SEBACEOUS CARCINOMA OF THE OCULAR ADNEXA: RADIOTHERAPEUTIC MANAGEMENT

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A total of 30 patients with histologically confirmed sebaceous carcinoma of the ocular adnexa were evaluated at our institution from 1974-1986. There were 18 women and 12 men in the series with a median age of 61 years. Ten cases received radiotherapy with curative intent. Four patients were treated definitively with doses ranging from 45-63.0 Gy over 4-7 weeks. Six patients received post-operative radiotherapy to the parotid bed and ipsilateral cervical lymph node chain for parotid metastases developing within 36 months of initial surgical treatment. Patients with lower lid lesions and significant pagetoid histologic components were more likely to develop parotid lymph node metastases. Local control at the primary site after radiation and/or surgery was 90% with follow-up ranging from 2-10 years. Overall disease specific actuarial survival at 5 years was 96%. Radiation therapy is an effective treatment modality in adnexal sebaceous carcinoma. With employment of careful technique and state-of-the-art technology, long term local control and survival with satisfactory cosmetic and functional results can be anticipated.

Radiotherapy, Sebaceous carcinoma, Meibomian gland adenocarcinoma, Pagetoid.

INTRODUCTION

Sebaceous carcinoma or meibomian gland carcinoma of the ocular adnexa is an unusual neoplasm. It was first described in the seventeenth century as arising from the tarsal glands by Heinrich Meibom, German Professor of Medicine (5). It comprises less than 1% of all orbital adnexal tumors, and accounts for as much as 5% of malignant neoplasms in this region (2, 3, 7, 10, 17, 19). The tumor usually presents as a recurrent painless mass in the eyelids or caruncle, and a diagnosis of recurrent chalazion is frequently associated with its presence. (Fig. 1) The histopathologic picture is sebaceous adenocarcinoma and its diagnosis can also be difficult with 20-50% of most published series reporting an error in the initial pathologic diagnosis (2, 4, 15, 17).

Meibomian glands are developed by the fourth month of intra-uterine life after lid fusion (1). The larger upper tarsal plate contains approximately 30-40 glands with the lower tarsal plate containing 20-30 glands (1). Histologically, the gland is lined by stratified squamous epithelium with acini separating supporting stroma from a layer of undifferentiated cells. Large lipid laden cells are centrally located in the acini. The tumor may often have a significant intra-epithelial component suggestive of pagetoid spread (Fig. 2). This has been shown to be a poor prognostic factor (10, 17, 18).

Treatment for this tumor has been primarily surgical, however, the French literature suggested radiotherapy to be of potentially curative value as early as 1936 (5, 15, 20). Our review of the English literature shows radiation therapy being administered with curative intent in fewer than 15 cases (2, 3, 6, 8, 9, 14, 19).

METHODS AND MATERIALS

From 1974-1986, 30 patients with sebaceous carcinoma of the ocular adnexa were seen and evaluated at Massachusetts General Hospital/Massachusetts Eye and Ear Infirmary. All cases were biopsy documented and slides reviewed by our ophthalmic pathologists. There were 18 women and 12 men. Median age was 61 (range 42-84). Twenty-eight patients initially presented with a painless mass. Sixteen patients had a significant intra-epithelial component suggestive of pagetoid spread. Ten patients presented with tumors in the lower lids, five in the lid and adjacent caruncle, three in the upper lids, five in the lid and adjacent caruncle, three

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both the upper and lower lids concomitantly, and two
were too extensive to determine tumor origin (Fig. 3a).
Surgical procedures consisted of biopsy only (four pa-
tients), simple excision (three patients), wide local excision
(ten patients), orbital exenteration (seven patients), su-
perficial or total parotidectomy with or without lymph
node dissection (six patients) (Fig. 3b).
Radiotherapy was used as either definitive or postop-
erative treatment in eleven cases. Five patients underwent
definitive irradiation (Table 1). Tumor volume included
the region of primary tumor involvement plus at least a
5 mm margin. For lesions with extensive intra-epithelial
changes, the adjacent fornix and bulbar conjunctiva were
covered when clinically appropriate. Individual lead eye
shields were used to reduce transmission to less than 2%.
One patient with a primary lesion less than 5 mm in di-
ameter in the lower lids without intra-epithelial changes
received 50.0 Gy via 6 MeV electrons. Two patients pre-
sented with extensive recurrent lesions greater than 5 mm
in diameter with pagetoid components. Both were treated
twice daily with electron technique of 63.0 and 53.19 Gy,
respectively. One patient with recurrent lower lid lesions
with pagetoid changes received 45.0 Gy on the 50 kV
unit. Six patients presented with parotid lymph node re-

