Discrimination between normal and glaucomatous eyes with visual field and scanning laser polarimetry measurements

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Abstract

Aim—To evaluate the ability of structural parameters (as determined by retinal nerve fibre layer (RNFL) measurements obtained with the scanning laser polarimetry (SLP-NFA/GDx)) and functional parameters (as determined by automated perimetry) to discriminate between normal and glaucomatous eyes.

Methods—In a case-control study, a total of 91 normal subjects and 94 patients with glaucoma underwent automated perimetry and RNFL measurements obtained with the SLP. Three independent scans of each eye were obtained and a mean image was created and used for further analysis. Only one eye per individual was randomly included in the study. The sensitivity (Se) and specificity (Sp) of 12 RNFL parameters were calculated according to the SLP internal normative database. The Se and Sp of the visual field (VF) global indices and the glaucoma hemifield test (GHT) were also calculated according to the instrument’s normative database. Receiver operator characteristic (ROC) curves were built for each SLP parameter and VF index. Fisher’s linear discriminant formulas (LDFs) were developed for VF indices (VF LDF), SLP measurements (SLP LDF), and both examinations (combined LDF).

Results—According to the SLP internal database, the parameters with better Se and Sp were: superior/nasal ratio (Se = 58.5%; Sp = 86.8%), and GDx the number (Se = 43.3%; Sp = 96.7%). The construction of an ROC curve for the number resulted in Se = 84% and Sp = 79%. The creation of LDFs improved both the sensitivities and specificities when compared with isolated parameters SLP LDF (Se = 90.4%; Sp = 82.4%), VF LDF (Se = 89.4%; Sp = 89.0%), and combined LDF (Se = 93.0%; Sp = 90.1%). The sensitivity to diagnose early and moderate glaucomatous damage observed with the GHT was lower than that obtained with the number (p<0.01).

Conclusions—Creation of LDFs enhanced the Se and Sp for both VF and SLP. Integration of SLP and VF in a combined LDF reached the highest Se/Sp relation, suggesting that these examinations may be additive concerning the diagnosis of glaucoma. The SLP parameter the number may be more sensitive than the GHT in diagnosing early and moderate glaucomatous damage.

There has been increasing evidence that retinal nerve fibre layer (RNFL) analysis may improve the diagnosis of early glaucomatous damage.¹⁻⁴ Hoyt and Newman first suggested that localised RNFL defects represent the earliest detectable defect in glaucoma. Sommer et al⁵ demonstrated that RNFL abnormalities may be detected up to 6 years before the development of visual field loss. Other authors have stressed that RNFL examination is a useful way of monitoring glaucomatous damage.⁶⁻⁸ Scanning laser polarimetry (SLP) measurement is based on the birefringent properties of the RNFL, which has its microtubules disposed in an organised, parallel fashion. This peculiar anatomy leads to a change in the state of polarised light as it passes through the RNFL, creating a retardation that is directly proportional to its thickness.⁹ Experimental and clinical studies have demonstrated that SLP provides quantitative¹⁰ and reproducible¹¹ measurements of the RNFL thickness, shown to be significantly lower among glaucomatous¹² and ocular hypertensive¹³ eyes when compared with healthy eyes, although considerable overlap is present between these groups.

Most of the studies investigating glaucoma require both anatomical and functional damage to define the disease, although a time interval exists between these.¹⁰ Hence, we designed a study in order to compare the ability of SLP structural parameters and automated perimetry functional measurements (used separately or in conjunction) to discriminate between normal and glaucomatous eyes.

Methods

After approval of the ethics committee of the University of Campinas and written consent, all subjects underwent a thorough ophthalmological examination including slit lamp biomicroscopy, applanation tonometry (Goldmann), gonioscopy, dilated retinal and optic nerve head examination (20 dioptre and 78 dioptre lenses), automated perimetry using the Humphrey field analyser II, program 24-2, full threshold strategy (Humphrey Systems, Dublin, CA, USA) and SLP, using the nerve fibre analyser-GDx (Laser Diagnostic Technologies, San Diego, CA, USA), software version 1.0.12.
The inclusion criteria for both the normal and glaucoma groups were best corrected visual acuity $\geq 20/30$, spherical equivalent $\leq +$ or $-5$ dioptries, age over 40 years (no upper limit), and two reliable Humphrey 24-2 visual fields. Patients in both groups were excluded if presented with history of systemic or ocular disease (except glaucoma) that could interfere with the scanning laser polarimeter or visual field results. We also excluded pseudophakic eyes and those with significant cataract—greater than mild lens opacification, according to the Lens Opacity Classification System III. One eye per patient was randomly selected if both eyes were eligible.

Normal subjects were recruited from volunteers among the medical staff, university members, spouses, and friends of patients. These were excluded if presented with pressure above 22 mm Hg or with a suspicious disc (that is, localised rim loss, optic disc haemorrhage, cup/disc asymmetry $>0.2$), or with glaucomatous visual field defects (as defined below).

Glaucoma patients were recruited from the glaucoma service of the University of Campinas. The inclusion criteria were: clinical diagnosis of primary open angle glaucoma with two or more IOP measurements above 22 mm Hg, optic nerve examination demonstrating glaucomatous damage (that is, cupping, localised rim loss, disc haemorrhage, or cup/disc asymmetry $>0.3$). Furthermore, a typical glaucomatous visual field defect had to be present on at least two reliable VF testings. This was defined as: (a) two or more contiguous points with a 10 dB loss or greater in the superior or inferior Bjerrum areas, compared with perimeter defined age matched controls; (b) three or more contiguous points, with a 5 dB or greater loss, in the superior or inferior Bjerrum areas. Neither the global indices nor the GHT were used to define glaucomatous or normal visual fields.

Patients were classified as having early, moderate, or severe glaucomatous damage according to the following criteria: (a) early damage: MD no worse than $-6$ dB and CPSD no worse than 1%; (b) moderate damage: MD between $-6$ dB and $-15$ dB, and CPSD no worse than 1%; and (c) severe damage: MD worse than $-15$ dB or CPSD worse than 1%.

To obtain RNFL measurements of each eye, we created a mean image, which was the average of three consecutive 15° images, centred on the optic nerve. Room lights were kept on and pupils were left undilated. In order to be included, each single image had to pass the software’s criteria of quality. A single examiner (RLP) obtained the images and delineated the disc margin.

The following RNFL parameters were collected: symmetry, superior ratio, inferior ratio, maximum modulation, average thickness, superior to nasal ratio, ellipse modulation, ellipse average, superior average, inferior average, superior integral, and the number. The meaning of each RNFL parameter has been reported elsewhere.

The sensitivity and specificity of each single parameter were calculated according to the GDx normative database. Values outside the 95% confidence limits of the internal software database, automatically labelled as “outside normal limits”, were considered abnormal.

The neural network variable, the number, was considered abnormal if greater than 70 (as suggested by the manufacturer). Additionally, an “all normal” variable was created and defined as abnormal if at least one of the 12 parameters measured by the NFA was “outside normal limits”.

