Carcinoma of the Eyelid Treated by Irradiation

Analysis of 157 Primary and 22 Recurrent Cases

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• **The eyelid is a frequent site for skin cancers of the face. Its location presents certain special problems in treatment from a cosmetic and functional standpoint. If untreated, a major deformity with possible loss of sight can result. This paper is a report of our treatment with irradiation of 157 primary tumors and 22 recurrent tumors. In 98 per cent of patients there was control of the tumor for more than five years and a good cosmetic and functional result.**

CANCER OF THE EYELID may properly be considered a subtype of facial cutaneous cancer. In addition to creating a cosmetic defect, it may, if neglected, cause serious impairment of vision. Radiation long has played a major role in the treatment of cancer of the eyelid (Baclesse,[1] Hunt,[2] Martin,[3] Pompa,[4] Stetson,[5] Traub,[6] Wildermuth[8]) and remains the most commonly used therapeutic agent. Radium therapy as practiced 30 to 40 years ago is far less widely used today because of its inconvenience in application and the difficulties inherent in accurate shielding of the cornea and lens. Although there is no doubt that skin cancer in this location can be cured with either irradiation or surgical operation if the treatment is adequate, radiotherapists and surgeons still frequently disagree as to which is the better method. The purpose of this paper is to evaluate the functional and cosmetic results of treatment of carcinoma of the eyelid, both in cases not previously treated and in recurrent cases previously treated elsewhere.

Nature of This Material

This report is based on the total experience of all cases of cancer of the eyelid seen by us in private practice during a 15-year period from 1943 through 1958. There were 171 patients, 90 of whom (53 per cent) were male. There were 179 separate tumors, 90 of which were on the left and 89 on the right. In seven patients there were two or more separate cancers of the eyelid (one patient had three). In four of these seven patients the lesions were located on the same side and in three on the opposite side. Two of the patients had two separate cancers of the eyelid when first seen and in the remaining five patients new cancers of the eyelid developed eight to ten years after the first primary tumor.

One hundred fifty-seven cancers of the eyelid were previously untreated when first seen by us; 22 cases were recurrent after previous treatment elsewhere. The results of treatment of these two groups will be discussed separately.

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The site of origin is usually on the skin of the eyelid, near to but distinctly separate from the palpebral margin. The basal cell variant tumor usually begins as a small mound-like, nonulcerated nodule which infiltrates the skin but is freely movable over the underlying tissues. As the nodule increases in size, it seems to have a pearly translucency, often associated with a faint telangiectasia on the surface. The rate of growth is variable; it may be so slow that ten to fifteen years elapse before the patient seeks treatment. In this series, 20 per cent of patients had an awareness of an eyelid growth for more than two years before seeking medical advice. Symptoms other than cosmetic are rare unless the lesion is larger than 10 millimeters or involves the palpebral margin, the conjunctiva or the inner canthus. Pain and discomfort are never prominent symptoms. If untreated, the tumor may grow large and will eventually ulcerate, extending onto the skin of the face and, occasionally onto the conjunctiva. Further neglect will result in invasion of the orbit, the periorbital tissues, erosion of the bone and finally intracranial extension.

Etiologic Factors; Age and Sex Incidence

As with other skin cancer, the highest incidence was in the fifth and sixth decades of life; 60 per cent of the cases in this series were in that age period (Chart 1). Five patients were in the second decade and ten in the third, which together made up only 8.5 per cent of the total series. Men were slightly more commonly affected than women—53 per cent and 47 per cent.

The most important factors in the background of cutaneous carcinoma are genetic and environmental. The genetic influence is manifested by deficiency in

the distribution of the protective pigmentary elements, which is related to vulnerability to the damaging effect of solar radiation. The carcinogenic influence of actinic radiation is expressed in the increased incidence of skin cancer in areas such as Southern California, where the number of new cases of skin cancer per 100,000 of population is eight times what it is in Illinois and the number of hours of solar radiation, by yearly average, is also eight times that occurring in Illinois.

Site of Lesion

Forty-six per cent of the tumors in the present series arose on the lower eyelid and 35 per cent in the region of the inner canthus (Figure 1). The relatively infrequent occurrence of eyelid cancer in the region of the outer canthus or the upper lid was similar to that reported by other investigators. In only one of the primary untreated cases was there extension of the tumor onto the conjunctiva. (This series does not include 18 cases of cancer which arose on the conjunctival surface and were seen during a similar period of this study.)

