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Multidisciplinary Management of Lacrimal Sac/Nasolacrimal Duct Carcinomas

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Abstract

Purpose—To determine rates of globe-sparing treatment and useful final visual function in patients with primary lacrimal sac/nasolacrimal duct carcinomas treated with multidisciplinary therapy.

Methods—The medical records of 14 patients with primary lacrimal sac/nasolacrimal duct carcinoma treated at 1 institution were retrospectively reviewed.

Results—The patients were 9 men and 5 women; the median age at diagnosis was 58.5 years (range, 45–73 years). Seven patients presented with epiphora, 7 with a palpable mass in the inferomedial orbit, and 2 with dacryocystitis. In 3 patients, the diagnosis of cancer was not considered until during or after dacryocystorhinostomy (DCR). Seven patients had squamous cell carcinoma, 2 transitional cell carcinoma, 2 adenoid cystic carcinoma, and 1 each adenocarcinoma, poorly differentiated carcinoma, and inverted papilloma with carcinoma in situ transformation. Nine patients underwent surgical resection of the lacrimal sac and nasolacrimal duct, resection of the medial upper and lower eyelids including canaliculi, partial ethmoidectomy, and medial maxillectomy. One patient underwent lacrimal sac biopsy only as another primary malignancy was discovered on the work-up for systemic disease. Four patients underwent orbital exenteration because of extensive involvement of the orbital soft tissue. Radiotherapy was recommended for 13 patients; in 1 patient, radiotherapy was not recommended because the patient had an inverted papilloma with carcinoma in situ transformation that was completely excised. The median radiation dose was 60 Gy. Eight patients received chemotherapy concurrent with radiation therapy (5 patients), as neoadjuvant treatment (1 patient), or for progressive or metastatic disease (3 patients). The median follow-up time was 27 months (range, 6–96 months). In 10 patients, the globe was spared. In 9 of these 10 patients, visual acuity was the same as at baseline or better than 20/40 at last follow-up.

Conclusions—With multidisciplinary therapy, the eye can be spared and reasonable visual function can be preserved in most patients with primary lacrimal sac/nasolacrimal duct carcinomas.

INTRODUCTION

Lacrimal sac and nasolacrimal duct malignancies are uncommon.^{1–3} Early symptoms are often nonspecific and can be mistaken for symptoms of benign and more common conditions such as idiopathic nasolacrimal duct obstruction or dacryocystitis. While in most cases the diagnosis of malignancy can be made when there are specific clinical findings such as a progressive mass in the area of the lacrimal sac/nasolacrimal duct, in some instances the diagnosis is made intraoperatively during routine dacryocystorhinostomy (DCR) when the surgeon notes a mass or other abnormal findings.⁴ Furthermore, in some instances, the diagnosis is missed even at DCR, and in these cases, the tumor can grow into the adjacent sinuses and the nasal cavity and cause significant morbidity.

Lacrimal sac/nasolacrimal duct tumors can be divided into epithelial and nonepithelial categories. The majority are epithelial in origin, and the majority of those are malignant.^{5–7} The reported lacrimal sac/nasolacrimal duct carcinomas include squamous cell carcinoma, transitional cell carcinoma, adenoid cystic carcinoma, adenocarcinoma, and other uncommon entities.^{8–12} In addition to carcinomas, lymphoid tumors, melanomas, and sarcomas can also rarely involve the lacrimal sac/nasolacrimal duct as a primary tumor site.^{10,11}

The treatment of primary lacrimal sac/nasolacrimal duct carcinomas typically involves wide surgical resection followed by radiation therapy and/or chemotherapy. Because of the anatomic location of the lacrimal sac and nasolacrimal duct and their proximity to the orbital soft tissue, the maxilla and maxillary sinus, and the ethmoid bone and ethmoid sinuses, a multidisciplinary surgical approach is often optimal. Some practitioners may shy away from attempting globe-sparing surgery because of concerns about a higher risk of local recurrence if the eye is spared and also because of concerns about ocular damage from radiation therapy.