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**Fig. 1.** Typical appearance of tumor in left upper eyelid of a 42-year-old patient with extensive pagetoid involvement and orbital extension. Patient refused recommended orbital exenteration.

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**Fig. 2.** Photomicrograph of sebaceous carcinoma with significant intra-epithelial component suggestive of pagetoid spread (arrow in black).
currence and no evidence of disease at the primary site within 36 months of original surgical treatment. Three underwent total parotidectomy and three underwent superficial parotidectomy. Postoperative radiotherapy consisted of combined photon/electron techniques to the parotid bed and ipsilateral cervical nodes of 45–61 Gy over 5–7 weeks (Table 2).

Follow-up information was obtained from medical record documentation and personal interviews. Local control and survival were calculated by the actuarial method. For patients with recurrent lesions on presentation, follow-up interval was determined from time of the most recent recurrence. For comparison, p-values were obtained by normal estimation of the binomial for comparison, and by log rank analysis for actuarial survival.

RESULTS

Local control at the primary site after radiation and/or surgery was 90% with follow-up interval ranging from 2–10 years. All six patients presenting with parotid lymph node recurrences, without evidence of disease at the primary site, and treated with resection and postoperative radiotherapy are without evidence of disease with follow-up ranging from 2–7 years (Table 2). They had lower lid lesions with significant pagetoid intra-epithelial components (p < .01). One of the 30 patients originally treated surgically failed distantly with radiographically documented CNS disease at 24 months. One patient treated with radiation alone was locally NED (no evidence of disease), but developed metastases in the lymph nodes at 36 months. He received combined photon/electron/interstitial radiotherapy. Subsequently, he had superficial parotidectomy with close margins. This patient developed pulmonary parenchymal disease 12 months later with local control at the primary site (Fig. 4).

Actuarial survival at 5 years was 96%. Because of the small number of patients, no difference was noted in treatment modality used, number of prior recurrences, or presence of orbital extension by log rank analysis. Overall, patients were followed for a median of 59 months (range 2–10 years). For the radiotherapy group, the median follow-up was 62 months (range 3–10 years).

DISCUSSION

Sebaceous carcinoma or meibomian gland carcinoma of the ocular adnexa may have an aggressive natural history with over 20% mortality reported in most series (2, 10, 11, 14, 17). Typically, initial treatment for limited lesions may be either radiation therapy or wide local excision. The recurrent extensive lesions and those with sig-

Table 1. Patients undergoing definitive irradiation

<table>
<thead>
<tr>
<th>Location</th>
<th>Pagetoid</th>
<th>Radiation (cGy/fx/days)</th>
<th>Local NED (mo.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower lid</td>
<td>+</td>
<td>5000/10/15</td>
<td>52</td>
</tr>
<tr>
<td>Lower lid</td>
<td>+</td>
<td>6300/29/21*</td>
<td>117</td>
</tr>
<tr>
<td>Upper lid</td>
<td>+</td>
<td>5319/25/21*</td>
<td>36</td>
</tr>
<tr>
<td>Lower lid</td>
<td>+</td>
<td>4500/04/05</td>
<td>45</td>
</tr>
</tbody>
</table>

* BID (twice daily fractionation).
significant intra-epithelial involvement or orbital extension may be considered for orbital exenteration. In spite of the widespread, erroneous impression that sebaceous carcinoma is "radioresistant" or "radioinsensitive," all of our patients were locally controlled at the primary site following definitive therapy. Actuarial disease specific survival was 96% at 5 years. Patients with lesions initially involving the lower lids with significant pagetoid components were more likely to recur in the parotid lymph nodes. These lymph node recurrences occurred from 6 to 36 months after initial treatment of the primary. The management of these patients was either definitive radiation therapy or combined superficial or total parotidectomy with postoperative radiotherapy to the parotid bed and ipsilateral cervical chain (21).

