Individuals with inherited retinal disease and their relatives or carers are in favour of genetic testing for a number of reasons and despite the fact that most inherited retinal diseases remain untreatable. The majority of respondents support diagnostic and predictive testing in both adults and children, but want counselling before testing. In view of these findings, it is hoped that there will be greater access to testing to bring the service provision into line with the aspirations of service users.

Conflict of interest

The authors declare no conflict of interest.

References

- 1 Bunce C, Wormald R. Causes of blind certifications in England and Wales: April 1999-March 2000. *Eye (Lond)* 2008; **22**(7): 905–911.
- 2 Koenekoop RK, Lopez I, den Hollander AI, Allikmets R, Cremers FP. Genetic testing for retinal dystrophies and dysfunctions: benefits, dilemmas and solutions. *Clin Experiment Ophthalmol* 2007; **35**(5): 473–485.
- 3 Pradhan M, Hayes I, Vincent A. An audit of genetic testing in diagnosis of inherited retinal disorders: a prerequisite for gene-specific intervention. *Clin Experiment Ophthalmol* 2009; **37**(7): 703–711.
- 4 Mackey DA, Héon E, Webster AR. Predictive DNA testing in ophthalmology. *Br J Ophthalmol* 2003; **87**(5): 633–638.
- 5 Pawlowitzki IH, Rütther K, Brunsmann F, von Gizycki R. Acceptability of prenatal diagnosis for retinitis pigmentosa. *Lancet* 1986; **2**(8520): 1394–1395.
- 6 Mezer E, Babul-Hirji R, Wise R, Chipman M, DaSilva L, Rowell M *et al.* Attitudes regarding predictive testing for retinitis pigmentosa. *Ophthalmic Genet* 2007; **28**(1): 9–15.
- 7 Furu T, Kääriäinen H, Sankila EM, Norio R. Attitudes towards prenatal diagnosis and selective abortion among patients with retinitis pigmentosa or choroideremia as well as among their relatives. *Clin Genet* 1993; **43**(3): 160–165.
- 8 Mezer E, Wygnanski-Jaffe T. Ethical issues in ocular genetics. *Curr Opin Ophthalmol* 2009; **20**(5): 382–386.
- 9 Sutherland JE, Day MA. Genetic counseling and genetic testing in ophthalmology. *Curr Opin Ophthalmol* 2009; **20**(5): 343–350.

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A poster presentation, including some of this data has been presented at the Royal College of Ophthalmologists Annual Congress 2010

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Sir, Combination intravitreal rituximab and methotrexate for massive subretinal lymphoma

Primary vitreoretinal lymphoma (PVRL), also known as primary intraocular lymphoma (PIOL), is a subset of primary central nervous system lymphoma (PCNSL), typically diffuse large B-cell lymphoma, which often manifests as posterior uveitis or sub-retinal pigment epithelial (RPE) infiltrates.¹ PCNSL treatment includes radiation and chemotherapy; however, the optimal therapy for PVRL without CNS involvement is unknown.² We report the efficacy of intravitreal rituximab and methotrexate in a patient with PVRL who presented with massive sub-retinal infiltration with RPE involvement.

Case report

An 83-year-old male patient presented with a 1-month history of progressive blurred vision OS. Visual acuities were 20/20 OD and hand motions OS. A relative afferent pupillary defect was present OS. Ophthalmic examination was normal OD. Trace vitritis and diffuse, confluent yellow-white subretinal infiltrates were seen OS (Figure 1). CBC, RPR, FTA-ABS, HIV, ACE, ESR, and chest CT scan were normal. Pars plana vitrectomy, subretinal aspiration biopsy, air-fluid exchange, endolaser, and 14% C₃F₈ instillation were performed.

Cytopathology revealed lymphomatous infiltrates with condensed chromatin and multiple nucleoli. Flow cytometry showed CD20⁺ staining. IgH gene rearrangement studies demonstrated monoclonal restriction consistent with diffuse large B-cell lymphoma.