Likewise, the sensitivity and specificity of the visual field (VF) global indices (MD, SF, and CPSD) and the glaucoma hemifield test (GHT) were calculated. The GHT was considered abnormal when the printout displayed the message “outside normal limits”, which refers to a value falling outside the 99% confidence interval. Additionally, MD, SF, and CPSD were considered abnormal when labelled with $p<5\%$ according to the Humphrey's database (Humphrey field analyser's II statistical software, STATPAC 2).

Subsequently, receiver operator characteristic (ROC) curves were plotted for each individual SLP parameter and VF index. The area under the curve was calculated and a z test was employed to determine if the area was significantly different from 0.5 (which indicates no discrimination). Cut-off points were arbitrarily selected to determine the best sensitivity/specificity relation for each single VF and SLP measurement.

Fisher’s linear discriminant functions (LDFs) composed of the best combination of SLP and VF measurements were created. The ability to discriminate between normal and glaucomatous eyes with the SLP LDF, the VF LDF, and the combined (VF+SLP) LDF was tested.

Comparisons were made with the Student’s $t$ test (for continuous variables), the $\chi^2$ test (Yates’s corrected), and the Fisher exact test (for the categorical data). $p$ Values of less than 0.05 were considered significant.

**Results**

A total of 185 eyes, 91 normal and 94 glaucomatous, were enrolled in this study. Among the 94 glaucomatous eyes, 14 were classified as having early glaucomatous damage, 30 had moderate, and 50 had severe damage (mean MD $= -11.09$ (SD 9.10) dB). Demographic data are displayed in Table 1. The mean age in the glaucoma group (64.7 (11.3)) was significantly higher than the normal group (47.3 (6.0)) (p<0.05). The cup/disc ratio was significantly higher among glaucoma patients (0.69 (0.12)) when compared with controls (0.32 (0.12)) (p<0.05). Because of the significant differences in age and cup/disc ratio, these were included as candidate variables in the linear discriminant function (LDF) analyses. The stepwise analysis, used to create the LDFs, demonstrated that both age and cup/disc ratios were weak variables, and therefore were not included in the final structural LDF formula.

There were statistically significant differences ($p<0.001$) between healthy and glaucomatous eyes for all VF global indices and SLP parameters.
parameters, except for symmetry (p = 0.12) (Tables 2 and 3) (Fig 1). When the NFA/GDx normative database was used, SLP parameters showed low sensitivities (Se) and high specificities (Sp) for the diagnosis of glaucoma (Table 4). Conversely, the “all normal” variable resulted in a sensitivity of 79.8% and a specificity of 56%. Based on the Humphrey’s internal database, VF global indices showed moderate sensitivities (over 70%), except for SF (Se = 33.0%), and high specificities (above 90%).

Areas under the ROC curves for all SLP parameters and VF indices were highly significant (p<0.001), except for symmetry (p = 0.184) (Table 5, Fig 2). Selection of cut-off points improved the sensitivity/specificity relation of all SLP parameters when compared to the results obtained with the GDx normative database. Individual parameters found to have better sensitivity/specificity relation were the number (Se = 84%; Sp = 79%), ellipse modulation (Se = 82%; Sp = 73%), and superior/nasal ratio (Se = 82%; Sp = 79%). Although highly significant ROC curves were observed for each VF parameter (p<0.001), we could not find, in our model, cut-off points to improve the sensitivity/specificity relation for SF and CPSD (Table 5).

A statistically significant area of 0.961 under the ROC curve was obtained for the VF LDF (p<0.01). With a cut-off point at lower than 0.547 as abnormal, it showed a sensitivity of 90.4%, and a specificity of 82.4%, with an accuracy of 85.9%.

The use of a combined discriminant function resulted in an increase of the sensitivity/specificity relation of all SLP parameters when compared to the results obtained with the GDx normative database, VF global indices showed moderate sensitivities (Se) and high specificities (Sp) for the diagnosis of glaucoma (Table 4).

### Table 1  Demographic data

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal subjects</th>
<th>Glaucoma patients</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (n)</td>
<td>91</td>
<td>94</td>
<td></td>
</tr>
<tr>
<td>Age (years (SD))</td>
<td>47.3 (6.0)</td>
<td>64.7 (11.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Race (black/white/Asians)</td>
<td>23/65/3</td>
<td>35/57/2</td>
<td>0.20</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>54/37</td>
<td>52/42</td>
<td>0.58</td>
</tr>
<tr>
<td>Spherical equivalent (dioptres)</td>
<td>+0.33 (0.91)</td>
<td>+0.69 (1.86)</td>
<td>0.22</td>
</tr>
<tr>
<td>Cup/disc ratio</td>
<td>0.32 (0.12)</td>
<td>0.69 (0.12)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

All values expressed as mean (SD).

### Table 2  Visual field global indices and the GHT in the normal and glaucomatous groups

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal subjects</th>
<th>Glaucoma patients</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD (dB) (mean (SD))</td>
<td>−0.83 (1.30)</td>
<td>−11.09 (9.10)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SF (dB) (mean (SD))</td>
<td>1.46 (0.45)</td>
<td>2.62 (1.92)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CPSD (dB) (mean (SD))</td>
<td>1.56 (0.98)</td>
<td>5.94 (3.69)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GHT outside normal limits</td>
<td>2 (2.2%)</td>
<td>68 (72.3%)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*p*Decibels (dB).

### Table 3  SLP parameters in normal and glaucomatous eyes

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal subjects</th>
<th>Glaucoma patients</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symmetry</td>
<td>0.95 (0.15)</td>
<td>0.93 (0.13)</td>
<td>0.12</td>
</tr>
<tr>
<td>Superior ratio</td>
<td>2.15 (0.50)</td>
<td>1.59 (0.36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inferior ratio</td>
<td>2.29 (0.56)</td>
<td>1.74 (0.41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Superior/nasal</td>
<td>1.85 (0.31)</td>
<td>1.44 (0.27)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Maximum modulation</td>
<td>1.41 (0.42)</td>
<td>0.83 (0.38)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Ellipse modulation</td>
<td>2.69 (0.71)</td>
<td>1.62 (0.65)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>The number</td>
<td>24.5 (17.71)</td>
<td>60.42 (25.05)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Average thickness</td>
<td>64.90 (13.68)</td>
<td>57.32 (25.07)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ellipse average</td>
<td>68.11 (14.29)</td>
<td>57.76 (10.36)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Superior average</td>
<td>74.72 (18.75)</td>
<td>59.18 (12.90)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Inferior average</td>
<td>80.15 (16.39)</td>
<td>65.23 (12.72)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Superior integral</td>
<td>0.22 (0.06)</td>
<td>0.18 (0.04)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

*p*Ellipticity (dioptres).

