COMMUNICATIONS

IMPLANTATION IRRADIATION OF EPITHELIOMATA OF THE EYELIDS AND ADJACENT AREAS*

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As far as is known the first description of a rodent ulcer was given by Jacob† (1827), who stated: "The characteristic features of this disease are the slowness of its progress, the peculiar condition of the edges and surface of the ulcer, and the comparatively inconsiderable suffering produced by it, its incurable nature except by extirpation, and it not contaminating the neighbouring lymphatic glands".

Apart from Jacob's comment that extirpation is the only cure, which fortunately no longer holds true, this description of a rodent ulcer remains accurate.

It is now seldom the lot of the ophthalmic surgeon to treat lesions as gross as that illustrated by Jacob, but he frequently has to deal with the condition in an early stage.

The guiding principles for the modern therapeutic approach to malignant lesions of the eyelids are to obtain complete obliteration of the growth and to insure against recurrence while maintaining full function of the eye and its adnexa with the best possible cosmetic result. The accepted methods of treatment are surgical removal, radiotherapy, or a combination of the two. To achieve the major aim of complete cure by excision, the amount of clearance may have to be quite extensive, and much re-constructive surgery is often required to obtain full function and good appearance.

The following series of eighteen cases is designed to demonstrate the effectiveness with which implanted radiation material will deal with basal cell or squamous epitheliomata on the eyelids or in the region surrounding the orbit without causing gross functional impairment or disfigurement.

PLACING OF RADIATION SOURCE

The surgeon should aim at inserting the needles adjacent to the lesion on its deeper aspect, so that the affected area is completely covered by the

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† Jacob founded two Eye Hospitals in Dublin, The Institute for the Curing of Diseases of the Eye and Ear (1817) and the Ophthalmic Hospital (1828); later, in 1831, he helped to start the present Royal City of Dublin Hospital.

radiation material. If the lesion is small, two needles or seeds in close parallel will suffice, the length of the needles depending on the extent of the epithelioma (Fig. 1*a*).

FIG. 1(*a*).—Two parallel needles.

FIG. 1(*b*).—Needles enclosing the lateral canthus.

Larger lesions may require three or more needles, according to the surface area involved. If the growth extends more deeply it may be necessary to place the needles in two planes enclosing a cube or block of tissue. In Case 2, a lesion of the lateral canthus required seeds occupying four sides of a pentagon leaving the medial part adjacent to the eyeball free (Fig. 1*b*).

In all the cases described a radiograph was taken of the needles or seeds in position from which the physicist could estimate the rate of dosage (Figs. 2*a*, *b*).

FIG. 2(*a*, *b*).—Radiographs of needles in position

METHOD OF INSERTION OF NEEDLES OR SEEDS

A skin incision is made large enough to admit the needle, and through this an iris repositor is pushed to form a tunnel to accept the needle. All the needles and seeds should be threaded to maintain them in position and to facilitate withdrawal, the threads being anchored to the skin by adhesive plaster. Sutures inserted into the skin and strapped to the forehead or cheek will serve to retract the eyelid being treated; a canthotomy may be necessary to mobilize the lid.

EIGHTEEN CASES TREATED BY IMPLANTATION IRRADIATION FOR RECURRENCE AFTER SURGICAL REMOVAL (Table)

In three cases (1, 11, 15) treatment was required for recurrence after apparently complete surgical removal, and in four further cases (4, 5, 8, 10) because of doubtful or incomplete clearance of the neoplastic tissue by surgery. In Case 14 (Fig. 3), there was some doubt at the time of surgery whether complete clearance had been obtained. This was clinically diagnosed as a case of molluscum sebaceum because of the appearance, mode of onset, and short history, but histologically this diagnosis, although not completely excluded, could not be confirmed by the pathologist who advised that the tumour should be treated as a carcinoma. As the lesion continued to be inflamed and to discharge 3 months after the attempted extirpation, a surgical opinion was sought. The advice received in consultation with the dermatological and radiological departments was for a wide excision of the upper eyelid; this was preferred to radiotherapy because of the danger of producing a cataract. It was pointed out that—provided that the lid was retracted sufficiently—the chance of damage to the eye by implanted radiotherapy was much less than if the major portion of the eyelid was removed. Treatment by radium was carried out, and examination of the lenses 7 years later showed no clinical evidence of cataract. Moreover the eyelid, with minimal evidence of the disease or treatment, is cosmetically and functionally excellent (Figs 4 and 5).

