

Cataracts in childhood leukaemia

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SUMMARY The incidence and severity of cataract were studied in 37 children who had completed treatment for acute lymphoblastic leukaemia. Twelve (32%) had posterior subcapsular lens opacities. Treatment had included corticosteroids and cranial irradiation, but no dose relationship was evident. The boys were more severely affected than the girls. Although none of the lens opacities was optically significant, clinicians should be aware of the potential risk to vision.

Following a recent observation in the United States that three out of 50 treated leukaemic children had small and asymptomatic posterior subcapsular lens opacities it was decided to examine the eyes of children treated for acute lymphoblastic leukaemia at the Hospital for Sick Children, Bristol.¹

Corticosteroids have a well established role in the treatment of leukaemia, and cranial irradiation is now routinely used to prevent meningeal relapse. Since both ionising radiation and steroids are cataractogenic, particular attention was paid to these factors.

Patients and methods

All children who had completed treatment and remained in remission were asked to attend for examination. Best corrected acuities were obtained and pupils dilated with cyclopentolate to allow detailed examination of the lens and retina.

Lens opacities were assessed with a slit-lamp and direct ophthalmoscope and were then carefully drawn to allow sequential assessment. Opacities were graded according to Crews' classification,² and, after taking into account other relevant factors such as squint or amblyopia, an estimate of the optical significance of the cataracts was made.

All assessments were made by one examiner, who was unaware of treatment protocols.

Results

In response to 38 postal requests 37 children aged between 8 and 22 years attended for examination,

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their disease having been diagnosed between 1967 and 1979. All were in remission and off treatment.

Seven of the 14 boys had evidence of posterior subcapsular cataract, but only five out of the 23 girls were so affected. A total of 12 children (32%) had lens opacity.

Crews² divided adult steroid induced cataract into four grades of severity. Only grades I (occasional posterior subcapsular opacities or vacuoles in the central region with or without distortion of the specular reflex) and II (small clusters of posterior subcapsular opacities remaining discrete) were seen. Details are given in Table 1.

All children had received steroids in various dosages and protocols. There was no dosage difference between affected and unaffected children (Table 2). A wide range of dosage was represented in each group. As little as 1.1 g/m² prednisone was associated with cataract, yet one child received 17.6 g/m² without ill effect. Mean daily dosages were not compared in view of the pulsed nature of the treatment.

Likewise both groups had similar doses of cranial irradiation, though the range of dosage was, as

Table 1 *Grades of severity of cataract in affected children*

Patient No.	Boys		Patient No.	Girls	
	Right	Left		Right	Left
1	II	II	8	I	I
2	II	II	9	I	O
3	I	II	10	I	O
4	I	I	11	I	O
5	I	I	12	I	O
6	I	O			
7	O	I			

Table 2 Total steroid dose and total cranial irradiation dose (nominal)

	Prednisone g/m^2	cGy
Lens opacities	6.5 (1.1–15.3)	2290 (2000–2400)
Normal	5.2 (1.1–17.6)	1940 (1800–2400), and 3 patients received none

Table 3 Average age at diagnosis of leukaemia and time after cessation of treatment

	Age at diagnosis (yr)	Time off treatment (yr)
Lens opacities	5.2 (1.8–11)	5.8 (2–10.5)
Normal	6.7 (1.8–15.1)	5.1 (0.3–10.4)

expected, much smaller. The only three children who received no cranial prophylaxis did not have lens opacities. Development of cataract could not be correlated with the radiation field geometry, fractionation, type of machine used, use of sedation, or the observation of restlessness during radiotherapy.

Those with lens opacities were on average younger at the time of diagnosis, but this difference was not significant (Table 3).

One boy with bilateral grade II lens opacities had a visual acuity of 6/15 in each eye, but he was also mentally retarded and highly myopic, and it was considered that the opacities were not fully responsible. The other boys with grade II cataracts had an acuity of 6/6 in each eye.

Discussion

With increasing acceptance that childhood leukaemia is no longer an inevitably fatal disease more attention is being focused on the long-term complications of treatment.³ Posterior subcapsular cataract appears to be one of these, though fortunately the visual consequences have been slight.

It is presumed that lens opacities result from a toxic effect of various therapeutic agents on the lens. Many agents have ocular toxicity⁴; this study has examined two of the most likely candidates.

Black *et al.* first observed the cataractogenic property of steroids in patients with rheumatoid arthritis.⁵ Males predominated, though this finding was not analysed further. Crews confirmed the original observation and noticed a dose relationship.² Dikshit and Avasthi⁶ made a similar observation in children with nephrotic syndrome treated with corticosteroids, and other authors have since contributed their observations.^{7–9}

The dose relationship has not been observed so

consistently as in adults, and a recent study in Leeds did not show such a relationship in children with nephrotic syndrome¹⁰; 14% had cataract and in only one child was vision reduced (to 6/9).

The pathogenesis of steroid cataract remains unclear and there is no animal model.¹¹

The incidence, severity, and localisation of the lens opacities in this study are consistent with a steroid aetiology, but the slight trend to unilaterality raises the possibility of a lateralising cause such as cranial irradiation applied asymmetrically due to head movement or tilt. Even with precise screening the lens would receive a small dose, due both to attenuation of the beam by the shielding and to scatter. X-irradiation causes posterior subcapsular cataract indistinguishable from those observed in this study. Merriam and Focht¹² have extensively studied the subject and correlated severity and time of onset with dosage. The mechanism appears to be inhibition of mitosis in the germinative epithelium of the lens causing cortical opacities after a latent period. The minimum cataractogenic dose in adults is about 200 cGy, but no detailed data exist for children, in whom the lens may be more sensitive.^{12,13}

Examination of two potential cataractogenic influences in this study has revealed no clear aetiology of lens opacities in treated leukaemia. A combination effect would be feasible. Individual susceptibility of certain children is also possible and has been suggested before in reference to steroid cataract.^{6,10} Whatever the mechanism, lens opacities do occur and it is important that clinicians should be aware of the potential threat to sight.

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