first visit and then monthly during follow-up. Fluorescein angiography was performed at baseline and whenever CNV activity was suspected. Bevacizumab reinjections were performed in cases with signs of CNV activity (one or more ETDRS lines lost associated with increased central foveal thickness (CFT) and/or macular haemorrhage).

Both groups were matched for age, previous photodynamic therapy, BCVA and CFT (Table 1). The

Table 1. Parameters of the two groups at baseline and during the first year follow-up (Group 1: eyes receiving only one initial bevacizumab injection; Group 2: eyes receiving three initial injections).

	Group 1 (107 eyes)	Group 2 (32 eyes)	p-value (Statistical test)
Age (years)	55 (12.1) 26 to 90	54 (15.8) 29 to 85	0.61 (Unpaired Student's *t*-test)
Spherical equivalent (D)	−11.61 (4.32) −1.75 to −25.00	−12.38 (5.34) +1.00 to −22.00	0.43 (Unpaired Student's *t*-test)
% pseudophakia	27%	22%	0.70 (Chi-square test)
% previous PDT	30%	41%	0.26 (Chi-square test)
Baseline			
No. letters read	49.9 (20.3)	55.4 (12.6)	0.29 (Chi-square test)
CFT	288.6 (93.4)	285.4 (73.5)	0.90 (Chi-square test)
3 months			
No. letters read	59.3 (19.6)	66.3 (14.4)	0.08 (Mann–Whitney)
CFT	236.8 (54.5)	219.3 (52.3)	0.06 (Mann–Whitney)
6 months			
No. letters read	58.5 (19.6)	65.8 (15.4)	0.07 (Mann–Whitney)
CFT	233.0 (52.5)	228.2 (51.4)	0.67 (Student's *t*-test)
9 months			
No. letters read	58.4 (20.0)	66.7 (15.9)	0.04 (Mann–Whitney)
CFT	232.8 (48.8)	243.5 (52.6)	0.35 (Student's *t*-test)
12 months			
No. letters read	58.4 (20.5)	64.0 (15.1)	0.31 (Mann–Whitney)
CFT	232.5 (51.0)	246.2 (63.2)	0.51 (Mann–Whitney)

Mean, standard deviation, range and p-values are shown; SD, standard deviation; D, diopters; PDT, photodynamic therapy; CFT, central foveal thickness.

changes in BCVA and CFT are shown in Table 1. The average number of total intravitreal injections required was 1.8 (SD 1.3, range 1–7) in Group 1 and 3.2 (SD 1.3, range 3–5) in Group 2. No significant differences were found for BCVA and CFT by the end of the first year (Table 1).

A statistically significant improvement in BCVA and decrease in CFT were found during a 12-month follow-up in both groups. This visual improvement occurred during the first 3 months in both groups, and visual acuity remained stable afterwards.

The presence of high levels of vascular endothelial growth factor (VEGF) and pigment epithelium-derived factor is suspected to be involved in the development of myopic CNV. Antiangiogenic therapies have been used to treat subfoveal myopic CNV (Figurska & Stankiewicz 2008; Gharbiya et al. 2009; Ikuno et al. 2009a,b).

The initial use of three IVB as a therapeutic protocol can be questionable because of the usual low activity of the myopic CNV. There is a further concern about the possible teratogenic effects on young patients of childbearing age.

The reduction in the number of intravitreal injections required may be of interest if it is confirmed that bevacizumab damages choroidal circulation (Ikuno et al. 2009a,b). The lower number of injections associated with a higher frequency of recurrences and 'unexpected' retreatments did not affect the final visual outcome. The higher risk of recurrences might imply a need for closer follow-up; however, a monthly follow-up is usually required in patients with CNV, so the frequency of follow-up visits would not be affected.

Limitations of the current study are the different number of eyes in both groups (107 versus 32) and being retrospective. The clinical investigators from all the centres used identical protocols. An assessment of the statistical power of the statistical tests used in the current study was performed and showed to be enough for a statistical power of at least 60% (standard sample size calculations).

According to our results, one IVB seems to be a useful procedure to treat CNV associated with high myopia, as a first-line therapy. The patients must be controlled monthly at least during the first year because of the risk of CNV reactivation. Clinical studies with longer follow-up are needed to evaluate the efficacy of this therapy in the long term.

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