BRIEF ARTICLES

Evaluation of Cutaneous Squamous Cell Carcinomas that Extend to the Parotid: the Value of Negative Surgical Margins

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ABSTRACT

While high-risk characteristics for cutaneous squamous cell carcinoma (cSCC) and the management of metastatic cSCC have received considerable attention in the literature, standard of care management for the positive MMS margin at the parotid fascia in cSCC has yet to be clarified. The aim of this study is to better define optimal management approaches for the positive deep Mohs Micrographic Surgery (MMS) margin at the parotid fascia. Inclusion criteria for this retrospective case series were patients presenting to the Saint Louis University with biopsy proven cSCC with a positive deep MMS margin at the parotid fascia who were referred to HNS and treated with curative intent. The following data were recorded: age; gender; NCCN high-risk factors; adjuvant surgical, medical, radiation (RT), or chemoradiation (CRT) therapies; outcomes; and follow-up data. Eight patients undergoing MMS had a positive deep margin at the parotid fascia. HNS performed 7 parotidectomies and 1 wide local excision (WLE), obtaining negative margins in 75.0% (6/8) of patients (5/7 parotidectomies and 1/1 WLE). Obtaining negative surgical margins (6/8 patients) resulted in a disease free survival (DFS) and overall survival (OS) of 27.8 and 43.6 months, respectively; compared to a DFS of 20.6 months and OS of 39.1 months for positive margins (2/8 patients). This study demonstrates that resection with negative surgical margins results in excellent long-term local and regional disease control, and overall survival for cSCC patients with positive deep MMS margin at the parotid fascia.

INTRODUCTION

In 2012, approximately 700,000 new cases of cutaneous squamous cell carcinoma (cSCC) were diagnosed in the US. Of these, approximately 5,500 progressed to nodal metastasis and 4,000 caused death, highlighting the considerable burden of the disease.[1] The preauricular area is a common site for cSCC as well as a region of particular morbidity and mortality as it overlies the parotid gland containing cranial nerve VII.[2] While high-risk characteristics for cSCC and the management of metastatic cSCC have received considerable attention in the literature, standard of care management for the positive MMS margin at the parotid fascia in cSCC has yet to be clarified.[3] The aim of this study is to better define optimal management approaches for the positive deep MMS margin at the parotid fascia.

METHODS

This retrospective case series was approved by the Saint Louis University Institutional Review Board. Initial inclusion criteria were all patients presenting to the Saint Louis University Departments of Dermatology and Otolaryngology - Head and Neck Surgery (HNS) with biopsy proven cSCC treated with curative intent from January 1, 2000 to January 1, 2014. Final inclusion criteria were patients with a positive deep MMS margin at the parotid fascia who were referred to HNS and treated with curative intent. The following data were recorded: age; gender; NCCN high-risk factors; adjuvant surgical, medical, radiation (RT), or chemoradiation (CRT) therapies; outcomes; and follow-up data. Patient medical records and the Social Security Death Index were reviewed to determine disease-free survival (DFS) and overall survival (OS), respectively.

RESULTS

MMS treated 325 patients with cSCCs in the preauricular, cheek, or temple anatomic regions. Of these patients, 56 (17.2%, 56/325) were referred to HNS for further evaluation. Fifty-four patients had 1 cSCC and 2 patients had 2 cSCCs. During individual chart review, 8 patients (2.5%, 8/325) undergoing MMS had a positive deep margin at the parotid fascia.

Patients with a positive MMS margin at the parotid fascia had a mean age of 77.1 years (range 57.2-90.2 years) and the majority were male (87.5%, 7/8). In this series, average tumor size was 2.8 cm (range 1.5 - 4.8 cm), 75.0% (6/8) were recurrent, and perineural invasion (PNI) was present in 50.0% (4/8) of cSCCs (Table 1). Of note, 62.5% (5/8) of cSCCs were well-differentiated and did not recur. Two of eight cSCCs were noted to have keratoacanthoma (KA) features, one of which metastasized to the parotid gland (Table 2).

