Severe diabetic retinopathy in adolescents

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SUMMARY This paper reports on 9 patients aged 13-18 years (mean 15.4) with severe diabetic retinopathy. Two patients were prepubertal and 4 were going through puberty. Hypertension was present in 2 patients, while 4 had proteinuria. Severe preproliferative disease was present in 3 patients initially and proliferative retinopathy in the remainder. In 5 this retinopathy was considered to be florid. Two patients seen prior to 1975 had pituitary ablation, while those seen after 1975 were treated by extensive argon and xenon arc photocoagulation. Proliferative lesions regressed in both groups. At the latest follow-up 7 of the 9 patients achieved a final visual acuity of 6/9 or better in at least one eye. One patient became blind. Proliferative retinopathy advances rapidly in adolescents, but photocoagulation, as used now, can maintain vision in most.

Severe diabetic retinopathy is rarely reported under the age of 18 because duration of disease before puberty is not thought to be of significance in the development of microvascular disease. Immerslund and Jackson et al. found no cases of proliferative retinopathy before the age of 18 in juveniles with as long as 17 years' duration of diabetes. Indeed, Jackson et al. found that only 14% of their post-pubertal insulin-dependent diabetics had any evidence of retinopathy. This is in contrast to the studies of Malone et al. who found that 75% of their diabetic children had vascular abnormalities noted on fluorescein angiography, with 7% having early proliferative disease in at least one eye. Frank et al., in a well controlled study, found no retinopathy in young diabetics with 0 to 4 years' duration of diabetes, 27% between 5 and 9 years', and 71% with over 10 years' duration. No proliferative retinopathy was noted in patients under age 18. The purpose of this report is to draw attention to the fact that, although rare, severe retinopathy can occur in adolescent diabetics, even before the onset of puberty, and to discuss possible treatment.

Patients

Between 1965 and 1982 9 adolescents with severe retinopathy were seen in the Hammersmith Hospital (HH) Diabetic Retinopathy Clinic (this represents approximately 0·5% of the new retinopathy patients). Details of the medical and eye data are given in Tables 1-3. The age of the 9 adolescents ranged from 13 to 18 years (mean 15·4 years), with a mean age at onset of diabetes of 5·7 years. The mean duration of diabetes was 9·7 years. Seven patients were female and 2 were male. They were followed up for a mean duration of 5·1 years (range 1-17 years). At presentation 6 had proliferative retinopathy, 5 with both new vessels on the disc (NVD) and new vessels elsewhere (NVE). Three had severe preproliferative retinopathy characterised by intraretinal microvascular abnormalities (IRMA), cotton-wool spots,

![Fig. 1 Comparison of initial and final visual acuity of all patients. Diagonal line is 'no change' line; those between it and the vertical axis improved, those between it and the horizontal axis deteriorated.](http://bjog.bmj.com/67/73-79)
venous beading, and extensive intraretinal haemorrhages and microaneurysms.

Visual acuity on presentation was 6/12 or better in 13 of 18 eyes (72%). During follow-up the visual acuity improved or remained stable in all eyes except those of patient 2. She became blind in both eyes due to thrombotic glaucoma. Seven of 9 patients achieved a final visual acuity of 6/9 or better in at least one eye (Fig. 1).

The diabetic control at presentation was poor in 6 cases but improved in 8 during follow-up. In most cases this improvement occurred after switching from single daily injections of insulin to multiple injections or, more recently, to continuous subcutaneous insulin infusion (CSII). With regard to the patients’ pubertal status (Tables 1A, 2A, 3A) at the time of presentation, 2 were prepubertal, 4 were entering puberty, and 3 were postpubertal. The systemic blood pressure was raised in 2 patients, and laboratory values of renal function were normal except for proteinuria in 4 patients (Tables 1B, 2B, 3B). Other systemic illnesses included anorexia nervosa, hyperlipidaemia, and diabetic cardiomyopathy in one patient each. Of the 4 patients who had blood rheology tested 3 had abnormal blood viscosity and one showed abnormal red cell deformability.