### Table 4  Sensitivity and specificity of SLP parameters and VF indices according to the GDx and Humphrey databases

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symmetry</td>
<td>18.1%</td>
<td>81.3%</td>
</tr>
<tr>
<td>Superior ratio</td>
<td>29.8%</td>
<td>89.0%</td>
</tr>
<tr>
<td>Inferior ratio</td>
<td>29.8%</td>
<td>91.2%</td>
</tr>
<tr>
<td>Superior/nasal</td>
<td>58.5%</td>
<td>86.8%</td>
</tr>
<tr>
<td>Maximum modulation</td>
<td>40.4%</td>
<td>87.9%</td>
</tr>
<tr>
<td>Ellipse modulation</td>
<td>26.6%</td>
<td>97.8%</td>
</tr>
<tr>
<td>The number</td>
<td>42.3%</td>
<td>96.7%</td>
</tr>
<tr>
<td>Average thickness</td>
<td>12.8%</td>
<td>98.9%</td>
</tr>
<tr>
<td>Ellipse average</td>
<td>22.3%</td>
<td>96.7%</td>
</tr>
<tr>
<td>Superior average</td>
<td>42.6%</td>
<td>95.6%</td>
</tr>
<tr>
<td>Inferior average</td>
<td>19.1%</td>
<td>95.6%</td>
</tr>
<tr>
<td>Superior integral</td>
<td>28.7%</td>
<td>84.6%</td>
</tr>
<tr>
<td>GHT</td>
<td>72.3%</td>
<td>97.8%</td>
</tr>
<tr>
<td>MD</td>
<td>83.0%</td>
<td>94.5%</td>
</tr>
<tr>
<td>SF</td>
<td>33.0%</td>
<td>97.8%</td>
</tr>
<tr>
<td>CPSD</td>
<td>79.8%</td>
<td>92.3%</td>
</tr>
</tbody>
</table>
Specificity relation. When the cut-off point was set at higher than −0.446 as abnormal, it showed an area under the ROC curve of 0.98, a sensitivity of 93.0%, a specificity of 90.1%, and an accuracy of 90.8%.

Combined LDF = 1.015 − (0.645 × ellipse modulation) + (0.017 × the number) − (0.24 × ellipse average) + (0.207 × SF) + (0.196 × CPSD)

Table 6 discloses the different sensitivities obtained with the GHT, the number (cut-off = 32), and the structural and functional LDFs according to the severity of the disease. The sensitivities obtained with the number and the structural LDF for the diagnosis of early/moderate glaucomatous damage were significantly higher than that obtained with the GHT (p = 0.009, and p = 0.0001, respectively).

**Discussion**

In the present study, RNFL retardation measurements obtained with the SLP were significantly higher in normal eyes compared with glaucomatous eyes, although there is a considerable overlap between both groups. The symmetry parameter was the only measurement not significantly different between the groups (p = 0.12). These findings are consistent with previous studies that stressed the large range of normal mean values of retardation.

Although the mean age was different among the groups, it did not influence our LDF analysis to discriminate between normal and glaucomatous eyes, as it proved to be a weak variable to be used in the LDF formula.

All individual SLP parameters showed low sensitivities and high specificities when the NFA/GDx database was used as reference and none of the individual RNFL measurements could correctly assign as outside normal limits the majority of glaucoma cases. There are two possible explanations for this finding. Firstly,
the normative database may be insufficient (in number or in variety), which may be influenced by the variability of the axis of corneal polarisation as recently reported by Greenfield et al. The SLP employs an anterior segment compensating algorithm, which assumes a fixed axis of corneal polarisation, and may not be adjusted to such physiological variability. Secondly, the use of the 95% confidence interval to define “outside normal limits” may be too stringent, decreasing the sensitivity in spite of a high specificity. As it is, the database may be useful to confirm the diagnosis of glaucoma, but not to detect early glaucomatous damage.

Construction of ROC curves for individual structural parameters and arbitrary selection of cut-off points significantly enhanced the sensitivity of all SLP parameters, reaching values around 80% for the number, ellipse modulation, superior/nasal, and maximum modulation. It is possible that modulation parameters and ratios are not greatly sensitive to changes in the axis of corneal polarisation, explaining the better sensitivity/specification relation obtained with this parameter. The number was the SLP parameter with the largest area under the ROC curve (0.87), leading to a sensitivity of 84%, a specificity of 79%, and an accuracy of 80.5%, with a cut-off set at 32. When analysing the same variable, Weinreb et al were able to build a ROC curve with an area of 0.78 when the cut-off point was set at 27, which resulted in a specificity of 82% and a sensitivity of 62%. The use of a cut-off point that would increase the sensitivity is desired in a test designed to provide early diagnosis of glaucoma, yet lower cut-off points for the number lead still to only moderate sensitivities in both studies. Similarly, other authors found that a cut-off for the number around 30 performed better than at the suggested 70.23

On the other hand, the analysis of functional parameters showed that, except for SF, VF indices showed better sensitivities than SLP measurements, according to the respective equipment databases. MD and CPSD were found to have sensitivities of 83% and 80%, respectively. The reason for the better sensitivities obtained with VF indices may be secondary to the large Humphrey's statistical database, or to a selection bias in our criteria for defining glaucoma (although both structural and functional damage were required for the patient to be included). The use of clusters of low sensitivity points may have artificially increased the sensitivity and specificity of indices such as the CPSD and the GHT, designed to detect focal differences or regional asymmetries. Nevertheless, the 72.3% sensitivity of the GHT shown in this series is similar to the 78% sensitivity reported by Asman and Heijl, and lower than that previously reported by Katz et al (Se = 94%). However, the latter study defined typical glaucomatous defects based on Goldmann's manual perimetry, which may have led to the inclusion of more advanced stages of glaucoma, artificially increasing the sensitivity.

The GHT has been described by some authors as the best single objective statistical criterion for the detection of glaucoma. The 72.3% sensitivity observed with the GHT was lower than that obtained with the number when its cut-off point was set at 32 (Se = 84.0%). This difference becomes greater when the sensitivities of both parameters are compared in the early/moderate damage group (the number = 75%; GHT = 45.4%) (p = 0.005).

The SLP LDF (Se = 86.3%) was also more sensitive in diagnosing early and moderate glaucoma when compared to the GHT (p<0.001) (Table 6). These findings indicate that the SLP neural network may be capable of showing change earlier than classic functional measures, consistently with the description that RNFL defects may occur long before visual field damage.

In this study, the creation of a VF LDF (Se = 89.4%; Sp = 89.0%) and a SLP LDF (Se = 90.4%; Sp = 82.4%) resulted in similarly high sensitivities and specificities, higher than any individual SLP parameter or VF index. When applied to the early and moderate subgroup, the SLP LDF reached slightly higher sensitivities than VF LDF, although the differences were not significant (p = 0.395).