Thirty-seven per cent of the patients in this series had one or more other unrelated skin cancers, either before or after treatment for the eyelid cancer (Table 1). Sixty-four per cent of the patients who were observed with a recurrent cancer of the eyelid after treatment elsewhere had other primary skin cancers. Only 4 per cent of all patients had a history of prolonged exposure to either sun or weather as a direct result of their occupation. Seven patients had decidedly heliophobic skin.

Associated Conditions

Fifteen patients at some time had neoplasms that were unrelated to the skin cancer or eyelid cancers. Twelve of the lesions were malignant, three were benign (Table 2). These data do not suggest etiological factors but emphasize that in an aging population a neoplastic process may develop in any organ at any time.

Diagnosis

The possibility of cancer exists when any tumor of the eyelid is present, whether ulcerated or not. As mentioned earlier, a cancer of the eyelid may be of considerable size before an ulceration develops. Biopsy always should be done. The specimen may be obtained readily with a punch after infiltration of the skin with a local anesthetic agent. Hemostasis is readily brought about with electrodesiccation. There is no evidence of any hazard associated with excising material for biopsy. Welch[7] reported a 14 per cent incidence of cancer of the eyelid noted in biopsy of 617 lid lesions at the Wilmer Ophthalmological Institute of the Johns Hopkins Hospital during a five-year period. A papilloma, a nevus or a chalazion were more commonly noted than was a cancer. A pigmented basal cell carcinoma might be confused with a melanoma grossly if one were to not take careful note of the slate-grey sheen which is characteristic of a pigmented basal cell. A chalazion usually can be differentiated grossly by its characteristic subcutaneous involvement and lack of overlying epidermal tissue.

TABLE 1.—*Patients with Other Cutaneous Cancer in This Series of Patients with Eyelid Cancer*

Location	157 Primary	22 Recurrent	Total
Head and neck	43	13	56
Upper extremity	5	1	6
Trunk	1	0	1
Lower extremity	0	0	0
More than one site	35	6	41
Per cent of total patients	32.8	64.0	37.0

TABLE 2.—*Noncutaneous Neoplasms in Patients with Cancer of the Eyelid*

Cancer breast	2
Cancer larynx	2
Cancer cervix	1
Cancer corpus	1
Cancer stomach	1
Cancer soft palate	1
Cancer nasal septum	1
Cancer in situ cervix	1
Leiomyosa colon	1
Melanoma	1
Pituitary adenoma	1
Mixed tumor, submaxillary gland	1
Cyst, mandible	1

TABLE 3.—*Pathology of Eyelid Carcinoma*

	Primary	Recurrent	Total
Basal cell	119	18	76.4%
Squamous cell	23	1	13.6%
Basosquamous	6	1	3.9%
Adenoid cystic	5	2	3.9%
No pathologic identification*	4	0	2.2%
Total	157	22	100 %

*Note: Two patients refused biopsy.

Pathologic Features

Basal cell carcinoma is the most common malignant tumor of the eyelid. It accounted for 76 per cent of the tumors in the present series (Table 3). Squamous carcinoma is next most common in frequency and accounted for 13 per cent of the tumors. Variants of these lesions include the basosquamous carcinoma, and the adenocystic variety of a basal cell carcinoma. In only four cases in the series was a microscopic report not available for review.

General Considerations in Treatment

The treatment of eyelid cancer does not differ materially from that of other facial skin cancer except for the need to avoid injury to the function of

the eye and its adnexa. Some physicians favor surgical treatment, others irradiation; and the tendency toward one or the other depends to a great extent upon their personal inclinations, training and experience. Cancer of the eyelid is seldom a fatal disease. It did not cause death in the present series. The problem of treatment, therefore, is not one of saving life but of effecting a cure with the least degree of functional and cosmetic deformity. The treatment of an eyelid cancer requires either the removal of an adequate surgical margin, or irradiation of a surrounding area of normal tissue to insure complete control of the growth.

The relative merits of irradiation and excision cannot be judged adequately by comparing results of treatment of only small early lesions. When properly applied, these two methods will produce comparable results. When a larger lesion (over 1.0 cm.) is present or when the tumor is located in the region of the inner canthus, the best cosmetic and functional result will usually be obtained by radiotherapy. Failures after either method of therapy may be followed by the use of the other, often with success. Only in the case of most advanced cancers, where there is invasion of the orbit, would we favor radical surgical extirpation as the primary method.