**TREATMENT**

The 9 patients could be categorised into 3 groups according to the type of treatment given initially for the severe retinopathy. In group A (Table 1A, B) no specific treatment was given because the retinopathy was at that time of severe background or preproliferative type and diabetic control was poor. In patient 3 the retinopathy improved with better control of the diabetes and hyperlipidaemia. However, in patient 1 the retinopathy became more severe at least temporarily despite optimal control with CSII. In patient 2 the retinopathy initially improved with resolution of the anorexia nervosa
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Table 2A  Pituitary ablation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Referral + year</th>
<th>Last Visit</th>
<th>Management</th>
<th>Control</th>
<th>Pubertal status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initial</td>
<td>After diag. of DR</td>
<td>Before</td>
</tr>
<tr>
<td>4</td>
<td>♀</td>
<td>5</td>
<td>17 1968</td>
<td>Single daily lente</td>
<td>bd Insulin (variable), thyroxine, prednisolone</td>
<td>Poor → Fair</td>
</tr>
<tr>
<td>5</td>
<td>♀</td>
<td>10</td>
<td>16 1976</td>
<td>Single daily lente</td>
<td>bd Insulin, no replacement</td>
<td>Poor → Fair</td>
</tr>
</tbody>
</table>

Table 2B  Pituitary ablation

<table>
<thead>
<tr>
<th>Patient</th>
<th>BP mmHg</th>
<th>Medical data</th>
<th>Visual acuity</th>
<th>Retinopathy</th>
<th>Eye treatment</th>
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</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>S urea mmol/l</td>
<td>S creat. µmol/l</td>
<td>Protein U g</td>
<td>Initial</td>
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<tr>
<td>4</td>
<td>120/70</td>
<td>3-7</td>
<td>69</td>
<td>—</td>
<td>6/5 CF</td>
</tr>
<tr>
<td>5</td>
<td>110/60</td>
<td>6-7</td>
<td>82</td>
<td>—</td>
<td>6/9</td>
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</tbody>
</table>

NVD=new vessel on optic disc. NVE=new vessel elsewhere. TD=traction detachment. RP=retinitis proliferans.

Table 3A  Photocoagulation

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Referral + year</th>
<th>Last visit</th>
<th>Management</th>
<th>Control</th>
<th>Pubertal status</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Initial</td>
<td>After diag. of DR</td>
<td>Before</td>
</tr>
<tr>
<td>6</td>
<td>♀</td>
<td>6</td>
<td>16 1977</td>
<td>Single daily lente</td>
<td>CSII 4/12</td>
<td>bd insulin</td>
</tr>
<tr>
<td>7</td>
<td>♀</td>
<td>3</td>
<td>15 1979</td>
<td>Single daily lente</td>
<td>bd insulin</td>
<td>—</td>
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<tr>
<td>8</td>
<td>♀</td>
<td>1</td>
<td>16 1980</td>
<td>Single daily lente, bd insulin 3 yr</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>9</td>
<td>♀</td>
<td>2</td>
<td>13 1981</td>
<td>Single daily lente</td>
<td>bd insulin, frusemid bd, prazosin TDS, digoxin bd, spironolactone</td>
<td>—</td>
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</table>

(Figs. 2A, B). Ten years later, following erratic control of the diabetes, first macular oedema then proliferative retinopathy developed. Extensive argon and xenon photocoagulation was ineffective in preventing rubeotic glaucoma in both eyes. This lead to complete blindness despite surgical attempts to control the glaucoma.

The 2 patients in group B (Tables 2A, B) were seen in the late 1960s and mid 1970s. Each had an yttrium-90 implant of the pituitary for severe proliferative
Table 3B  Photocoagulation

<table>
<thead>
<tr>
<th>Patient</th>
<th>BP mmHg</th>
<th>Medical data</th>
<th>Visual acuity</th>
<th>Retinopathy</th>
<th>Eye treatment</th>
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<tbody>
<tr>
<td></td>
<td></td>
<td>S urea mmol/l</td>
<td>S creat. µmol/l</td>
<td>Protein U g</td>
<td>Initial L R</td>
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<td>135/90</td>
<td>6-6</td>
<td>61</td>
<td>—</td>
<td>6/5</td>
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<tr>
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<td>110/70</td>
<td>3-1</td>
<td>68</td>
<td>—</td>
<td>6/36</td>
</tr>
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<td>3-2</td>
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<td>9</td>
<td>130/100</td>
<td>6-0</td>
<td>69</td>
<td>1-6</td>
<td>6/18</td>
</tr>
</tbody>
</table>

RPE=retinal pigment epithelium. S/A=same as above.