The use of functional and structural variables in a combined LDF improved the overall sensitivity/specificity relation, reaching a 92.5% sensitivity and a 90.1% specificity. Enhancement of sensitivity and specificity in this model suggests that VF and SLP parameters may be additive in the diagnosis of glaucoma. These findings are consistent with those reported by Caprioli, who described that the combination of functional (VF indices) and structural parameters (computer derived variables of the optic nerve and RNFL indirect measures) in a linear discriminant function improved the capability to diagnose glaucoma. This method of analysis correctly classified 87.8% of the studied eyes, compared to a 77% precision with a functional LDF, and a 76% precision of a structural LDF. Higher labelling accuracies were achieved with the LDFs developed in the present study (90.3% for the functional LDF, 85.9% for the structural LDF and 90.8% for the combination of structural and functional parameters).

Although the LDFs were not tested in an independent sample, we estimated the bias of the ROC curve with a k-fold cross validation on randomly chosen training variables and the test sets of variables. This approach resulted in an estimated decrease of 1.6% in the area under the structural LDF ROC curve and of 1.8% for the combined LDF.

Weinreb et al also developed a structural LDF, based on SLP readings that could increase the ability to differentiate between normal and glaucomatous eyes with early to moderate visual field damage (ROC curve of 0.89, a sensitivity of 74% and a specificity of 92%). The application of the LDF proposed by those authors in our sample resulted in an overall sensitivity and specificity of 85.1% and 88.8%, respectively.

Furthermore, that formula resulted in a sensitivity of 77.2%, when used in our early and moderate glaucoma groups (defined with the...
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same criteria as Weinreb et al. These results are similar to those reported in that original series (Se = 74%) and apparently validate that formula. Nevertheless, the estimated sensitivity of our SLP LDF (86.3%) was higher than Weinreb’s when applied to the same subgroup of patients, although the difference was not statistically significant (p = 0.269). The lack of significance may be due to the small number of early/moderate glaucoma patients in the present study. Further evaluations on larger samples are needed to address this issue. Interestingly, the two formulas share three variables in common: average thickness, ellipse modulation, and ellipse average. The fourth variable included in our LDF, the number, took part in only one of the best set of 20 models of three predictors used in Weinreb’s LDF.

Direct comparisons between the present study and previous reports of SLP performance to detect glaucoma may not be straightforward, in part because population samples seem to have distinct spectra of glaucomatous damage. The 96% sensitivity and 93% specificity reported by Tjon-Fo-Sang and Lemij when using the SLP to detect glaucoma were obtained with a previous version of the NFA. The calculation of mean retardation was processed in six selected areas and avoided areas crossed by vessels. Although their study included patients with a range of MD loss (mean MD = −10.33 dB, ranging from −31.5 to 0.76 dB) similar to ours (mean MD = −11.09 dB, ranging from −27.6 to 4.16 dB), the GHT was necessarily outside normal limits, which was not an inclusion criterion in our study. The use of the NFA-GDx instead of the original NFA may account for some differences in the results, particularly because the normative database and the methods employed by Tjon-Fo-Sang and Lemij are different from the data analysis included in the software used in this study. Additionally, new features of the NFA-GDx were developed in order to evaluate the quality of the captured image and to reduce interoperator and intraoperator variability of the image acquisition.

In conclusion, this study showed that integration of multiple SLP variables on a LDF improved the ability to differentiate between normal and glaucomatous eyes more than any individual SLP parameter. The application of a linear discriminant model also suggested that visual field indices and SLP parameters may be additive concerning the diagnosis of glaucoma. Further studies are necessary to validate these LDFs in different population samples. Finally, as far as we are aware, this is the first report to indicate that the SLP parameter the number may be more sensitive to the detection of glaucomatous damage than the GHT, especially in the early/moderate damage group.

The authors have no proprietary interest in any product discussed in this presentation or a competing instrument.

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Surgically induced diffuse scleritis: comparison of incidence in phacoemulsification and conventional extracapsular cataract extraction

Surgically induced diffuse scleritis (SIDS) is a recognised but less well reported cause of pain and reduced vision following cataract extraction. We have previously reported on complications of conventional extracapsular cataract extraction in which SIDS was the second most common. Recently, we conducted an audit of patients undergoing phacoemulsification cataract extraction to compare the incidence of SIDS in these patients relative to that found in the ECCE group.

Methods and results

From a computerised departmental database, 666 consecutive patients who had undergone phacoemulsification cataract surgery with intracocular lens (IOL) implantation under a single consultant firm were identified. The case notes were examined and all postoperative complications arising within the first 3 months were documented. The patients' preoperative ophthalmic and general medical histories were also recorded to identify additional risk factors. The results of the study were compared with those from a previously published retrospective study of 682 consecutive patients who underwent conventional extracapsular cataract surgery (ECCE) under the same consultant firm at a time when ECCE was the preferred technique.

Final visual acuities reached 6/12 or greater in 80% of phacoemulsification patients and 67% of ECCE patients. The commonest complications occurring in both groups and in the National Cataract Surgery Survey (NCSS) 1997–8 are listed in Table 1.

Comment

Ten (1.5%) of the patients who underwent phacoemulsification cataract extraction (including one whose procedure was combined with trabeculectomy) were diagnosed with SIDS. This was approximately half the proportion (21% (3.1%)) of the ECCE group, but was the second commonest complication in both groups of patients. However, it does not feature in the list of postoperative complications reported in the National Cataract Surgery Survey 1997–8. SIDS has previously been described as an underdiagnosed clinical entity and it may be failure to recognise it which explains its absence from the national statistics.

Patients who had undergone previous ipsilateral iris surgery (trabeculectomy, Scheie's procedure, or YAG iridotomy) appeared to be at increased risk, although this only attained statistical significance in the phacoemulsification group (p=0.009). General anaesthesia was associated with higher statistical risk for ECCE patients only (p=0.009). It is unclear why this should have been the case. Intraoperative complications did not increase the risk of developing SIDS, and there was no association with concurrent ocular or systemic disease. The mean age of the SIDS patients in the ECCE group was approximately 11 years younger than that in the phako group (62.5 vs 73.6). It is our practice to take a thorough history from the postoperative patient. Severe pain, especially that waking the patient from sleep, is a common feature. Examination of the patient both on the slit lamp and in daylight is conducted, the latter to recognise the characteristic violaceous injection of the scleral vasculature. B-scan ultrasonography is performed to measure scleral thickness. Relative thickening compared to the contralateral eye or absolute thickness greater than 1.8 mm supports the diagnosis. Affected patients usually show a favourable response to a combination therapy with oral non-steroidal anti-inflammatory agents, topical steroids, and a topical cycloplegic. SIDS should be considered in the differential diagnosis of a painful red eye postoperatively. Prompt diagnosis and appropriate therapy lead to early resolution of SIDS and improved visual outcome.