We herein report on 14 patients with primary lacrimal sac/nasolacrimal duct carcinomas who underwent surgical resection followed by adjuvant radiation therapy and in some cases concurrent chemotherapy and radiation therapy. Our goal was to determine rates of globe-sparing treatment and useful final visual function in patients with primary lacrimal sac/nasolacrimal duct carcinomas treated with multi-disciplinary therapy. The Institutional Review Board of The University of Texas MD Anderson Cancer Center approved this study.

METHODS

After Institutional Review Board approval was obtained, the clinical records of 14 consecutive patients diagnosed with a primary lacrimal sac/nasolacrimal duct carcinoma between December 2001 and June 2012 were retrospectively reviewed. Information recorded from each patient's chart included age at diagnosis, sex, ethnicity, primary cancer diagnosis, presenting signs and symptoms, type of surgery (e.g., dacryocystectomy, removal of canalicular portion of eyelids, partial maxillectomy, ethmoidectomy), details of radiation therapy and chemotherapy, whether lacrimal bypass surgery was performed at the time of primary cancer surgery or later, and time interval between surgery and radiation therapy.

Patients with lymphoid tumors or metastatic lesions of the lacrimal sac/nasolacrimal duct were excluded from this study.

RESULTS

Clinical Characteristics and Presenting Symptoms and Signs

Of the 14 patients in this study, 9 were men, and 5 were women. The age at diagnosis ranged from 45 to 73 years (mean, 58.5 years). Ten patients were Caucasian, 2 were Hispanic, 1 was Asian American, and 1 was African American. Symptoms and signs were unilateral in all patients; 8 patients had lesions on the right side, and 6 had lesions on the left side.

The main primary symptom or sign that led to the diagnosis was epiphora in 6 patients (42%), a palpable mass in 7 patients (42%), and dacryocystitis in 2 patients (14%). In 3 patients (21%), the diagnosis of malignancy was not considered until during or after routine DCR. In 2 of these patients, epiphora recurred or failed to resolve after DCR, which prompted re-evaluation. In the other patient, the diagnosis was made intraoperatively when the surgeon noted abnormal-appearing tissue in the area of the lacrimal sac.

Primary Cancer Diagnosis and Anatomic Characteristics

The primary cancer diagnosis was squamous cell carcinoma in 7 patients (50%), transitional cell carcinoma in 2 (14%), adenoid cystic carcinoma in 2 (14%), and adenocarcinoma, poorly differentiated carcinoma, and inverted papilloma with severe dysplasia in 1 patient each (7%). In all patients, the lacrimal sac or nasolacrimal duct was believed to be the location of the primary malignancy. In all patients, the mass involved the lacrimal sac fossa, portions of the medial maxillary bone, and varying degrees of the ethmoidal sinuses. In 4 patients, the lacrimal sac mass extended into the deep orbital soft tissue, necessitating an orbital exenteration.

Treatment and Side Effects

Nine patients underwent surgical resection of the lacrimal sac and nasolacrimal duct in addition to removal of the canalicular portion of the upper and lower eyelids, a partial ethmoidectomy, and a medial maxillectomy. One of these 9 patients, a patient with adenoid cystic carcinoma, required excision of the medial wall of the orbit. Four patients (1 each with squamous cell carcinoma, transitional cell carcinoma, poorly differentiated carcinoma, and adenocarcinoma) required an orbital exenteration because of extensive involvement of the orbital soft tissue. One patient underwent biopsy of the lacrimal sac/nasolacrimal duct mass as a second primary malignancy was discovered in his lung at the time of the work-up for systemic disease. This patient underwent systemic chemotherapy and radiation therapy as primary treatment for both malignancies. One patient who had been treated for an inverted papilloma two years prior to presentation had transformation to carcinoma in situ. No patient underwent a primary DCR as part of the initial surgical plan.