HNS performed 7 parotidectomies and 1 wide local excision (WLE), obtaining negative margins in 75.0% (6/8) of patients (5/7 parotidectomies and 1/1 WLE). In the 2 patients who had positive margins after HNS parotidectomies, RT was utilized (of note, 1 patient with positive margins after HNS deferred parotidectomy several months until a palpable mass was found on physical exam). Obtaining negative surgical margins (6/8 patients) resulted in a DFS and OS of 27.8 and 43.6 months, respectively; compared to a DFS of 20.6 months and OS of 39.1 months for positive margins (2/8 patients). For the entire cohort, DFS was 25.7 months and OS was 42.5 months.
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DISCUSSION

In this cohort, negative surgical margins improved DFS by 7.2 months and OS by 4.5 months (Table 1).

Negative surgical margins provide patients with high-risk cSCC the best possible outcome, a definitive cure, and thus remains the treatment goal.[4] MMS remains the first-line treatment for high-risk cSCC, as it provides thorough surgical margin evaluation, which allows a positive deep margin at the parotid fascia to be identified and further managed by HNS.[5] Interestingly, the finding of a positive deep surgical margin led to the identification of microscopic disease in the parotid gland that was not detected with preoperative CT scans in two patients (Table 2). This early detection of microscopic regional disease may have contributed to the improved outcomes observed in our cohort.

When confronted with the positive deep MMS margin at the parotid fascia, standard of care management has yet to be definitively defined. This finding has clear prognostic and therapeutic implications as involvement of the parotid has been associated with worse outcomes.[2] Patients with a positive deep margin at the parotid fascia should undergo HNS evaluation and surgical management, as this is the most appropriate next step.[5] Surgical Continuity of Care, MMS handing off a positive deep margin at the parotid fascia to HNS, provides the patient the best opportunity to achieve negative surgical margins, and thus delivers the best possible outcome.

Clinicians have several options for treatment when the MMS margin is positive at the parotid fascia, including HNS excision, RT, CRT, or a combination of HNS excision and adjuvant RT or CRT[5]. This study substantiates previous findings, further confirming the importance of obtaining negative surgical margins for cSCC with parotid involvement.[5] When negative surgical margins are unobtainable or there is lymph node involvement, surgery plus RT has been shown to be superior to either treatment modality individually.5 Today, patients with highly locally invasive or metastatic disease would be candidates for the recently FDA approved PD-1 inhibitor, cemiplimab.[6]

The limitations of this study include the following: it is a small retrospective case series and lacks randomization and blinding. A multi-institution prospective randomized control trial is needed to provide definitive evidence based standard of care management recommendations for high-risk and invasive cSCC.

Table 1. Patient demographics, tumor characteristics, and outcomes.

Variable	N (%)	Mean	Range
Patient Demographics:			
Age, years		77.1	57.2 - 90.2
Gender			
Male	7 (88%)		
Female	1 (13%)		
Tumor Characteristics			
Size, cm		2.8	1.5 - 4.8
Location			
Cheek and temple	3 (38%)		
Preauricular	5 (63%)		
Recurrent tumors	6 (75%)		
Primary tumors	2 (25%)		
Histology			
Well-differentiation	5 (63%)		
Moderate-differentiation	3 (38%)		
Keratoacanthoma[a]	2 (25%)		
Acantholytic	1 (13%)		
Perineural Invasion	4 (50%)		
Perineural Inflammation	1 (13%)		
Lymphovascular Invasion	1 (13%)		

Summary of outcomes			
Entire cohort	8 (100)		
Follow-up, months		23.1	0.0 - 64.4
Disease-free survival		25.7	4.0 - 64.4
Overall survival		42.5	15.0 - 85.0
Negative margins after HNS	6 (75%)		
Disease-free survival		27.8	6.0 - 64.4
Overall survival		43.6	16.0 - 85.0
Positive margins after HNS	2 (25%)		
Disease-free survival		20.6	4.0 - 37.1
Overall survival		39.1	15.0 - 63.2

Abbreviations: HNS, otolaryngology – head and neck surgery.
[a]Two cSCCs had keratoacanthoma features. One was well-differentiated, and the other was moderately-differentiated and metastasized to the parotid gland.

Table 2. Patient characteristics, management approaches, and outcomes.