Brain MRI and CSF studies were negative for CNS disease. Following neuro-oncology consultation regarding treatment options including chemotherapy, blood–brain barrier disruption, and radiation, systemic therapy was deferred by the patient. Monthly intravitreal injections of rituximab (1 mg/0.1 ml) and methotrexate (400 mcg/0.1 ml) for 3 months were undertaken. Rapid regression of the subretinal lesions was observed by 2 months and visual acuity improved to finger counting at 3 feet. The retinal examination was stable at 18 months with no evidence of CNS involvement.

Comment

Rituximab is a chimeric monoclonal antibody targeting the CD20⁺ B-cell marker, while methotrexate inhibits folate metabolism and DNA synthesis. Intravitreal monotherapy for PIOL has been described,^{3–5} while combination intravitreal methotrexate 200 mg/0.05 ml (half the standard dose) and rituximab 1 mg/0.1 ml has been reported once previously.⁴ The rationale for combination therapy stems from conventional combination chemotherapy for systemic diffuse large B-cell lymphoma, which may include high-dose systemic methotrexate and intrathecal rituximab.⁶ The complete ocular remission in our patient following three doses of combination methotrexate and rituximab at 18-months follow-up suggests that this dosing strategy warrants further investigation. Further studies are needed to determine its long-term efficacy, and CNS

Figure 1 Fundus photograph montage prior to therapy (a) showing massive yellow subretinal infiltrates with cystic-appearing spaces throughout the posterior pole and the majority of the peripheral retina. Fluorescein angiography revealing early mottled hyperfluorescence of the posterior pole with extensive leakage and perivascular staining (b, c). Spectral domain optical coherence tomography (SD-OCT) scan showing elevated neurosensory retina but no evidence of retinal infiltration (d). Cytopathological evaluation from a subretinal aspiration biopsy revealing a cellular infiltrate with cells larger than mature lymphocytes with condensed chromatin and multiple prominent nucleoli (e). Abundant necrotic cells are also seen (e, black arrows). Repeat fundus photograph montage (f) 2 months following initiation of combination rituximab and methotrexate therapy showing marked eradication of the subretinal lymphoma within the macula and retinal periphery. These areas resolved completely by the final 18-month follow-up. Horizontal macular SD-OCT scan showing resolution of the previously seen neurosensory elevation with some RPE thickening and subretinal fibrosis (g, yellow arrows).

surveillance with the aid of a neuro-oncologist is advisable.

Conflict of interest

The authors declare no conflict of interest.

References

- Chan CC, Buggage R, Nussenblatt RB. Intraocular lymphoma. *Curr Opin Ophthalmol* 2002; **13**: 411–418.
- Nussenblatt RB, Chan CC, Wilson WH, Hochman J, Gottesman M. International Central Nervous System and Ocular Lymphoma Workshop: recommendations for the future. *Ocul Immunol Inflamm* 2006; **14**: 139–144.
- Smith JR, Rosenbaum JT, Wilson DJ, Doolittle ND, Siegal T, Neuwelt EA *et al*. Role of intravitreal methotrexate in the management of primary central nervous system lymphoma with ocular involvement. *Ophthalmology* 2002; **109**: 1709–1716.
- Kitzmann AS, Pulido JS, Mohny BG, Baratz KH, Grube T, Marler RJ *et al*. Intraocular use of rituximab. *Eye* 2007; **21**: 1524–1527.
- Ohguro N, Hashida N, Tano Y. Effect of intravitreal rituximab injections in patients with recurrent ocular lesions associated with central nervous system lymphoma. *Arch Ophthalmol* 2008; **126**: 1002–1003.
- Rubenstein J, Ferreri AJ, Pittaluga S. Primary lymphoma of the central nervous system: epidemiology, pathology and current approaches to diagnosis, prognosis and treatment. *Leuk Lymphoma* 2008; **49**(Suppl 1): 43–51.

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Sir,
Patient, surgical, and lens-related factors, and their association with Hydroview intraocular lens opacification

We read with interest Rimmer *et al*'s letter¹ published in January suggesting a higher incidence of Hydroview lens (Bausch and Lomb) calcification in those implanted between late 2000 and mid-2001. The main cause of opacification was thought to be silicone in the lens packaging.^{2,3} As the packaging did not change between 1997 and 2001,² Rimmer *et al*'s observations suggest that other aetiological factors might be involved.