As early as 1956, the English literature recognized the usefulness of radiotherapy in the management of this disease. Straatsma reported a case of recurrent meibomian gland carcinoma that received over 6000 R to the right external canthus and over 5750 R to the right preauricular region using orthovoltage technique (19). Similarly, Ide et al. reported on a patient initially receiving 6800 R over 11 days and receiving an additional 5000 R over 24 days following local recurrence 6 months later (9). Harvey and Anderson reported a patient treated with 5300 R who was free of disease at 5 years (7). Hendley et al. summarized the case histories of three patients treated with doses of 4800, 5000, and 6600 cGy, respectively over 3–5 weeks with one of the patients recurring in the parotid region 6 months later (8). Nunnery et al. scored all five of their patients as having failed radiotherapy, although their results indicate that two patients were locally controlled with evidence of regional nodal disease outside of the radiation fields and one patient did not complete the prescribed treatment course (14).

High dose irradiation to the eyelids can produce an acute, brisk conjunctival reaction before similar changes take place on the keratinizing epithelium of the skin of the outer lid. With high total doses and fraction sizes, lid deformity leading to chronic corneal irritation may cause serious ocular morbidity. We have found, however, that when a portion of the tarsus is irradiated to tumor doses of 50–60 Gy, the lid may appear somewhat atrophic, but its function is generally preserved. Individualized lead eye shields can be used to protect as much of the bulbar conjunctiva, globe, and cornea as possible. With more comprehensive orbital irradiation, a decrease in lacrimal function has been reported (12, 16). Clinically severe dry eye syndrome may develop with a dose of 32–45 Gy (16). Therefore, it is important to protect the lacrimal system from unnecessary irradiation. One of our patients complained of significant dry eye symptomatology and this patient was s/p prior extensive tarsorrhaphy. Corneal ulceration, retinal damage, or cataract formation have not been observed.

Table 3. Eye function following radiation therapy

<table>
<thead>
<tr>
<th>Location</th>
<th>Dose (cGy)</th>
<th>Visual acuity</th>
<th>Lacrimal function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lower lid</td>
<td>5000 OD</td>
<td>20/20</td>
<td>- (52)</td>
</tr>
<tr>
<td>Lower lid</td>
<td>6300 OD</td>
<td>20/60</td>
<td>+ (60)</td>
</tr>
<tr>
<td>Upper lid</td>
<td>5319 OS</td>
<td>30/20</td>
<td>O (36)</td>
</tr>
<tr>
<td>Lower lid</td>
<td>4500 OS</td>
<td>20/40</td>
<td>+ (45)</td>
</tr>
</tbody>
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+= Normal lacrimal function; O = Slightly/moderately decreased function; − = Markedly decreased function (time of last ophthalmic exam in months).
Radiation treatment of ocular and adnexal tumors requires careful radiologic and clinical evaluation to determine tumor anatomy and define the target volume precisely. Care must be taken to shield non-target tissue and to design treatment fields which will prevent cataracts, retinal damage, and dry eye syndrome (12, 13, 16). Superficial tumors can be controlled with doses of 50 Gy in 3–4 weeks. In cases with extensive intra-epithelial changes, the adjacent fornix and bulbar conjunctiva may need to be included in the target volume and doses between 50–60 Gy may be used. Radiation beam energy and fractionation schemata must be tailored to the individual case. All of our patients treated by radiotherapy have maintained satisfactory visual and lacrimal gland function at the time of last ophthalmic exam (Table 3).

CONCLUSION

Radiation therapy is an effective treatment modality in the management of early sebaceous carcinoma of the ocular adnexa. Surgery should be reserved for extensive lesions or lesions recurrent after radiation therapy. Irradiation of the parotid bed and ipsilateral cervical lymph node chain, in conjunction with parotid debulking, can successfully control parotid lymph node metastases. Elective radiation therapy to the parotid and/or ipsilateral cervical nodes should be considered for patients with extensive recurrent lesions and patients with widespread intra-epithelial changes. With employment of careful technique and state-of-the-art technology, long-term local control and survival with satisfactory cosmetic and functional results can be anticipated (Fig. 5).

REFERENCES