	Location/ size	Tumor Features	Physical Exam/ Imaging/ Consults	Surgical Management	Disease-free survival/Overall Survival
1	Left preauricular/2.6x1.4cm	Recurrent, PNInv, well-differentiated	CT: negative. Pre-MMS HNS consult	1. Slow Mohs[a]: 1 stage. Positive margin at parotid fascia. 2. HNS: superficial parotidectomy and neck dissection. Intra- and peri-parotid LN levels II, III, and V positive with ECS. Margins negative. 3. Adjuvant RT.	DFS: 64.4mo / OS: (CoD unknown) 73.4mo
2	Left preauricular /3.0x2.3cm	Recurrent s/p LN2; moderately differentiated with keratoacanthoma features, PNInf;	CT: negative	1. MMS: 1 stage. Positive margin at parotid fascia. 2. Slow Mohs: 2nd stage (excision processing). Positive deep margin. 3. HNS: parotidectomy. Parotid gland positive; LNs negative. Positive margins. Pt declined further surgery. 4. Adjuvant RT (positive re-excision margins).	DFS: 37.1mo/ OS: currently alive, 63.2mo
3	Right temple and cheek/2.2x1.6cm	Recurrent s/p 2 excisions; well-differentiated, PNInv, lymphovascular invasion; muscular invasion	P/E: parotid mass. CT: positive	1. MMS: 4 stages. Positive margin at parotid fascia. 2. Pt declined parotidectomy. 3. Palpable mass noted on P/E during 2month f/u 4. HNS: superficial parotidectomy and neck dissection. Parotid gland and parotid LNs positive with ECS. Positive margin. 5. Adjuvant RT (positive re-excision margins and to recurrence)	DFS: 4mo (metastasis in subcarinal LN, received subsequent RT to chest)/ OS: (CoD unknown) 15mo
4	Right preauricular/4.8x2.3cm	Well-differentiated, acantholytic, PNInv	CT: parotid invasion. Pre-	1. Slow Mohs: 1 stage. Positive margin at parotid fascia. 2. HNS: parotidectomy and neck dissection. Parotid gland positive;	DFS: 6mo /OS: currently alive, 21mo

			MMS HNS consult	LN negative. Margins negative.	
5	Left temple and cheek/1.5x1.0cm	Recurrent, moderate-differentiation, PNInv	No imaging	1. Slow Mohs: 3 stage. Positive margin at parotid fascia. 2. HNS: re-excision, superficial parotidectomy, and neck dissection. Parotid gland negative. Margins negative.	DFS: 20.8mo/ OS: (CoD unknown) 39.7mo
6	Right preauricular/3.2x2.7cm	Moderate-differentiation	CT: negative	1. Mohs: 6 stages. Positive margin at parotid fascia. 2. HNS: re-excision and parotidectomy. Parotid gland negative. Margins negative.	DFS: 9.6mo/ OS: (CoD unknown) 26.4mo
7	Left preauricular/3.3x2.1cm	Recurrent s/p ED&C and excision, well-differentiated with keratoacanthoma features	No imaging	1. Slow Mohs: 1 stage. Positive margin at parotid fascia. 2. HNS: re-excision and superficial parotidecomy. Parotid gland negative. Margins negative.	DFS: no follow-up/ OS: (CoD unknown) 16mo
8	Right temple and cheek/ 2.0x2.0cm	Recurrent, well-differentiated	No imaging	1. Slow Mohs: 1 stage. Positive deep margin. 2. HNS: re-excision. Margins negative.	DFS: 38.0mo/ OS: currently alive, 85 mo

Abbreviations: PNInv, perineural invasion; CT, computed tomography; MMS, Mohs Micrographic Surgery, frozen sections only; HNS, otolaryngology-head and neck surgery; ECS, extracapsular spread; RT, radiation therapy; DFS, disease-free survival; OS, overall survival; CoD, cause of death; LN2, liquid nitrogen; PNInf, perinerual inflammation; ED&C, electrodessication and curettage.

[a]Slow Mohs: MMS with staged excision pathology; permanent sections only.

[b]Patient differed parotidectomy until parotid swelling was found on physical exam during follow-up. Local and distant metastases were noted on computed tomography scan.

CONCLUSION

This study and others demonstrate that resection with negative surgical margins results in excellent long-term local and regional disease control, and overall survival for patients with high-risk and invasive cSCC.[4] When caring for complex patients with invasive cSCC we utilize an early, collaborative, and multidisciplinary approach with HNS that includes the concept of Surgical Continuity of Care. Surgical Continuity of Care means when managing the MMS positive deep margin we collaborate closely with HNS in an attempt to obtain negative surgical margins prior to RT, CRT, or other treatment modalities when treating patients with curative intent. Tumor free surgical margins remain the treatment goal for invasive and locoregional cSCC, because a clear surgical margin provides the best outcome for our patients.

Conflict of Interest Disclosures: None.

Funding: None.

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