Technique of Radiation

We prefer intermediate voltage radiation with a half-value layer of about 0.16 mm. copper for all tumors except those invading bone. A margin of 2 to 3 mm. on all sides of the tumor beyond its apparent gross extension is mandatory. After the application of an anesthetic agent to the conjunctiva with an eye-dropper, a gold eyeshield is placed in the conjunctival sac to protect the cornea and deeper tissues. A second shield with a portal of the required size is placed over the cancer of the eyelid and taped securely. Five hundred roentgens in air are administered twice weekly for a total of 3,000 r. A mild epidermal reaction is usually noted to reach a peak about 10 to 15 days after treatment has been completed. The cornea itself is quite resistant to doses of this order, even if unprotected. If the palpebral margin is included, the cilia usually fall out and do not regenerate. A bland ointment is useful in preventing cracking and crusting during and immediately after treatment. We do not favor radon seeds, contact radium or radium needles, although they have been used in the past by other investigators with considerable success.

The mild reaction which represents the peak effect in uninvolved skin is transient; in the average person the erythema subsides within 20 days or so after the final treatment. Usually the slight atrophy and loss of elasticity at the site of the former lesion is detectable only on close inspection. Sometimes but not often depigmentation in the treated area will persist for months and color will not be restored until the area is exposed in moderation to actinic radiation, natural or artificial. Such admirable cosmetic results are the rewards of proper choice of quality of irradiation, fractionated over the three-week period. Only for persons who are intensely heliophobic, with very thin, "red-headed" skin, is this technique unsatisfactory. For them the routine approach is discarded in favor of individualization: Their problem is manageable by smaller increments per treatment, over a longer total treatment time, use of a harder beam of x-radiation (h.v.l. $= 0.25\pm$), or even a lesser total dose. Also, when the lesion is deeply infiltrating, especially into palpebral cartilage, a higher quality of irradiation and greater fractionation is important in the avoidance of chondritis due to the avascularization secondary to more caustic irradiation. With such precautions, a cancericidal effect in cartilage is customary without undesirable sequelae.

Many physicians, predominantly surgeons, have written extensively of the complications of radiotherapy in eyelid lesions. More often than not, their observations in this regard are based on experience with poorly treated cases in which complications developed mainly through too caustic irradiation, inadequate fractionation, overtreatment or some combination of these factors. Our experience is reassuring. No cataracts were noted in this series. In one patient, glaucoma developed five years after treatment and necessitated surgical therapy. In only three cases was persistent telangiectasia noted and in only one case was there persistent ectropion, and it was mild. The suppleness of roentgen therapy, its adaptability to the peculiar requirements of a neoplasm in a location adjacent to the eye cannot be excelled by any other method of therapy. Surgical excision will destroy either the lacrimal duct or gland in lesions located about the inner canthus, and these structures are resistant to irradiation. In none of this series was tearing a persistent complication of therapy. This treatment does not require hospitalization as does surgical care.

An analysis of the results of treatment in our experience will be reported in two parts: First, 157 cases of primary previously untreated eyelid cancers and, second, 22 cases of recurrent eyelid cancers which were first seen by us after failure of previous treatment.

Treatment of Primary Eyelid Cancer

One hundred fifty-seven patients with primary untreated eyelid cancer were seen in our office from 1943 through 1958, representing our total experience. These cases included only those in which the cancer reasonably could have arisen on the eyelid;

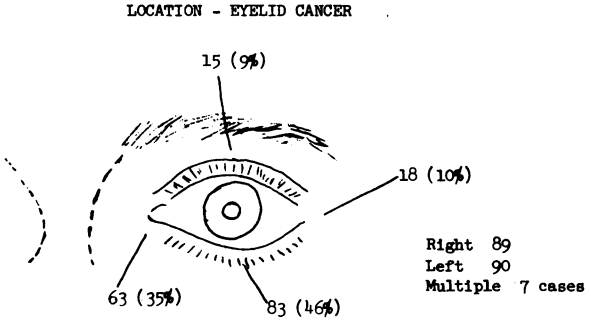

Figure 1.—Sites of lesions in 179 cases of cancer of the eyelid.

