

Orbital recurrence of retinoblastoma successfully treated by combined therapy

R R Goble, J McKenzie, J E Kingston, P N Plowman, J L Hungerford

Abstract

Five children with an orbital recurrence of retinoblastoma have been successfully treated by a combination of excision biopsy of the tumour mass, radical orbital radiotherapy, and systemic chemotherapy. Nine previous children, consecutive with the five presented here, died from disseminated retinoblastoma after failure of earlier treatment programmes for orbital recurrence. An aggressive therapeutic approach is justified by this improvement in survival.

Orbital recurrence of retinoblastoma after enucleation has carried a poor prognosis, with the mortality rate ranging from 94 to 100% and a mean survival of 14 months.^{1,2} Deaths occur from the effects of direct extension into the central nervous system and from metastatic disease. Recommended treatment now includes local surgical excision of the recurrent orbital tumour with radical orbital radiotherapy and systemic chemotherapy.¹ We report on five children successfully treated in this manner (for summary of details see Table I).

Case reports

CASE 1

In July 1980 a 17-month-old girl was referred with a squint of recent onset and right leucocoria. An examination under anaesthetic (EUA) revealed bilateral multifocal retinoblastomas. The right eye was enucleated in view of the size of the tumours in this eye. Histological examination showed a poorly differentiated retinoblastoma with evidence of choroidal invasion but no optic nerve involvement.

At a routine follow-up EUA 18 months after enucleation a mass was found in the right socket. Excision biopsy confirmed this to be an orbital recurrence of retinoblastoma. Routine staging investigations including chest x ray, technetium bone scan, bone marrow aspirate, cerebrospinal fluid cytology, and CT head scan showed no evidence of extraorbital spread. The patient was treated with radical orbital radiotherapy to a dose

of 50 Gy in 26 fractions over 40 days and with intravenous vincristine and cyclophosphamide chemotherapy. She has been off treatment for over seven years and remains disease free.

CASE 2

In March 1985 a 7-year-old girl presented with a right panuveitis and secondary glaucoma. Medical treatment failed, and four months after presentation she underwent cyclocryotherapy, lensectomy for secondary cataract, and biopsies of some iris nodules and a white friable mass at the inferior ora serrata. These indicated a diagnosis of retinoblastoma, and the eye was enucleated.

Eight months after enucleation the patient was referred to this centre with a right orbital mass. A recurrence of retinoblastoma was confirmed by excision biopsy. Staging investigations were negative for metastatic retinoblastoma, and she received orbital radiotherapy to a dose of 44 Gy in 22 fractions over 30 days together with systemic chemotherapy with vincristine, cyclophosphamide, cisplatin, etoposide (OPEC protocol), and intrathecal methotrexate. She has been off treatment for over three years and remains well and disease free.

CASE 3

A 6-year-old girl was noticed to have right leucocoria in July 1986. Coats's disease was suspected, and a transcleral biopsy was performed. Histological examination revealed a retinoblastoma, and the eye was enucleated. Extension of necrotic tumour tissue through the biopsy site was noted.

The patient was referred to this centre three months later with a right orbital mass. Excision biopsy of the lump confirmed an orbital recurrence of retinoblastoma, and systemic staging investigations showed no evidence of metastatic spread. The patient was treated by orbital radiotherapy to a dose of 45 Gy in 23 fractions over 37 days and received systemic chemotherapy according to our OPEC protocol together with intrathecal methotrexate. She remains disease free 27 months off treatment.

CASE 4

A 2½-year-old boy was referred in January 1987 with a suspected orbital recurrence of retinoblastoma nine months after a left enucleation and insertion of a Castroviejo implant. The enucleated specimen showed no evidence of transcleral or optic nerve spread. On examination a diffuse mass was detected anterior to the implant which was calcified on orbital CT scan.

TABLE I Summary of cases

Case	Sex	Age at diagnosis of RBL (months)	Interval from enucleation to recurrence (months)	Disease status (time off treatment in months)
1	F	17	18	CR (84)
2	F	92	8	CR (38)
3	F	72	3	CR (27)
4	M	19	9	CR (24)
5	F	5	6	CR (8)

RBL=retinoblastoma. CR=complete remission.

St Bartholomew's
Hospital, London,
Department of
Ophthalmology
R R Goble
J McKenzie
J L Hungerford

Department of Paediatric
Oncology
J E Kingston

Department of
Radiotherapy
P N Plowman

Moorfields Eye Hospital
J McKenzie
J L Hungerford

Correspondence to:
Mr John Hungerford,
Department of
Ophthalmology,
St Bartholomew's Hospital,
West Smithfield, London
EC1A 7BE.