Table 1  Postoperative complications requiring intervention

<table>
<thead>
<tr>
<th>Complication</th>
<th>Phako (%)</th>
<th>ECCE (%)</th>
<th>NCSS (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Astigmatism*</td>
<td>–</td>
<td>9.5</td>
<td></td>
</tr>
<tr>
<td>Cystoid macular oedema</td>
<td>1.95</td>
<td>1.3</td>
<td>0.05</td>
</tr>
<tr>
<td>SIDS</td>
<td>1.5</td>
<td>3.1</td>
<td></td>
</tr>
<tr>
<td>Uveitis</td>
<td>1.35</td>
<td>2.3</td>
<td>5.6</td>
</tr>
<tr>
<td>Posterior capsule opacification</td>
<td>0.75</td>
<td>1.9</td>
<td>0.4</td>
</tr>
<tr>
<td>Endophthalmitis</td>
<td>0.6</td>
<td>&lt;1</td>
<td>0.03</td>
</tr>
<tr>
<td>Corneal decompensation</td>
<td>0.3</td>
<td>–</td>
<td></td>
</tr>
<tr>
<td>Subluxed IOL</td>
<td>0.15</td>
<td>&lt;1</td>
<td>0.05</td>
</tr>
<tr>
<td>Iris prolapse/wound dehiscence</td>
<td>0.15</td>
<td>&lt;1</td>
<td>1.2</td>
</tr>
<tr>
<td>Hyphaema</td>
<td>0.15</td>
<td>–</td>
<td>1.1</td>
</tr>
</tbody>
</table>

*Astigmatism requiring suture removal.

References


Total exudative detachment as a first presentation of von Hippel Lindau disease

Von Hippel Lindau disease is a rare condition characterised by retinal and central nervous system haemangioblastomas. It is also associated with renal cell carcinoma, phaeochromocytoma, and pancreatic, and epididymal cysts.

The disease usually presents with neurological symptoms and/or visual disturbance; angiomata if seen in the retina can often be treated in an attempt to prevent progression to retinal detachment.

We report a young girl with von Hippel Lindau disease whose initial presentation was with a total exudative retinal detachment.

Case report

A 14 year old girl presented to the eye casualty department with no perception of light in her left eye. She gave a 2 month history of gradual, painless loss of vision, but had delayed previously mentioning her symptoms. Past ocular history was unremarkable; an optometrist visit a year previously was normal. She was otherwise well.

Slit lamp examination on the left revealed a quiet anterior segment, with retinal folds visible abutting the posterior lens capsule (Fig 1A). The right eye was entirely normal. An ultrasound B-scan showed a left total funnel retinal detachment (Fig 1B). Computed tomograph scan demonstrated normal orbits.

The patient’s identical twin was also present and was examined: both her eyes were normal. At this stage the family history proved helpful. The patient’s father had recently been diagnosed with renal cell carcinoma and pituitary vascular tumours. The paternal line had a cluster of various carcinomas, including three relatives with cerebellar tumours. Further investigation revealed at least one of these to be histologically...
confirmed haemangioblastoma. The possibility of von Hippel Lindau disease was raised and the patient's father was screened: the diagnosis was confirmed with polymerase chain reaction analysis; showing a frame shift mutation (single base pair deletion [G]) in codon 195 (exon 3) of the von Hippel Lindau gene. Subsequent extended family screening has revealed the same mutation in the patient and nine other living relatives (Fig 2), including the patient's identical twin. Five of these relatives have clinical manifestations of the disease, and in one case an asymptomatic stage 1 renal cell carcinoma was diagnosed and successfully resected.

Miss AB's left eye has subsequently developed pupil block glaucoma which is currently well controlled medically. It remains blind with a rigid total retinal detachment. The cause of this detachment is most likely to be an optic nerve or retinal haemangioblastoma; however, no causal lesion was identified on ultrasound or computed tomography (CT).

The few retinal vessels that can be seen (Fig 1A) do not show any abnormality. Her other eye remains normal and screening for signs of the disease elsewhere has proved negative.

Comment
This case highlights the importance of considering von Hippel Lindau disease as a diagnosis when confronted with a patient with an unexplained exudative retinal detachment.

Von Hippel Lindau disease has an autosomal dominant inheritance pattern with an incidence of one in 36 000; with a 70% prevalence of ocular haemangioblastomas. Von Hippel Lindau gene mutation carriers have a 35% probability of visual loss by age 50.1

Ocular angiomas occur commonly in the superotemporal mid-peripheral retina, less commonly on the optic disc (8%), and at the posterior pole (1%).2 If left untreated, lesions can cause vitreous haemorrhage, macular oedema, epiretinal membrane formation, and exudative or tractional retinal detachment. This last complication is well demonstrated in our patient's case, with a 2 month delay between onset of symptoms and first presentation.

Treatment comprises laser photocoagulation of angiomas less than one disc diameter.3 Cryotherapy, or vitreoretinal surgery with trans-scleral drainage and endolaser may be indicated in larger lesions,4 especially if vitreous traction is present.5 Early treatment necessarily offers a better prognosis.

This case underscores the value of taking a good family history in order to detect hereditary diseases, which can then be confirmed with genetic molecular analysis. The importance of identification and subsequent screening of von Hippel Lindau gene mutation carriers (both affected and unaffected) is exemplified in our patient's family—with the potential benefit of early diagnosis and treatment of asymptomatic retinal and cerebellar haemangioblastomas, as well as potentially fatal tumours. The screening should be maintained regularly, as the protean manifestations of von Hippel Lindau disease may occur de novo at any age.6

Figure 2 Family pedigree.

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References

Anomalous venous drainage of a plexiform (pial) arteriovenous malformation mimicking an indirect carotidcavernous sinus fistula

We report a case of a 35 year old man who presented with proptosis of the left globe and congested episceral and retinal veins. We present angiographic evidence to show that the venous engorgement of the left orbit was related to anomalous venous drainage of a previously posteriorly draining parietal arteriovenous malformation (AVM).

Case report
A 35 year old man presented complaining of a 3 month history of a red eye and a 1 month history of progressive swelling and protrusion of the left eye. His only significant past medical history was that of a subarachnoid haemorrhage from an intracranial AVM 7 years previously for which he had undergone stereotactic radiosurgery. Ocular examination revealed a visual acuity of 6/5 in either eye. There was a 5 mm axial displacement of the left globe with normal ocular motility. The proptosis was non-pulsatile, non-reducible, and Valsalva manoeuvre was negative. There was no audible bruit. Anterior segment examination was unremarkable aside from congested episceral vessels. Examination of the fundus revealed dilated and tortuous retinal veins but a normal arterial system. There was no disc swelling.