not included were cases of extension of lesions which arose either on the surrounding facial skin or on the conjunctival surface. The age incidence, the anatomic location, and the histologic patterns are noted in Chart 1, Figure 1 and Table 3. Seventy-six per cent of these lesions were 1 cm. or less in greatest diameter, an additional 18 per cent were 1 to 2 cm. across, and 6 per cent were between 2 and 6 cm. Twenty-three per cent of these neoplasms were ulcerated (Table 4). Of these patients, 146 were treated solely by irradiation after biopsy. The 11 remaining patients were treated by various means: Six by surgical excision, one by excision and graft and two by radium, all with complete control of disease. One patient was untreated because of associated melanoma, and expired as the result of melanoma eight months after the diagnosis of the eyelid cancer. One other patient was treated by electrocoagulation; recurrence was noted in ten months. The patient subsequently was treated with 3,000 r, and at last report, five years following this treatment, had recurrence. Of the 146 patients treated with primary radiation therapy, 139 had no recurrence and were free of disease at the time of this report. The roentgen dosage is noted in Table 5; 85 per cent of the patients received 3,000 r during a three-week period.

Seven of the 146 patients treated primarily with irradiation were not cured following the first treatment of 3,000 r in air. In Table 6 these failures with irradiation are summarized and the treatment at the time of recurrence is noted. Two of these cases may not in reality be true recurrences. The patient in Case 1 had persistent disease one month following treatment and it is likely that the field which was treated primarily did not adequately cover one margin of the lesion. This area then was treated and the disease thereafter was controlled for five years. The patient in Case 7 was noted to have either a recurrence or a new lesion 12 years after the original treatment in our office, and has sought treatment elsewhere. It is likely that this is a second primary lesion, although we have

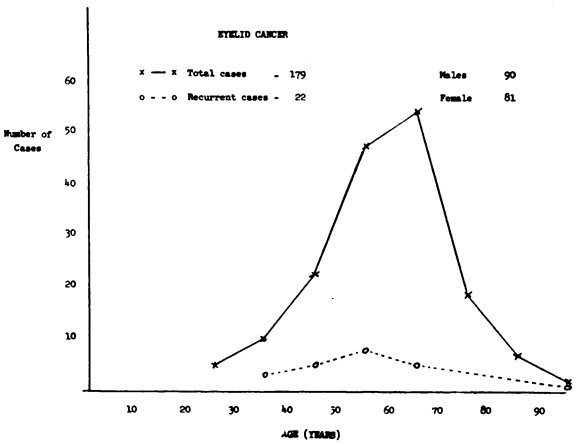

Chart 1.—Relation of incidence of eyelid cancer to age of patient.

TABLE 4.—*Appearance of Eyelid Cancer*

	Untreated Eyelid Cancer	Recurrent Eyelid Cancer	Totals
Nonulcerated	77%	59%	134 cases
Ulcerated	23%	41%	45 cases

TABLE 5.—Primary Eyelid Cancer—Irradiation Treatment

Air Dose (r)	Cases
2,500	1
2,900	1
3,000	129
3,500	8
3,750	1
4,000	3
4,500	3

TABLE 6.—*Treatment of Irradiation Failures (All had 3,000 r initially)*

Case No.	Free Interval	Treatment of Recurrence	Result
1.	1 mo.	3000 r	NED 5 yr.
2.	7 mo.	a. Excision	
		b. Exenteration orbit 5 yr. later	Recurrent 6 yr.
3.*	2 yr.	1600 r	NED 7 yr.
4.	3½ yr.	Electrocoagulation	NED 5 yr.
5.	6 yr.	Excision, graft	Recurrent 1 yr.
6.	7 yr.	Excision	NED 1 yr.
7.	12 yr.	Lost to follow-up	?

NED—No evidence of disease.
*Recurrence clinical—not proven by biopsy.

not so stated. A third patient had a suspicious recurrence two years following treatment. Biopsy was not done but the lesion was retreated with 1,600 r and the patient remained well for seven years without recurrence. In the four remaining cases of failure of treatment, 3,000 r was given as the initial treatment. The lesions recurred seven months, three and a half years, six years and seven years after

TABLE 7.—*Methods of Treatment to Control Recurrent Eyelid Cancer*

Previous Treatment	Treatment Resulting in Control				
	Electrocoagulation	Excision	X-ray	Radium	Exenteration
Electrodesiccation failure	....	....	6	....	....
Irradiation failure	....	3	1	....	1
Radium failure	....	1	2	....	1
Surgical failure	1	....	2	....	2

treatment, and all recurrences were proven by biopsy. Two of these patients were treated by electrocoagulation and excision and were well at the time of this report, one year and five years after the second treatment. In two other cases radical wide surgical excision was used, one with graft, and in neither case was the disease controlled. One of the patients had recurrent cancer one year after the treatment and the other finally was treated by exenteration of the orbit and a partial maxillary resection. It is difficult to be certain that the tumor in this last mentioned case is a recurrence of the original eyelid cancer, since the patient has had literally hundreds of primary skin cancers of the head and neck region and developed a tumor which was described in the exenteration specimen as a minor salivary gland carcinoma similar to a lesion he had on the cheek. These lesions were entirely different histologically from the original basal cell carcinoma which arose on the eyelid.