FIG. 3.—Case 14, before operation.

FIG. 4.—Case 14, after operation, lid open.

FIG. 5.—Case 14, after operation, lid closed.

COMPLICATIONS

(a) *Lens Change*.—In Case 3 three radon seeds were implanted to the medial part of the right lower eyelid for a rodent ulcer. A cortical change in the infero-nasal quadrant of the lens was detected 4 years later. This opacity had not appreciably changed after a further $3\frac{1}{2}$ years, and the visual acuity was then 6/9 in each eye. It is not certain that some lens change was not present before radiation was applied, and there is no note indicating whether the eyelid was retracted sufficiently at operation to avoid the possibility of radiation cataract. This patient, who was aged 49 at the time of treatment, sustained an occlusion of the central retinal vein of the right eye 5 years and

3 months after the operation. Her blood pressure was 165/70 and the other eye showed marked nipping of the retinal veins at the arterio-venous crossings. In view of the hypertension and arterial changes it is quite probable that the thrombosis of the central retinal vein was incidental to the irradiation to the right lower eyelid. The distance between the thrombosis and the source would make the radiation received at the site of the occlusion of negligible intensity, particularly as there was no subsequent stenosis of the tear passages despite the seeds being placed within 3 mm. of the canaliculus.

No other patient developed a lens change. Case 7 was noticed before treatment to have some coronary congenital lens opacities, and this appearance was unchanged when he was last examined $2\frac{1}{2}$ years later, when the visual acuity in the treated eye was 6/6.

(b) *Pain*.—Cases 11, 14, and 15 admitted to some degree of discomfort. Two of them were not particularly disturbed by these symptoms, but the third (Case 14—suspected of having molluscum sebaceum) did have some pain in the region of the affected eye 18 months after irradiation with 6,000 in 4 days (Figs 3, 4, 5). This pain was diagnosed as an “atypical neuralgia” and disappeared after treatment with Bellargal tablets for one month; 7 years later the patient was still free from symptoms but suffered an occasional mild attack of episcleritis. It had been noted at the first ophthalmological examination in May, 1955 (*i.e.* 4 months before radiation), that there was bilateral superficial corneal scarring with marginal vascularization, so that the subsequent attacks of mild episcleritis were unconnected with the irradiation.

(c) *Epiphora*.—Case 16 (Fig. 6), who presented with a large excavating ulcer at the inner side of the medial canthus, has never been particularly worried by epiphora since his treatment, although his tear ducts are probably at least partially blocked. There did appear to be some measure of patency on syringing $3\frac{1}{2}$ years after treatment (Figs 7 and 8), although the radium needles had been placed within 2 or 3 mm. of the lacrimal passages. 6 years after therapy the patient was quite comfortable with no sign of recurrence.

FIG. 6.—Case 16, before operation.

FIG. 7.—Case 16, after operation.

FIG. 8.—Case 16, general appearance after operation.

Case 3 (Fig. 9) had three radon seeds placed within 3 or 4 mm. of the lower lacrimal punctum without subsequent stenosis of the canaliculus or epiphora.

(d) *Late Radiation Reaction.*—Cases 3, 16, and 17 had a “late” radiation reaction in the treatment area some months afterwards, which presented as areas of induration about 3 mm. in diameter. These lesions were not painful and cleared in a few weeks with local application of antibiotic ointment. A precautionary biopsy was done in Cases 3 and 17.

(e) *Effects on Skin, Tarsal Plate, and Conjunctiva.*—Cases 11 (Fig. 10) and 16 (Figs 7 and 8) have an avascular appearance of the skin in the treated areas; the appearance is not very noticeable and certainly not more objectionable cosmetically than the results of plastic surgery might be.

FIG. 9.—Case 3, after operation.

FIG. 10.—Case 11, appearance of skin after operation.

In Case 16 the appearance of the area nasal to the medial canthus is probably much better than could have been expected from plastic reconstruction had the necessary generous excision been carried out, since the lesion was deeply erosive.