Accepted for publication
23 August 1989

Excision biopsy of the mass provided histological confirmation of the diagnosis of recurrent orbital retinoblastoma, but subsequent staging investigations showed no evidence of extraorbital spread. The patient underwent radical orbital radiotherapy to a dose of 40 Gy in 20 fractions over 28 days together with systemic and intrathecal chemotherapy. He remains disease free two years after completion of treatment.

CASE 5

A 5-month-old girl developed a right convergent squint and leucocoria in December 1987. Unilateral retinoblastoma was diagnosed and the right eye was enucleated. Histologically the resected end of the optic nerve was free from tumour, but a cluster of tumour cells was found round a vessel in the sclera on sectioning.

Six months after the enucleation the patient was referred to this centre with a swelling of her right upper eyelid. Following excision biopsy and routine staging investigations a diagnosis was made of orbital recurrence of retinoblastoma with no extraorbital spread. Orbital radiotherapy was limited to 34 Gy in 17 fractions over 26 days by a marked skin reaction. She received adjuvant systemic and intrathecal chemotherapy. There is no evidence of disease on follow-up eight months after completion of therapy.

Discussion

In a previous study from the Paediatric Ocular Oncology Units of St Bartholomew's and Moorfields Eye Hospitals 10 patients were described who had no evidence of extraorbital spread at the time of diagnosis of orbital recurrence of retinoblastoma.¹ Of these 10 the first nine died from disseminated retinoblastoma. The tenth patient was treated by excision biopsy of the orbital recurrent tumour, radical orbital radiotherapy, and systemic chemotherapy. She is the index patient of the present series (case 1).

In our previous reported study¹ distant relapse was by far the commonest cause of death follow-

ing orbital recurrence of retinoblastoma, and this was also found in Reese's series of 25 patients, none of whom survived despite treatment by orbital exenteration and radical orbital radiotherapy.³

In our previous study¹ three out of four exenterations for orbital recurrence were found to be incomplete histologically. One child, who received chemotherapy but no radiotherapy after incomplete exenteration, died from direct intracranial extension of retinoblastoma despite having no evidence of widespread tumour on re-presenting with an orbital recurrence.¹ After the survival of case 1 the next four patients to present with an orbital recurrence were treated in a similar way. The success of the new therapeutic approach may be justified by the fact that nine consecutive deaths after previous treatment methods have been followed by five consecutive survivors from recurrent retinoblastoma in the orbit when we adopted a more aggressive regimen. To date, where treatment failed, all deaths from orbital recurrence have occurred within two years and most within one year. Four out of the five patients treated with our new regimen have survived more than two years and are hopefully cured.

We would suggest that orbital exenteration is unlikely to achieve complete surgical clearance of all recurrent tumour, radical orbital radiotherapy will not prevent the development of metastatic diseases, and that chemotherapy alone cannot eradicate residual orbital disease. Accordingly we would recommend that simple excision biopsy of the orbital tumour mass should be performed and that this should be combined with radical orbital radiotherapy and systemic chemotherapy.

Mr J L Hungerford and Dr J E Kingston gratefully acknowledge the support of the Imperial Cancer Research Fund.

- 1 Hungerford JL, Kingston JE, Plowman PN. Orbital recurrence of retinoblastoma. *Ophthalmic Paediatr Genet* 1987; 8: 63-8.
- 2 Reese AB. *Tumors of the eye*. New York: Harper and Row, 1963: 155-6.
- 3 Reese AB. *Tumours of the eye*. London: Cassell, 1951: 138.



Orbital recurrence of retinoblastoma successfully treated by combined therapy.

R R Goble, J McKenzie, J E Kingston, et al.

Br J Ophthalmol 1990 74: 97-98
doi: 10.1136/bjo.74.2.97

Updated information and services can be found at:
<http://bjo.bmj.com/content/74/2/97>

	<i>These include:</i>
References	Article cited in: http://bjo.bmj.com/content/74/2/97#related-urls
Email alerting service	Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Notes

To request permissions go to:
<http://group.bmj.com/group/rights-licensing/permissions>

To order reprints go to:
<http://journals.bmj.com/cgi/reprintform>

To subscribe to BMJ go to:
<http://group.bmj.com/subscribe/>