Radiation chorioretinopathy

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SUMMARY Three cases of postradiation retinopathy are reported. The findings are analysed. The exudates described by many authors are really infarcts of the choroid lobules. Chorioretinopathy is proposed as a better descriptive term, and three types are suggested. Diagnosis of the condition is important to spare unnecessary enucleation, as the infarcted areas may resemble a recurrence. Predisposing factors are discussed.

Radiation retinopathy might occur as a reaction to irradiation after cobalt-60 local application to a retinoblastoma. The condition usually occurs several months or years after the presumed complete cure of the tumour, and it produces a more or less marked disturbance of vision which causes great alarm to both the patient and the doctor. The following cases demonstrate the series of events caused by such a complication.

Case reports

CASE 1

A female infant aged 1½ months presented on 18 May 1982 with a central raised mass with ill-defined and irregular margins involving the macular region of the left fundus. The right eye was enucleated because of retinoblastoma in an advanced stage, which proved on pathological examination to be well differentiated. A C-shaped cobalt-60 10 mm diameter applicator was applied over the macular area and embracing the optic nerve on its temporal margin, giving a dose of 19 000 rad over the base of the mass and 4000 rad over its apex. Seven days later the applicator was removed and the mass showed a good response in the form of few haemorrhages on the surface together with some diminution of the size and with well defined margins. A week after that the mass became much smaller and completely avascular, an indication of a good reaction to the local radiation therapy. The patient was followed up every month, with no change in either the size or pattern of the remaining mass.

On 30 November 1983 the mass started to show changes in the form of minute haemorrhages on the

surface and around its margins; deep, white patches had appeared around the mass and throughout the fundus, together with intervening telangiectases. The white patches were well defined, avascular, and deep to the retinal vessels. They were separate and appeared as a mosaic, but some coalesced to form relatively large triangular areas with the apex towards the optic disc. At the periphery some patches were large and pearly in appearance and were suspected of being recurrences. One month later the lesions were more severe, with an increase in the haemorrhages and telangiectatic vessels, while the mass remained small in size but covered with haemorrhages.

A course of external beam irradiation was started one week later, as the condition was wrongly diagnosed as a recurrence. After 12 sittings of this treatment, when the eye had received another 4000 rad, the fundus showed severe telangiectasis and diffuse haemorrhages, some of them preretinal, throughout the central and peripheral regions. Some of the preretinal haemorrhages were observed to increase in size when the eye was slightly pressed during movement to facilitate examination of the periphery.

Three months later the massive haemorrhages were completely absorbed, but few small haemorrhages and telangiectatic vessels remained. Recurrences in the form of small or large haemorrhages occurred every now and then, probably owing to pressure on the eye by the patient affecting thin walled telangiectatic vessels. The deep white patches remained, though they were small and had a slightly pigmented dimpled centre. The optic nerve showed atrophy, and the patient's vision deteriorated to hand movements. The patient is still under observation and has shown no subsequent changes.

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CASE 2

A male infant 7 months old presented with a large mass in the left macula. The right eye was normal. On 10 November 1982 a C-shaped cobalt-60 applicator 15 mm in diameter was applied over the macula and embracing the optic disc. Seven days later the applicator was removed and the mass showed marked improvement. It became smaller and showed well defined margins and a nodular surface indicating areas of calcification.

Routine follow-up was carried out weekly, bi-weekly, and monthly, with the mass showing continual reduction in size and increase in calcium deposition. From the start the patient was given a course of chemotherapy.

Six months later and while the patient was still under chemotherapy the nasal side of the mass started to show a few haemorrhages, and a recurrence was suspected. Two weeks later a course of external beam irradiation of 1500 rad was started on the assumption that the previous local irradiation had been insufficient for such a relatively large mass. One month later haemorrhages on the surface of the mass and throughout the fundus were seen, together with deep polygonal white patches of different sizes giving in some areas a mosaic appearance, choroidal in nature, and deep to the retinal vessels. Haemorrhages and telangiectatic superficial retinal vessels were present throughout the fundus. At the end of the irradiation course most of the telangiectatic vessels had disappeared, but many deep white patches remained.