Postoperative radiation therapy was delivered to 12 patients with a median dose of 60 Gy (range, 56–70 Gy). One patient declined recommended radiation therapy, and 1 patient with carcinoma in situ was advised against radiation therapy. Seven patients received proton radiation therapy, and the other 5 received intensity-modulated photon radiation therapy. With protons, an eye deviating technique was used to minimize the radiation dose to the cornea. Ten patients had postoperative radiation therapy at MD Anderson; the other 2 patients had postoperative radiation therapy at other facilities closer to their home communities. The interval between surgery and initiation of radiation therapy ranged from 4 to 8 weeks after surgery (median, 6 weeks.) In 1 patient with transitional cell carcinoma, radiation was delivered for an unresectable regional recurrence in the hypopharynx 4 years after radiation was delivered for a primary lacrimal sac tumor. This patient had had an orbital exenteration as the primary surgical treatment for his lacrimal sac tumor.

The main side effects of radiation therapy were superficial keratopathy partly due to radiation exposure and also partly due to moderate lower eyelid ectropion in 2 patients and nasocutaneous fistula, neovascular glaucoma, and mucositis in 1 patient each. Visual acuity in the 8 patients who had globe-sparing surgery and were treated with high-dose radiation therapy was the same as at baseline or improved by one line in 4 patients (range, 20/20 to 20/20-1), decreased by 1 line in one patient (20/20 to 20/25), decreased by 3 lines or less in 2 patients (from 20/20 to 20/40 and from 20/25 to 20/50), and decreased from 20/25 to hand motion in the 1 patient with neovascular glaucoma. The median postoperative follow-up time for the 6 patients whose visual acuity was unchanged after treatment was 24 months (range, 6–46 months), and the median postoperative follow-up time for those with decreased vision was 20.5 months (6–45 months). No patients reported symptomatic diplopia. One patient went on to have lacrimal bypass surgery (conjunctivo-DCR) 26 months after cancer surgery and proton radiation therapy to address persistent epiphora.

Eight patients (57%) received chemotherapy. Of these, 5 received chemotherapy concurrent with radiation therapy (in 1 patient, this treatment was primary therapy), 3 received chemotherapy for local-regional recurrence or metastasis, and 1 received neoadjuvant chemotherapy to reduce the tumor bulk prior to surgery. One patient who underwent globe-sparing surgery had recurrence in the orbit while he was receiving radiation therapy in the immediate postoperative period. This patient had chemotherapy added to his radiation therapy regimen and was without evidence of disease at last follow-up.

In 5 patients, chemotherapy consisted of cisplatin (30–40 mg/m²) alone or in combination with docetaxel. One patient was treated with the EGFR inhibitor erlotinib as part of a regimen for treatment of metastatic disease, this patient has previously been treated with carboplatin and taxotere initially but subsequently developed a recurrence. One patient was treated with carboplatin plus paclitaxel.

Survival and Predictors of Orbital Exenteration

The median follow-up time for the entire cohort was 27 months (range, 6 to 96 months). At the time of this writing, 10 patients (71.4%) are alive with no evidence of disease. Three patients (21%) died of metastatic disease at 7 months, 30 months, and 48 months after the initial diagnosis. These 3 patients had not responded to multiple rounds of chemotherapy and had significant orbital involvement, which necessitated orbital exenteration in 2 patients and resection of the medial wall of the orbit in the other patient. One patient was found to have a recurrence in the submandibular lymph node and is actively undergoing management of his recurrent disease.

The 4 patients who underwent orbital exenteration had a median maximum tumor diameter of 30 mm (mean maximum tumor diameter, 30.6 mm) at presentation, while the 10 patients who underwent globe-sparing surgery presented with a median maximum tumor diameter of 20 mm (mean maximum tumor diameter, 23.2 mm) at presentation. This difference was not statistically significant ($P=0.14$), but as expected, there was a trend towards more aggressive surgery for larger tumors. The patient who underwent neoadjuvant chemotherapy to reduce tumor size (50 mm in greatest diameter at presentation) avoided an orbital exenteration but also skewed the dataset. Had this patient been excluded, the data would have indicated that patients who required an orbital exenteration had a significantly larger tumor size at presentation. There was no difference observed in the primary cancer diagnosis between patients who had exenteration and those who did not. All patients who underwent an orbital exenteration required a free flap for reconstruction, while only 4 of the 10 patients who underwent globe-sparing surgery required free flaps.