In summation, in 157 primary eyelid cancers treated in our practice there was no mortality or metastasis ascribable to the lesions treated. At the time of this report, 21 patients were dead of intercurrent disease, primarily cardiovascular, although four died of other primary cancers. Only three of 157 patients, our total experience in primary treatment, had persistent disease at the time this report was written. One of these patients went elsewhere and the results of whatever treatment was given are not known. Two patients are still under our care with residual active disease. This means that in 98 per cent of the cases in the series the disease is controlled, with the possibility that in the still refractory cases control may still be brought about. No correlation between the histopathologic features, the size of the lesion or the duration of symptoms before treatment seemed significant in the present failure to control the disease in these three cases.

Treatment of 22 Eyelid Cancers Recurrent At First Visit

Twenty-two patients, all with microscopic proof of cancer, received multiple therapy before we treated them. Electrocoagulation had been used in 19 cases, surgical excision in eight, one course of x-ray therapy in seven, multiple courses of x-ray therapy in two, radium therapy in six and beta irradiation in one. Fifteen of the 22 had had two of these procedures, six had had three and one had had four. The patients' ages ranged from 37 to 91 and were rather equally divided between the 4th, 5th and 6th decades. The time interval from the first diagnosis of an eyelid cancer to the treatment of the patients in our office averaged three years, with a range from one to fifteen years. In five cases the lesions were still recurrent more than five years after initial treatment (six years in two cases, ten years in one and fifteen years in two).

Twenty of these 22 patients were free of eyelid cancer at the time of this report. In two the lesions remained uncontrolled. In all but one case curative therapy was completed within two years of admission. In that exceptional case, therapy took six years. In four cases control was obtained with the first treatment, nine with the second, two with the third, four with the fourth, one with the fifth. Of the two uncontrolled cases, one has been treated once and one has been treated six times. Ten of the 20 cases which are at present controlled have been controlled for five or more years.

The treatment that brought about control in these 20 cases was as follows: In 11 cases, x-ray therapy, in four surgical excision, in four radical orbital exenteration, in one electrocoagulation (Table 7).

Electrocoagulation is not considered to be a suitable treatment for a recurrent eyelid cancer. Previous radiation therapy does not foreclose the use of irradiation again, and the end results are surprisingly good, both cosmetically and functionally. One would expect that surgical excision would be mandatory after failure with radiation, but the results do not confirm this.

DISCUSSION

A report of five-year results in cancer of the eyelid is not revealing because of the rare instance of death as a result of this neoplasm. None of the deaths in this series were due to eyelid cancer. Many patients in the series were in the geriatric range and died of intercurrent disease. In only four of the 179 cases was the disease not controlled at the time of this report. We feel that this neoplasm can be successfully treated in all cases. There is no reason for not attempting curative treatment of a recurrent lesion. In none of the cases in this series did metastasis develop, either in the neck or elsewhere. One

patient had a metastatic squamous cancer in the node in the upper jugular chain ten years after control of a primary carcinoma of the eyelid. However, this patient had had multiple skin cancers on the face and, a year before the appearance of the metastatic lesion in the neck, had had a squamous cancer of the homolateral ear excised, and this is the most likely source of the metastatic extension.

The lack of serious complications in the cases in the present report removes any doubt about the safety with which radiation is used. The excellent cosmetic appearance of these patients cannot be equalled by surgical treatment.

The natural history of this neoplasm with its dilatory growth pattern and local persistence of tumor without metastasis suggests that early diagnosis and treatment is far less important than adequate primary treatment. The careful positioning of a radiation port with proper shielding of both the surrounding skin and the underlying eye require meticulous attention to detail on the part of the therapist. The frequent occurrence of multiple eyelid cancers in the same patient makes careful follow-up for an indefinite period an important consideration. It is impossible, except on theoretical grounds, to distinguish late recurrence of an eyelid cancer from primary new eyelid cancer. In view of the long natural history of this neoplasm, we believe that freedom from persistent or recurrent disease for three to five years after treatment does not assure there will be no late recurrence.

Neglect of this growth necessitated radical exenteration of the orbital contents in five patients in this series.

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