Three months later haemorrhages started to appear again over and in the retina surrounding the mass but not at the periphery of the fundus. These absorbed after a short time, to reappear every now and then. As the patient was under chemotherapy a cytomegalovirus retinopathy was suspected, but cultures from saliva and urine were negative. When the condition was discovered, the chemotherapy was not stopped, as a recurrence was suspected.

CASE 3

A 40-day-old male baby presented on 4 December 1979 with an advanced retinoblastoma in the left eye which necessitated enucleation. Examination of the right fundus revealed a crescentic mass embracing the upper and temporal area of the optic disc margin. Photocoagulation was done, but, as the mass was considered to be incompletely affected, a C-shaped, 7 mm diameter applicator was inserted above and temporal to the optic nerve. The mass responded satisfactorily, and the patient was considered to be completely cured. A monthly routine follow-up was carried out.

On 27 January 1981, that is about one year after

insertion of the cobalt-60 plaque, a black circular pigmented patch about 1.5 disc diameters was seen outside the macular area. The patch was flat, polygonal, and had a slightly raised irregular white mass at its upper and medial margin. Its centre was dimpled and faintly pigmented (Fig. 1). A recurrence was suspected, and a routine examination at short intervals was resumed. Six months later a few telangiectatic vessels were discovered above and temporal to the peripapillary mass.

The clinical picture remained unchanged for about two years, but on 12 April 1983, that is just over three years after application of the disc, an unusual picture was seen. Several white patches of regular polygonal margins close to each other and in mosaic formation covered the area above the macula and reached the previously detected lesion (Fig. 2). The new patches were not pigmented, were of various sizes, and were shallow at the centre. A few coalesced, and some were large, measuring about 2 disc diameters. They were all deep to the retinal vasculature. After a time certain changes occurred. The first patch to be discovered became white, with only a trace of pigment at its shallow centre. The other patches have remained unchanged up to the present.

Discussion

Radiation retinopathy is not often noted as a complication of radiotherapy for malignant melanoma or

Fig. 1 A late stage of the early choroidal infarct (arrow) together with the newly developed infarcts.

Fig. 2 Choroidal infarcts forming a mosaic with regular polygonal margins bridging the region above the macula.

retinoblastoma. Reese¹ refers only to postradiation vascular changes, while Ellsworth² relates the condition to vascular necrosis produced by damage to the endothelium of the retinal vasculature.

Stallard^{3,4} states that complications due to radiation therapy by application of cobalt-60 discs in the treatment of retinoblastoma occur when a large dose is applied, and especially if there is more than one mass or if the tumour is large or embraces the large branches of the central retinal artery. At the same time he refers to the role of the early vascular damage in destruction of the tumour mass. This vascular damage includes both a narrowing of the small vessels and rupture of the capillaries. He reported 15 cases of late complications of radiation. The delay before their appearance ranged from 9 to 18 months and even 4-5 years in one case. The resulting haemorrhage may be very small or large enough to necessitate enucleation. In four of his cases perivascular exudates occurred—after 11 months in two cases and after three years in a third, and with circinate form in the fourth. The exudates were chiefly present in the inner nuclear layer. He related the macular changes to choroidal vascular involvement.

MacFaul and Bedford⁵ reported on the delayed effect of radiation treatment of intraocular tumours. They stated that radiation retinopathy rarely occurs after irradiation of the whole eye and that retinal and choroidal changes are seen commonly after local irradiation of retinoblastoma or malignant melanoma and are usually apparent some months after the completion of the treatment. The vascular

changes were narrowing and obliteration of the retinal arteries, veins, and capillaries, with perivascular sheathing if massive radiation had been carried out, especially if the plaque was applied a few millimetres from the optic disc. Haemorrhages and exudates appeared early and sometimes late in and around the treated area after focal irradiation of a juxtapapillary retinoblastoma. Exudates are generally hard and white, presumably owing to phagocytosis of the tumour debris or haemorrhage together with infarction of choroid and retinal tissue close to the tumour.

In a study of the fundus by fluorescence angiography in three cases of malignant melanoma treated with cobalt plaque in which postradiation retinopathy occurred Hayreh⁶ concluded that the retinopathy takes various forms: a focal obliteration of the capillaries due to endothelial damage, microaneurysms or telangiectasia or both, and neovascularisation. Cotton wool spots sometimes present were thought to be due to focal occlusion of small retinal arterioles producing retinal infarcts. A circular cobalt plaque was applied in his first case, a C-shaped plaque in the second, and possibly a circular one in the third.