DISCUSSION

Our findings suggest that with multidisciplinary management of primary lacrimal sac/nasolacrimal duct carcinomas, including surgery, radiation therapy, and in some instances chemotherapy, the globe can be spared in most cases and most patients can achieve reasonable visual outcomes. Furthermore, the overall survival rate for our cohort of 14 patients was close to 80% with a median follow-up time of 27 months. Two of the three patients who died had had orbital exenteration as their initial surgical treatment. As such, the globe-sparing approach used in the majority of patients in this cohort did not lead to a higher risk of local recurrence, distant metastasis, or death compared with orbital exenteration.

In our series, 1 patient experienced regional recurrence in the hypopharynx and was treated with additional radiation therapy. Another patient had a recurrence in the orbit while receiving radiation therapy in the immediate postoperative period. This patient had chemotherapy added to his regimen and was without evidence of disease at last follow-up. Lastly, one patient who was initially found to have synchronous squamous cell carcinoma of the lung and nasolacrimal sac was found to have a recurrence to the submandibular lymph node 16 months after his original diagnosis. The patient subsequently underwent a neck dissection and is being considered for additional chemotherapy and or radiotherapy.

Our local-regional control rates and survival data are better than those of previous studies.^{13–16} In a series of 71 patients with lacrimal sac carcinomas from Shanghai published by Ni et al in 1982, the mortality rate was 43.7% despite orbital exenteration and other radical surgical measures.¹⁷ The authors recommended, “A malignant tumor beyond the confines of the lacrimal sac should be treated with exenteration or an even more radical operation depending on the extent of involvement”. The authors further wrote, “Once a tumor infiltrates beyond the lacrimal sac wall and into the orbit, even orbital exenteration combined with lateral rhinotomy does not improve the prognosis”. The mortality rate for the patients in this study was 37.5% for all patients and 50% in the subset with large and invasive lesions. In a more recent series of 115 patients with lacrimal sac tumors that included both benign and malignant lesions, the overall recurrence rate was 23%, but in the subset of patients with malignant epithelial carcinomas (as in our study), the recurrence rate was 41% and the mortality rate was 13.6%.² In the study by Ni et al,¹⁷ we could deduce from the data reported that the mortality rate was similar following globe-sparing surgery and orbital exenteration (35% and 40%, respectively.) In other published series, these data were not specifically provided and could not be deduced.

The decision whether to do an orbital exenteration is individualized and is mostly based on the degree of extension of the lacrimal sac carcinoma into the orbital soft tissue. Orbital exenteration was done in only 4 patients in our series despite the fact that many more of the tumors were associated with orbital and paranasal sinus extension. Orbital exenteration did not lead to better survival in our series—in fact, 2 of the 3 patients who died underwent orbital exenteration, suggesting that this procedure was used in patients with more aggressive tumors that led to poor outcomes regardless of radical surgery. The 3 patients in our series who died were patients with rapidly growing, high-grade carcinomas with multiple short-interval recurrences. Based on the review of the literature as well as our experience, we do not believe the treatment approaches would be different based on the various tumor histologies other than the possibility of receptor marker expression in individual tumors that may open the possibility of using targeted adjuvant systemic treatments concurrent with radiation therapy. An example of this would be expression of Her-2 receptor expression in adenocarcinomas which may justify the use of Herceptin either in the adjuvant setting or for treatment of metastatic disease.

Continued surveillance—including a careful clinical examination of the orbit and nasal cavity and computed tomography of the head and neck every 3 months during the first year, at least every 6 months during the second year, and annually thereafter—is recommended for all patients after multidisciplinary management of lacrimal sac/nasolacrimal duct carcinomas. In cases where MRI was the initial imaging modality, repeated MRI's during the follow-up period would be appropriate to allow for comparison with baseline. In addition, an MR may be recommended in patients in whom there is concern for perineural spread.

Radiation therapy was recommended for 13 of the 14 patients in our series and was delivered at high doses consistent with protocols used for other epithelial malignancies of the head and neck. Three patients developed radiation-related toxic effects, but only 1 experienced significant loss of visual function. Photons and protons were used with similar frequency; however, more recently, preference has been given at MD Anderson to using proton radiation therapy given the possibility of limiting the radiation doses to the cornea, optic nerve, and optic chiasm while treating the lacrimal sac and paranasal sinuses. Proton radiation therapy is also associated with less risk of radiation dose to more posterior skull base structures. The potential risk of ocular damage with high-dose radiation therapy can be mitigated with careful planning of radiation therapy and relatively globe-sparing radiation techniques.