Case 3 (Fig. 9) had a contracture of the conjunctiva in the lower fornix near the punctum, which is obvious only on eversion of the eyelid, and there is no displacement of the lid margin.

Case 17, who already showed some lid retraction pre-operatively (Fig. 11), had a minor retraction of the lower eyelid 6 months after the operation (Fig. 12), but this was not causing symptoms.

FIG. 11.—Case 17, before operation.

Fig. 12.—Case 17, after operation.

DISCUSSION

The results in the eighteen cases (Table) suggest that a cure rate of 100 per cent. is not improbable with implantation irradiation in the treatment of epitheliomata of the eyelids and adjacent regions without causing appreciable disfiguration.

TABLE
CLINICAL HISTORIES OF EIGHTEEN PATIENTS

Case No.	Date of Treatment	Age (yrs)	Description and Site of Lesion	Type	Therapy	Dosage	Surgery	Follow-up after Radiation (yrs)
1	April, 1952	68	Lump on middle two-thirds of lower lid "for many years"	Basal cell	Radium needles 2×1.3 mg. in a quadrantic field	6,300 r in 5 days 6½ hrs	Resection extending over middle two-thirds 12 months previously	7
2	April, 1952	57	Nodule at outer canthus	Basal cell	Radon seeds 4×1 mc. four sides of a pentagonal area (Medial side free)	5,600 r in 6 days	Biopsy only	7
3	May, 1952	49	"Thickening" at medial part of right lower lid for 6 months	Basal cell	Radon seeds 3×1 mc. one on conjunctival surface, one underneath skin, and one on lid margin	5,200 r in 6 days		10
4	June 1952	57	Small papilliferous mass on outer third right upper lid	Basi-squamous carcinoma	Radium needles 2×0.6 mg. horizontally between tarsal plate and orbicularis muscle	5,000 r in 7 days	Incomplete removal 2 months earlier	7½
5	July, 1952	55	"Wart" on upper lid	Contained carcinoma-tous cells	Radium needles 2×0.6 mg. placed horizontally deep to lesion	In situ 5 days dose approx. 5,500 r	Removal ? incomplete	10
6	June, 1953	50	Indurated lump on right lower lid for 2 years	Probably basal cell	Radium needles 2×0.6 mgm. placed horizontally	5,750 r in 5 days	No histology	2 mths. (went abroad shortly after treatment.)
7	January 1954	57	Recurrent ulceration of nodule on left lower lid	Probably basal cell	Radium needles 2×1.3 and 2×0.6 mg. in a rectangle	6,000 r in 6 days	No histology	2½
8	April, 1954	40	Lump on left upper lid	Squamous cell	Radium needles 2×1.3 mg. placed horizontally	5,400 r in 3 days 18 hrs	Incomplete removal	18 mths
9	July, 1954	?	Marginal ulcer of outer third of left lower lid	Basal cell	Radium needles 4×1.3 and 2×0.6 mg. rectangular field	6,000 r in 5 days	Biopsy	10
10	June, 1954	50 approx	"Wart" on upper lid	Squamous cell	Radium needles 2×0.6 mg. placed horizontally	5,040 r in 6 days	Removal ? incomplete	7