Retinopathy. In patient 5 argon laser therapy was first attempted, but the proliferative retinopathy became more aggressive in both eyes (Figs. 3A, B). In both patients 4 and 5 the retinopathy regressed following pituitary ablation (Fig. 3C). Both patients had residual areas of retinitis proliferans with mostly fibrous tissue. The vision in the left eye of patient 4 remained poor because of the pre-existing traction retinal detachment involving the macula.

The 2 patients in group C (Tables 3A, 3B) first presented between 1977 and 1981. Three had severe proliferative diabetic retinopathy (PDR) (Fig. 4A), while one had only early NVE (Fig. 4A). Because of the aggressiveness of the retinopathy and the young age of the patients photocoagulation with both argon and xenon was performed. Each eye received between 1500 to 3000 argon burns (mean 2264 burns) as well as 300 to 1000

![Fig. 2](http://bjo.bmj.com/)  Patient 2. A: Fluorescein angiogram of right macula at presentation. Note widespread leakage and capillary nonperfusion.

![Fig. 2B](http://bjo.bmj.com/)  Same as Fig. 2A but 2 years later, shows only a few leaking microaneurysms.
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Fig. 3 Patient 5. A: Fluorescein angiogram of right disc when patient first seen. Shows leakage from new vessels on the disc, venous beading, and dilatation.

Fig. 3B From colour photograph of inferior nasal area of patient seen in Fig. 3A, showing deterioration of disc new vessels after argon laser photocoagulation.

Fig. 3C Disc of patient seen in Fig. 3A following pituitary ablation. New vessels on disc have disappeared.

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xenon burns (mean 565 burns). The retinopathy improved in all cases. In patients 7 and 9 the reduced visual acuity was initially due to macular oedema and ischaemia (Figs. 4B 4C). In patient 7 the oedema resolved, but she remained with subsequent atrophy of the retinal pigment epithelium in both maculae. This accounted for the abnormal final visual acuity. Residual areas of inactive fibrovascular tissue (retinitis proliferans) were noted in patients 6, 7, and 9 (Fig. 4D). In patient 6 visual acuity remained at 6/9 in the left eye due to pre-existing preretinal traction over the macula (Fig. 5).

The general health has been fair to good during the follow-up period in 7 of the 9 patients. The only death occurred in patient 9, due to rapidly progressive nephropathy and cardiomyopathy.

Discussion

The 9 cases reported in the present study are of a much younger age (mean 15.4 years) and with a shorter duration of diabetes (mean 9.7 years) than previous studies have indicated. Among juvenile diabetics the mean age of onset of PDR is said by Beetham5 and Deckert et al.6 to be 29.6 and 36.5 years respectively. This occurred after a mean duration of diabetes of 20.5 years.

The prevalence of PDR among adolescent diabetics is low. Deckert et al.4 found that only 2% of their juvenile diabetics with PDR were under the age of 20. In more recent studies78 PDR was seen in only 2 diabetics (age 18 or under) out of the 267 children and young adults examined. These figures are in agreement with the present series of 9 cases, which represent approximately 0.5% of the new retinopathy patients at the Hammersmith Hospital.

Many authors9-10 believe that good control is essential in preventing the development of severe retinopathy. In 6 of our 9 cases there was a long-standing history of poor diabetic control on
presentation with severe retinopathy. This is consistent with the series of Valone and McMeel, in which 13 of 14 adolescents presenting with severe PDR were poorly controlled. One would therefore expect the retinopathy to improve with good control if diabetic control is of ultimate importance. Yet in all 3 of our cases on CSII the retinopathy continued to progress. It may be that, once diabetic retinopathy reaches a certain stage, good control is no longer an influencing factor. Optimal metabolic control has recently been shown to increase somatomedin levels while decreasing abnormally high growth hormone levels. This change in hormonal balance could stimulate progression of the retinopathy as reported in diabetics on CSII and in children treated for Mauriac's syndrome. The role that hormonal
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may have to be administered under general anaesthesia. After photocoagulation the neovascularisation regressed in all 4 group C patients. Visual acuity improved or remained normal. Thus the visual prognosis can be good if aggressive treatment with both xenon and argon photocoagulation is administered promptly.

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