The most common carcinomas encountered in our cohort were squamous cell carcinoma and transitional cell carcinoma, which is believed by some pathologists to be closely related histologically to squamous cell carcinoma. Less frequent carcinomas in our cohort were adenoid cystic carcinomas, adenocarcinomas, and other poorly differentiated carcinomas. A similar distribution of carcinoma types has been reported in prior series of lacrimal sac tumors. Among the malignant epithelial malignancies in the series of Ni et al and Stefanyszyn et al, squamous cell carcinoma was the most common type, followed by transitional cell carcinoma and then less common entities such as adenocarcinoma, adenoid cystic carcinoma, mucoepidermoid carcinoma, and poorly differentiated carcinoma.^{2,17–21}

Lacrimal sac/nasolacrimal duct carcinomas are uncommon tumors and can be easily mistaken for more benign processes such as idiopathic nasolacrimal duct blockage or chronic dacryocystitis. One important take-home message of our study for the general oculoplastic surgeon is to be on the lookout for any unusual findings during a DCR, including a mass lesion in the sac or duct area or soft tissue growth. If such a finding is encountered, the tissue should be sampled at the time of DCR, and the DCR should be aborted until the results of biopsy are confirmed and an imaging study of the area can be obtained and reviewed. The other recommendation is to pay special attention to patients with epiphora or dacryocystitis that does not resolve after a routine DCR. Failure of such symptoms to resolve in the early postoperative period may indicate an underlying malignancy and should prompt immediate computed tomography of the head and neck region to rule out the rare but important possibility of an underlying lacrimal sac/nasolacrimal duct carcinoma.

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TABLE
Characteristics of 14 patients with lacrimal sac and/or nasolacrimal duct carcinomas

Patient	Age (years)	Sex	Tumor Type	Presenting Sign or Symptom	Globe Sparing Surgery?	XRT	Chemotherapy	Follow up Time (months)	Status at last follow up
1	63	Male	Transitional Cell Carcinoma	Dacryocystitis	Yes	70 CGE	Cisplatin	27	NED
2	73	Male	Transitional Cell Carcinoma	Epiphora	No	66 Gy	None	96	NED
3	53	Female	Inverted Papilloma with Carcinoma in situ transformation	Mass	Yes	None	None	41	NED
4	45	Male	Adenocarcinoma	Epiphora	No	60 Gy	Multiple including erlotinib and carboplatin	30	Dead
5	46	Female	Squamous cell Carcinoma	Dacryocystitis	Yes	60 CGE	None	58	NED
6	69	Male	Poorly Differentiated Carcinoma	Mass	No	70 Gy	Cisplatin	7	Dead
7	73	Male	Squamous cell carcinoma	Epiphora	Yes	60 CGE	None	38	NED
8	48	Male	Squamous cell Carcinoma	Epiphora	No	60-70 Gy	*	27	NED
9	54	Male	Squamous Cell Carcinoma	Mass	Yes	56 CGE	None	18	NED
10	63	Male	Squamous cell Carcinoma	Epiphora	Yes	70 CGE	Cisplatin and Docetaxel	16	Active disease
11	48	Female	Adenoid Cystic Carcinoma	Mass	Yes	60 Gy	Cisplatin	48	Dead
12	67	Female	Squamous cell Carcinoma	Mass	Yes	Declined	Carboplatin and Paclitaxel	17	NED
13	70	Male	Adenoid Cystic Carcinoma	Mass	Yes	60 Gy	Cisplatin	6	NED
14	47	Female	Squamous cell Carcinoma	Mass. Epiphoria	Yes	60 Gy	None	7	NED

NED, no evidence of disease; XRT, external beam radiation therapy.

* Patient treated at an outside institution and chemotherapy records were unavailable; CGE- Cobalt Grey Equivalent