Blodi and Watzke⁷ stated that the effect of radiation on the retina and retinal tumours consists of vascular changes mainly in the form of thinning of the vessel wall leading to haemorrhages and in modification of the neoplastic cells.

Char *et al.*⁸ noted that, in five out of seven cases of posterior pole melanoma, radiation retinopathy developed after treatment, with resultant decrease in vision. They stated that this type of retinopathy is a form of occlusive vascular disease with a predilection for capillaries, causing obliteration of the lumen, formation of microaneurysms, telangiectasis, neovascularisation, cotton wool spots, circinate macular exudates, perivasculitis, and haemorrhages. They also stated that radiation retinopathy with a resultant decrease in vision is probably much more common than has been reported, since its onset is usually two to three years after therapy and may be as long as 15 years. Because of this complication they ceased using cobalt plaque in the management of posterior pole melanomas.

C-shaped cobalt plaques were used in the reported cases as a treatment for posterior peripapillary or macular retinoblastoma. This treatment was considered to be more suitable than external beam irradiation with its possible complications to the lens or the surrounding skin of the orbit. It has now been discontinued, as the three reported cases showed a typical postradiation retinopathy described by the above mentioned authors.

My interpretation of the accompanying so called

exudates is different. These exudates are actually choroidal infarcts of different sizes according to the size of the affected choroidal terminal arteriole. The choroidal lobules, so called by Hayreh,⁹ with their central terminal arterioles act as separate physiological units and become infarcted if the supplying vessel is occluded. Infarcted lobules become white and have a polygonal outline; together with neighbouring infarcted lobules they form a mosaic having the same appearance as is seen during fluorescein angiography of the normal choroid.

Choroidal infarcts, like cerebral infarcts, are usually initially white, because there is hardly any anastomosis and the vessels occluded are so small that obliteration is usually complete from the start. Actually the grey and yellow exudates described by Blodi & Watzke⁷ are choroidal infarcts, as their figs. 2, 3, and 4 show.

If a large choroidal vessel is involved, all the lobules supplied by this vessel become infarcted, producing the diffusely oedematous triangular areas with the apex towards the central region described by Amalric.¹⁰

Because of oedema due to rapid onset of the infarction the margins of the lobules coalesce, and the area looks as if it is one large patch. When the oedema subsides, the area resumes its mosaic form.

The condition can be considered as a chorioidopathy due to a late toxic effect of radiation treatment. It is usually accompanied by the characteristic retinopathy, as in cases 1 and 2, but sometimes it occurs alone or with only very little retinopathy as in case 3. The condition should be termed radiation chorioretinopathy, as the choroid is nearly always constantly involved.

Postirradiation toxicity may be divided into two types:

Type 1. Early radiation toxicity. This is common and occurs in nearly every case. It is a good sign, as it denotes the necrosis of the tumour with rupture of its capillary contents.

Type 2. Late radiation toxicity. This may be (a) mainly retinopathic, which is uncommon; (b) mainly choroidopathic, which is rare; or (c) chorioretinopathic, which is the commonest.

The late type may occur months or even years after the irradiation. Sometimes it comes in episodes; each

is probably predisposed to by small unnoticed traumata such as rubbing the eye, which cause bleeding from the extremely friable telangiectatic small vessels and capillaries.

It seems that the application of a cobalt plaque, especially the C-shaped type, over masses in the macula or near the disc causes direct pressure on the main ciliary and retinal vessels which are present in this area. This is why it is agreed that tumours in this region should be treated by other means if possible such as photocoagulation or external beam irradiation. However, the retinopathy occurred in one unreported case which had the plaque applied at the equator and in another case in which external beam irradiation was the only treatment. It thus seems that factors other than overdosage or proximity to the macula or the optic disc may play a part in producing the condition. As the retina is a part of the nervous system, one should not be surprised by the similarity of the late radiation effect to that which occurs in the brain or the spinal cord after radiation, either directly or to neighbouring structures.¹¹

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