A computed tomography (CT) scan of the brain and orbits revealed an AVM in the left primary sensory cortex, proptosis of the left globe and a dilated superior ophthalmic vein (Fig 1). A magnetic resonance image (MRI) with angiography confirmed the presence of an AVM in the left periorbital region which was fed by the left middle cerebral artery and the pericallosal branch of the left anterior cerebral artery (Fig 2). The dominant venous drainage was via a large superficial vein upwards to the superior sagittal sinus. Although the AVM did not appear to have changed significantly in overall size when compared with previous angiograms (Fig 3), it was clear that there had been significant changes in the venous structures distant to the AVM. A relative constriction at the junction of the ipsilateral transverse and sigmoid sinuses had developed (Fig 4) and as

Figure 1 CT scan of the orbits showing dilated superior ophthalmic vein. The majority of the venous outflow from the cavernous sinus is via the superior ophthalmic vein which is markedly dilated as seen in this scan.
a consequence there was a relative hold up to the filling of the sigmoid sinus. The AVM therefore now drained anteriorly via a collateral circulation into the cavernous sinus. The later phases of the angiogram revealed that there was relatively little downward venous outflow from the cavernous sinus and the majority of this venous outflow was therefore shunted via the superior ophthalmic vein which was markedly dilated as a consequence. The patient’s symptoms of unilateral proptosis and venous engorgement were therefore a manifestation of increased blood flow through collateral shunts that had developed as a consequence of a stricture in the principal drainage channel of the existing AVM, which itself had not changed significantly in size.

Figure 2  Anterior segment photographs showing the dilated episcleral vessels in the left eye.

Figure 3  Cerebral angiogram dated 1994. A moderately sized arteriovenous malformation is shown fed by branches of the left middle cerebral and anterior cerebral arteries. It is drained by a large superficial vein which continues into the superior sagittal sinus.

Comment

Arteriovenous malformations (AVM) are lesions which consist of racemose networks of arterial and venous channels which communicate directly rather than through a normal capillary bed. These communications are of two types: fistulous and plexiform. In the fistulous type an arterial channel empties directly into a venous channel, while in the plexiform type one or more arterial channels feed a vascular conglomerate that comprises multiple arteriovenous communications from which one or more venous channels emerge as draining veins. The fistulous types are usually supplied by meningeal branches of the external carotid artery and therefore they are also known as dural AVMs. The plexiform type, in contrast, are supplied by branches of the cerebral or cerebellar arteries and hence are also known as pial AVMs. The AVM most commonly encountered by the ophthalmologist is the acquired caroticocavernous sinus fistula, a dural AVM whose characteristic neuro-ophthalmic presentation results from the arterialisation of the orbital venous system. Proptosis and orbital venous engorgement secondary to direct arterialisation of the venous system has also been reported in dural AVMs involving the torcular herophili and the Galenic system. The more common plexiform (pial) AVMs typically present with complications that arise from the massive venous runoff that is generated by the associated arteriovenous shunts—namely, intracranial haemorrhage, seizures, and recurrent headache.

Symptomatic orbital drainage of plexiform (pial) AVMs is rare and when it does occur the AVM is usually in an anterior location. Unilateral proptosis associated with anterior shunting has previously been described in a child with bilateral sigmoid sinus hypoplasia, but has never been described in a patient with a posteriorly located plexiform AVM. Our case is also extremely unusual in that we have angiographic evidence which shows that these collateral channels developed as a result of an acquired stenosis at the junction of the transverse and sigmoid sinus, previously its dominant route of venous drainage. The aetiology of this focal stenosis is unknown. It is unlikely to be a consequence of the stereotactic radiosurgery as the site of the stenosis is remote to the previously treated area. It is more likely that the stenosis represents a response to the chronic endothelial damage that is known to accompany the hyperdynamic circulation of AVMs.

This case serves to illustrate that not all adults who present with proptosis and venous engorgement of the globe have a caroticocavernous sinus fistula and other anomalies of venous drainage must occasionally be considered.

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mal fatiguability of muscles due to deficiency

autoimmune disorder where there is abnor-

Myasthenia gravis is defined as an acquired

an infant

onset of generalised myasthenia gravis.

about 70% cases, ocular symptoms mark the

plegia, both unilateral and bilateral, constitute

Case report

We examined a 10 month old male child who

in childhood myasthenia gravis. Which comprises approxi-

1 Case report

We examined a 10 month old male child who

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Childhood myasthenia gravis in

Myasthenia gravis is defined as an acquired

autimmune disorder where there is abnor-

mal fatiguability of muscles due to deficiency

of acetylcholine receptors caused by circulat-

ing antibodies directed against them. Ocular

myasthenia is a form of myasthenia gravis

clinically involving only the levator palpebrae

superioris, the orbicularis oculi, and the

extraocular muscles. Ptosis and ophthalmople-

zia, or areflexia. On ocular examination, the

patient had moderate ptosis of the right upper

lid with absence of any voluntary movement of the right eyeball. Ocular

movements of the left eye appear to be

normal. The child was attentive to both visual

and auditory stimuli and frequently changed

his head posture to look in the direction of

origin of the visual or auditory stimuli. The

pupillary reactions were normal in both eyes.

In the primary gaze position, the visual axes

of both eyes were parallel (Fig 1). The child

was examined twice after a period of sleep

and similar findings were recorded again.

Examination of the anterior and posterior

segment of both eyes under general anaesthesia

was unremarkable. The forced duction test

was negative. Based on the above findings, a

negative diagnosis of an intracranial space

occupying lesion was made. However, a

contrast enhanced computed tomographic (CT)

scan of the head and orbit revealed no abnor-

malities. Cerebrospinal fluid examination was

also normal.

The child was subsequently subjected to an

diagnosis of childhood myasthenia gravis.

1 0.15 mg/kg body weight intravenously), which was unequivocally definite, with complete resolution of the ptosis

and ophthalmoplegia (Fig 2). A repetitive

stimulation of the left median nerve demon-

strated a significant decremental response

(22%). Subsequently, a serum analysis of anti-

acetylcholine receptor binding antibodies

and modulating antibodies was performed. Ab-

normal titres of anti-acetylcholine receptor

binding antibodies (5.8 nmol/l; normal is less

than 0.8 nmol/l) were present which con-

firmed the diagnosis of childhood myasthenia

gravis. A contrast enhanced CT scan of the

thorax was normal. The child was started on

tablet neostigmine 3 mg once daily along with

oral prednisolone (0.5 mg/kg body weight)

and followed up regularly. Marked improve-

ment of the ptosis and ophthalmoplegia was

observed which persisted at 1 year of follow

up. Systemic steroids were gradually tapered

off after 6 months.

Comment

Our patient was diagnosed to have juvenile

myasthenia gravis, which comprises approxi-

mately 1% of all cases of myasthenia gravis. It

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Phototoxic maculopathy following uneventful cataract surgery in a predisposed patient

Operating microscope light induced foveal damage is a well recognised occurrence following ocular surgery including complicated cataract extraction, complex anterior segment procedures, and vitrectomy surgery.1 An increased risk of phototoxicity is associated with an operating time greater than 100 minutes, increased body and therefore retinal temperature, unfiltered blue light, and hyperoxygenemia.2

We report a patient who developed a phototoxic lesion during routine cataract surgery possibly related to underlying systemic lupus erythematosus (SLE) and hydroxychloroquine treatment. We examine the measures taken to prevent recurrence with second eye surgery and the implications for routine cataract surgery are discussed.