A study set up at Bristol assessed the impact of Hydroview opacification on vision (Central and South Bristol Research Ethics Committee Ref 05/Q2006/163).⁴ We re-evaluated the data from this study to investigate the associations of opacification with patient, surgical, and lens-related factors. Data were gathered through a review of medical records, patient interview, and examination.

Data from 215 patients who had Hydroview lenses implanted in Bristol were analysed: 125 had clear

lenses, 89 had evidence of opacification, and 1 lens could not be assessed. No statistically significant association was demonstrated between opacification and any of the patient- (Tables 1 and 2) or surgery-related factors (Table 3) tested. However, this is likely to be a result of the small number of patients at subgroup analysis level.

There was a marked association of opacification with certain runs of consecutive lens serial numbers (Table 4). Serial numbers relate only to the order in which the lenses are manufactured and are sequential. Our study will have selection bias, as all patients had surgery over a similar time period and those symptomatic would be more likely to enrol. There will be a high number of certain runs of serial numbers and a high number of opacified lenses. However, variation in the proportion of lenses opacified (3–79%) across the serial numbers tested strongly suggests an association between opacity and certain runs of serial numbers.

Although these data must be viewed with respect to the context, ie, as a retrospective observation rather than as prospective evidence, they do question the supposition that the sole cause for opacification was the

Table 1 Association between lens opacification and ocular pathology

	IOL opacified			P-value ^a
	No (n = 125)	Yes (n = 89)	Total (n = 214)	
<i>Diabetic retinopathy in the study eye</i>				
No	117 (58.8%)	82 (41.2%)	199 (100%)	0.89
Yes	8 (53.3%)	7 (46.7%)	15 (100%)	
<i>Glaucoma in the study eye</i>				
No	109 (57.4%)	81 (42.6%)	190 (100%)	0.52
Yes	16 (66.7%)	8 (33.3%)	24 (100%)	
<i>Uveitis in the study eye</i>				
No	123 (58.3%)	88 (41.7%)	211 (100%)	>0.99
Yes	2	1	3 ^b	
<i>Vitrectomy in the study eye</i>				
No	119 (59.5%)	81 (40.5%)	200 (100%)	0.35
Yes	6 (42.9%)	8 (57.1%)	14 (100%)	

^aContinuity-corrected χ^2 -test or two-tailed Fisher's exact test was used if frequencies were small.

^bToo few for percentage calculation.

Table 2 Association between lens opacification and systemic pathology

	IOL opacified		Total	P-value ^a
	No	Yes		
<i>Hypertension</i>				
No	51 (60.7%)	33 (39.3%)	84 (100%)	0.684
Yes	74 (56.9%)	56 (43.1%)	130 (100%)	
Total	125 (58.4%)	89 (41.6%)	214 (100%)	
<i>Ischaemic heart disease</i>				
No	100 (61.0%)	64 (39.0%)	164 (100%)	0.225
Yes	25 (50.0%)	25 (50.0%)	50 (100%)	
Total	125 (58.4%)	89 (41.6%)	214 (100%)	
<i>Cerebrovascular event</i>				
No	120 (58.3%)	86 (41.7%)	206 (100%)	1.000
Yes	5 (62.5%)	3 (37.5%)	8 (100%)	
Total	125 (58.4%)	89 (41.6%)	214 (100%)	
<i>Inflammatory condition</i>				
No	122 (58.1%)	88 (41.9%)	210 (100%)	0.867
Yes	3 (75.0%)	1 (25.0%)	4 (100%)	
Total	125 (58.4%)	89 (41.6%)	214 (100%)	
<i>Cancer</i>				
No	121 (58.5%)	86 (41.5%)	207 (100%)	1.000
Yes	4 (57.1%)	3 (42.9%)	7 (100%)	
Total	125 (58.4%)	89 (41.6%)	214 (100%)	
<i>Gender</i>				
Male	48 (55.8%)	38 (44.2%)	86 (100%)	0.624
Female	77 (60.2%)	51 (39.8%)	128 (100%)	
Total	125 (58.4%)	89 (41.6%)	214 (100%)	

^a χ^2 -test was performed with continuity correction asymptotic significance two-sided.