TABLE—continued

Case No.	Date of Treatment	Age (yrs)	Description and Site of Lesion	Type	Therapy	Dosage	Surgery	Follow-up after Radiation (yrs)
11	December, 1953	46	Recurrent ulceration of skin of right lower lid below margin	Basal cell	Radium needles 4 × 0.6 mg. rectangular field	5,500 r in 6 days	Resection and skin graft 18 months previously	6
12	January, 1955	40	Ulcerated patch with rolled over edge on medial third of right lower lid "increasing in size over 18 months"	Basal cell	Radium needles 4 × 0.6 mg. in rectangle	5,000 r in 6 days	Biopsy only	7½
13	March, 1955	60	Linear ulceration of over one third of margin of left lower lid	Basal cell	Gold radon seeds 2 × 2 mc. (length 2 cm.) deep to growth on tarsal plate, parallel to lid margin	5,000 r in 5 days	Biopsy only	2
14	September, 1955	53	Infected ulcerated area, with indurated margins, of left upper lid	Molluscum sebaceum	Radium needles 6 × 0.6 and 2 × 1 mg. (short) deep to and surrounding lesion	6,000 r in 4 days 1 hr.	Resection 4 months previously, apparently incomplete	7
15	August, 1955	65	Thickening at lateral canthus of left eye	Basal cell	Radium needles 2 × 1.3 and 2 × 0.6 mg. Rectangle	4,240 r in 4 days	"Papilloma" removed 1947	5
16	May, 1956	50	Ulcer, 1 × 0.8 cm., penetrating deeply below right medial canthus—8 months history	"Rodent ulcer"	Radium needles 4 × 1.3 and 2 × 0.6 mg. arranged in rectangle 1 × 1.3 mg. placed diagonally across rectangle	5,750 r in 5 days	—	6
17	October, 1956	68	Rodent ulcer left lower lid, 6 × 7 mm.	"Rodent ulcer"	Radium needles 6 × 0.6 mg. 2 below horizontally 2 above horizontally 1 vertical at either side	5,976 r in 5 days	—	14 mths
18	October, 1956	70	Nodule right lower lid below margin, 5 × 3 mm.	"Rodent ulcer"	Radium needles 2 × 0.6 mg. parallel to and below margin, deep to growth	2,910 r in 4 days	—	2½

The first possible complication that springs to mind is irradiation cataract. Prevention of lens change by the use of a lead shell is not a feasible proposition except for short periods since much abrasive damage may be done by the shell unless it has been specially moulded; in addition it is questionable if the thickness of the shell rather than the lead is not the main factor in the protection of the crystalline lens from the gamma ray which is the harmful

element. It is certainly probable that retraction of the eyelid for a distance of 1 cm. from the cornea appears to have the desired effect. If the upper lid has to be retracted, it will probably be necessary to strap upwards the lower lid to protect the cornea.

Epiphora, as we have seen from Cases 3 and 16, is not an essential sequel of implanting radiation material in close proximity to the lacrimal drainage apparatus, provided that the channels are not damaged by surgical trauma. A dosage necessary to kill malignant cells should not necessarily lead to the formation of scar tissue. Emphasis must be laid on the proper control of dosage, the estimation of which by radiographs is not essential when sufficient experience has been gained to be able to judge from the skin reaction the approximate intensity of the radiation.

VARIATION OF RADIATION INTENSITY WITH DISTANCE FROM A RADIUM NEEDLE

The energy of the gamma rays emitted by radium, or radon, sealed in a platinum container is high enough for the reduction in intensity caused by absorption in tissue to be neglected, at least insofar as distances of a few centimetres are concerned. Under normal therapeutic conditions, therefore, the variation of radiation intensity in the neighbourhood of such a radiation source is determined by the absorption in the walls of the platinum container and by the operation of the inverse square law.

In the simple case of a very small spherical source, a point source, the variation of intensity with distance from the source will depend directly on the inverse square law and can hence be evaluated very easily. In the more usual case in which radium needles are used which may be long in comparison with the distances in question, the calculation is not so simple. The principles involved remain the same, but account must be taken of the fact that different parts of the relatively long needle lie at different distances from the point at which the intensity is to be calculated. Allowance must also be made for the effects of absorption in the platinum walls of the needle at oblique angles of traverse. The problem can be expressed in a mathematical form based on the Sievert Integral. This formula can be evaluated to give the variation of radiation intensity in the neighbourhood of a radium needle of given length and wall thickness. Typical results of such a calculation are given in a Table, which shows that the decrease in intensity with increasing distance from the source is not as great as would be expected from a simple application of the inverse square law, although it approaches this as the distance from the source becomes greater.

The dose rate is reduced as the distance from the "plane" of the needle implant increases. Presuming that at 3 mm. the dose rate is 100 per cent. at 5 mm. it will be 55 per cent., at 10 mm. 17 per cent., and at 20 mm. 5 per cent.

SUMMARY

Eighteen cases of epithelioma of the eyelids and adjacent areas treated by implantation irradiation are described.

As far as is known up to the present time, there has been no recurrence in any of the patients treated, five of whom had treatment over 10 years ago. Cosmetically the results are excellent and most of the complications encountered are in fact avoidable.

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