Case report
A 39 year old woman presented with blurred left vision and glare. One year previously she had been diagnosed with SLE for which she had been taking hydroxychloroquine 200 mg and prednisolone 5 mg daily for 18 months. She had bilateral subcapsular cataracts and underwent routine left phacoemulsification and lens implant surgery under general anaesthesia.

Directly after surgery, the patient noted two confluent blind spots immediately below fixation in the left eye. When first seen by us the left visual acuity was 6/9, intraocular pressure was 16 mm Hg, and the eye was quiet with a well centred posterior chamber lens implant. Fundal examination of the left eye showed two well circumscribed areas of coarse mottled retinal pigment epithelial (RPE) disturbance, approximately one and a half disc diameters in size, superotemporal to the fovea (Fig 1). There was no subretinal fluid or haemorrhage associated with these lesions. A fluorescein angiogram supported these findings (Fig 2) and the lesions were felt to be consistent with photic injury.

The patient was keen to proceed with right phacoemulsification and lens implantation because of anisometropia. She had stopped her hydroxychloroquine immediately after the first operation and the following precautions were agreed with the patient before surgery in the second eye: the use of the microscope filter throughout surgery, switching off the second eye: the use of the microscope filter throughout surgery.

Comment
Phototoxic lesions are defined as the retinal lesions produced after a relatively short exposure to an intense light source such as the operating microscope.3 Historically, these lesions were typically located inferior to the fovea as a result of the slight downgaze of the eye during extracapsular cataract surgery and a coaxial microscope beam directed inferor to the fovea.4–6 The incidence of retinal phototoxicity from the operating microscope has been reported at between 0% and 28%, with large series reporting angiographic evidence of retinal phototoxicity in 3–7% of cases.5

Retinal phototoxic lesions first appear as well circumscribed outer retinal whitening (oedema) with mild disturbances of the RPE often with a light border visible after a few days.4 Ophthalmoscopically, a subtle discrete margin can be seen. After the first week, lesions are characterised by coarse alterations of the RPE layer with fluorescein angiography demonstrating characteristic early discrete mottled hyperfluorescence with late staining but no leakage.7

Certain photosensitising drugs, such as hydroxychloroquine, have been reported to predispose to the development of retinal phototoxic lesions. However, there are no published reports of a similar association with systemic photosensitive conditions such as SLE. It has been suggested that patients who have SLE have increased numbers of chromosome breaks and rearrangements correlated with a low molecular weight chromosome damaging agent (clastogenic factor) present in lymphocytes that sensitises them to near ultraviolet light (360–400 nm) light.8 The presence of this photoactivated agent explains why SLE patients show an aggravation of their characteristic skin condition after exposure to sunlight. Certain pharmacological agents, such as hydroxychloroquine, which is used in the treatment of SLE, can also predispose to the development of phototoxicity. The mechanisms behind the predisposition to phototoxicity in humans of chloroquine and its derivatives are less clear. However, it is known that these drugs accumulate in the RPE layer of the retina and can cause drug induced lysosomal abnormalities including diminished vesicle fusion, diminished exocytosis, and reversible “lysosomal storage disease.”4 These two different predisposing mechanisms to phototoxicity presumably coexisted in this patient and may have significantly increased her risk.

References

Figure 1 Left eye showing two well circumscribed areas of coarse mottled retinal pigment epithelial disturbance.

Figure 2 Fluorescein angiogram of left eye.
Several procedures were undertaken to prevent the occurrence of a phototoxic lesion in the second eye. These included the use of ultraviolet filters on the microscope, although air can also be used in the anterior chamber to defocus the light from the retina as can light barriers on the cornea or in the microscope. The time and power of coaxial illumination from the microscope was minimised by turning the microscope off when instruments were not in the eye, and the patient’s eye was kept in downgaze so that the operating microscope’s axis was aligned off the patient’s visual axis so that any phototoxic lesion would be extraveeal and not cause a homonymous scotoma. Since animal studies have demonstrated a benefit of altering core ocular temperature,1 the patient’s body temperature was kept low to reduce the temperature within the eye. Alternatively, irrigation solutions may be cooled relative to room temperature to help reduce intraocular temperature. It has been shown that an increase in inspired oxygen markedly enhances retinal phototoxicity and so a low inspired oxygen concentration was used for the patient during the procedure.1 The patient discontinued hydroxychloroquine treatment following the surgery to her left eye but ophthalmologists should be aware of the risk of phototoxic retinal lesions in patients taking photosensitising pharmacological agents particularly for underlying potential photosensitising systemic conditions. Consideration should be given to stopping treatment before surgery and taking appropriate surgical precautions.

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References

Bilateral uveitis after intravesical BCG immunotherapy for bladder carcinoma
Intravesical bacille Calmette-Guerin (BCG) is indicated for the treatment and prophylaxis of carcinoma of the urinary bladder and has been associated with arthritis.7 HLA-B27 has been positive in all cases with uveitis.7 We describe a patient who is HLA-B27 negative with isolated bilateral uveitis after intravesical BCG therapy.

Case report
A 70 year old man presented to the eye casualty department with a 4 day history of bilateral, red, painful, and photophobic eyes. He had no systemic complaints. He had no ophthalmic history of note. He had a medical history of hypertension, gout, and recurrent papillary transitional cell carcinoma of the bladder. Eight weeks previously he had been seen by a urologist for haematuria and increased frequency. A diagnosis of recurrent papillary cell carcinoma was made by cystoscopy and biopsy. A 6 week course of weekly intravesical BCG therapy was commenced. His medications on presentation were Adalat (nifedipine) and amlopidine. He was allergic to penicillin and aspirin.

On ocular examination his visual acuities were 6/12 right eye and 6/6 left eye. A diagnosis was made of bilateral anterior uveitis. He had 2+ cells and posterior synechiae bilaterally. No keratic precipitates were seen. He had a right sided epipretinal membrane.

Laboratory studies showed an erythrocyte sedimentation rate of 66 with the rest of haematological studies normal. Biochemistry showed a raised sodium, urea, and creatinine, which were longstanding. Tests for anti-nuclear antibodies and rheumatoid factor were negative. Angiotensin converting enzyme was normal and Treponema pallidum antibodies were not detected. HLA-B27 was negative. Chest and pelvis radiographs were normal. His uveitis was resolved completely on topical steroid therapy and mydriatics. There was no recurrence of his uveitis over the subsequent follow up period of 3 months.

Comment
There have been no reported cases of intraocular BCG causing isolated uveitis in a patient that is HLA-B27 negative. There have been 26 reported cases of reactive arthritis secondary to intravesical BCG.7 About 8% of these cases were associated with uveitis.7 All the reported cases of combined arthritis and uveitis were HLA-B27 positive.7 8 In the BCG related arthritis the mean time of presentation was 10.5 days after the last BCG therapy.9 Our patient started having ocular symptoms 10 days after his last BCG therapy.1 A review of 1278 patients treated with intravesical BCG for bladder cancer, 95% had no complications.1 There were no reported cases of uveitis. Arthritis and arthralgia accounted for 0.5% of the complications.1


Intravesical BCG contains live attenuated Mycobacteria bovis bacillus Calmette-Guerin used to treat bladder cancer.10 This was proved microbiologically and histologically. This presentation was delayed with the patient presenting 14 months after his last intravesical BCG therapy. Intravesical BCG contains live attenuated mycobacteria. The intravesical BCG promotes a local acute inflammatory and subacute granulomatous reaction with macrophage and lymphocyte infiltrates in the superficial bladder.10 The exact mechanism of action is unknown but the antiinflammatory effect seems to be T lymphocyte dependent.12 This enhanced cell mediated immunity results in recognition and suppression of neoplastic cells.12 It has been hypothesised that the systemic inflammatory response is seen as part of an immune response initiated by BCG and then continued by cross reactivity with particular host proteins presented by the class I MHC receptor.12

It is impossible to definitively prove that intravesical BCG caused our patient’s bilateral anterior uveitis. The possibility of an infective aetiology by active mycobacterium must also be considered. If this were the case, definitive diagnosis could have been established by sending a specimen of aqueous for acid fast staining, culture, and polymerase chain reaction (PCR).13 It is plausible that intravesical BCG can cause acute inflammatory and hypersensitivity reactions in the eye secondary to a systemic inflammatory response.13 Contrary to previous thought, HLA-B27 need not be a determining factor for uveitis associated with intravesical BCG.1 This is the first case of isolated bilateral anterior uveitis presumed secondary to intravesical BCG in a patient who is HLA-B27 negative.

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References

NOTICES
Childhood blindness
The latest issue of Community Eye Health (No 40) discusses new issues in childhood blindness, with an editorial by Clare Gilbert, senior lecturer at the International Centre for Eye Health. For further information please contact: Journal of Community Eye Health, International Centre for Eye Health, Institute of Ophthalmology, 11–43 Bath Street, London EC1V 9EL, UK (tel: +44 (0)20 7608 6910; fax: +44 (0)20 7250 3207; email: eyeresource@x.ucl.ac.uk; website: www.jceh.co.uk). Annual subscription (4 issues) £235/US$40. Free to workers in developing countries.

International Centre for Eye Health
The International Centre for Eye Health has published a new edition of the Standard List of
Medicines, Equipment, Instruments and Optical Supplies (2001) for eye care services in developing countries. It is compiled by the Task Force of the International Agency for the Prevention of Blindness. Further details: Sue Stevens, International Centre for Eye Health, 11–43 Bath Street, London EC1V 9RL, UK (tel: +44 (0)20 7608 6910; email: eyeresource@ucl.ac.uk).

Second Sight

Second Sight, a UK based charity whose aims are to eliminate the backlog of cataract blind in India by the year 2020 and to establish strong links between Indian and British ophthalmologists, is regularly sending volunteer surgeons to India. Details can be found at the charity website (www.secondsight.org.uk) or by contacting Dr Lucy Mathen (lucymathen@yahoo.com).

Specific Eye Conditions (SPECS)

Specific Eye Conditions (SPECS) is a not for profit organisation which acts as an umbrella organisation for support groups of any conditions or syndrome with an integrat eye disorder. SPECS represents over fifty different organisations related to eye disorders ranging from conditions that are relatively common to very rare syndromes. We also include groups who offer support of a more general nature to people with retinitis pigmentosa and their families copy with the everyday concerns caused by retinitis pigmentosa. This service is especially valuable for those recently diagnosed with retinitis pigmentosa, and all calls are taken in the strictest confidence. Many people with retinitis pigmentosa have found the Society helpful, providing encouragement, and support through the Helpline, the welfare network and the BRPS branches throughout the UK. (tel: +44 (0)1280 821 334; email: lynda@brps.demon.co.uk; web site: www.brps.demon.co.uk)

3rd Interdisciplinary Symposium on the Treatment of Autoimmune Disorders

The 3rd Interdisciplinary Symposium on the Treatment of Autoimmune Disorders will be held in Leipzig, Germany on the 6–8 June 2002. Topics to be covered include: basic aspects of autoimmune diseases, experimental therapeutic concepts, and clinical studies providing novel concepts or a novel focus on established therapies. There will also be the presentation of the Nils-Illa-Richter Award (application deadline is April 2002, further details on the web site). Further details: Prof. Dr. med. Michael Sticherling, Department of Dermatology, University of Leipzig (email: sticm@medizin.uni-leipzig.de; website: www.autoimmun.org); Fördergesellschaft zur Therapie von Autoimmunerkrankungen e.V. (email: autoimmun.org@gmx.de).

International Society for Behçet’s Disease

The 10th International Congress on Behçet’s Disease will be held in Berlin 27–29 June 2002. Further details: Professor Ch Zouboulis (email: zoubbere@zedat.fu-berlin.de).

Singapore National Eye Centre 5th International Meeting

The Singapore National Eye Centre 5th International Meeting will be held on 3–5 August 2002 in Singapore. Further details: Ms Amy Lim, Organising Secretariat, Singapore National Eye Centre, 11 Third Hospital Avenue, Singapore 168751 (tel: (65) 322 8374; fax: (65) 227 7290; email: Amy_Lim@snec.com.sg).

BEAVRS Meeting

The next BEAVRS meeting will be held in the Dalmahoy Hotel near Edinburgh on 31 October to 1 November 2002. Further details: Susan Campbell, Medical Secretary, Gartnavel General Hospital (email: susan.j.campbell.wg@northglasgow.scot.nhs.uk).

CORRECTIONS

We regret that an error occurred in a paper that appeared in the May 2001 issue of the BJO by Lauande-Pimentel et al (Discrimination between normal and glaucomatous eyes with visual field and scanning laser polarimetry measurements, 2001;85:586–91).

After revision of the paper the authors found that the published cut-off point of the structural linear discriminant formula (LDF) was incorrect. The original formula described by Lauande-Pimentel et al is:

\[ LDF = -3.131 + (0.994 \times \text{ellipse modulation}) - (0.017 \times \text{the number}) - (0.086 \times \text{average thickness}) + (0.111 \times \text{ellipse average}) \]

The correct suggested cut-off point, defined as abnormal, is <0.43 instead of <-0.547. The use of such formula, with the suggested cut-off point, resulted in an enhancement in the sensitivity (90.4%, specificity = 82.4%) of the scanning laser polarimeter to detect glaucomatous changes.

An error occurred in the article: Additive effect of unoprostone and latanoprost in patients with elevated intraocular pressure Br J Ophthalmol 2002;86:75–9. The authors should have been listed as Tin Aung, Paul T K Chew, Francis T S Oen, Yiong-Huak Chan, Lennard H Thean, Leonard Yip, Boon-Ang Lim, Jade Soh, and Steve K L Seah.

An error occurred in the article: Fluoxetine oral administration increases intraocular pressure. Br J Ophthalmol 1996;80:678. The authors should have been listed as C Costagliola, I. Mastropasqua, I. Steardo, N Testa.