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Mohs micrographic surgery versus wide local excision for sebaceous adenocarcinoma of the eyelid : Analysis of a national database

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Summary *Background:* Sebaceous adenocarcinomas are rare and potentially aggressive tumors, which typically arise in the periocular region. Surgical treatments for eyelid sebaceous adenocarcinomas include Mohs micrographic surgery (MMS) and wide local excision (WLE). The objective of this study was to compare long-term survival outcomes of MMS versus WLE techniques for eyelid sebaceous adenocarcinomas.
Methods: A retrospective analysis was performed using data obtained from the Surveillance, Epidemiology, and End Results (SEER) cancer registry database. We analyzed cases diagnosed from 1998 to 2015 within the database. Patients diagnosed with sebaceous adenocarcinoma were identified using ICD codes. Cases were limited to primary sebaceous adenocarcinomas involving specifically the eyelid region. The main outcomes were assessed by Kaplan-Meier (KM) survival and Cox proportional hazards model.
Results: Sixty-seven cases of MMS were compared with 114 cases of WLE for eyelid sebaceous carcinoma. Overall KM survival rates for MMS compared to WLE at 5-year (75.6% vs. 70.3%) and 10-year follow-up (69.2% vs. 46.9%) did not show significant difference by logrank ($P = 0.062$). Similarly, after adjusting for demographic, tumor, and treatment characteristics, there was no significant difference in cancer-specific survival (HR 0.45, 95% CI 0.03-6.92, $P = 0.57$) and overall survival (HR 0.94, 95% CI 0.50-1.74, $P = 0.83$) when MMS surgical technique was compared with WLE techniques.

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Conclusions: Our adjusted analyses demonstrated no differences in overall survival or cancer-adjusted survival for patients with eyelid sebaceous adenocarcinomas treated with MMS compared with WLE. In areas requiring preservation of tissue because of cosmetic or functional purposes, MMS is a reasonable surgical approach.

Introduction

Sebaceous adenocarcinomas are rare and potentially aggressive tumors that typically arise in the periocular region. Sebaceous adenocarcinomas affect predominantly the meibomian and Zeis glands in the periocular region and are the fourth most common eyelid neoplasm.[1] Reported risk factors include elderly age,[2] Asian background,[3,4] females,[5-7] prior radiotherapy, and genetic factors.[8]

Sebaceous adenocarcinoma can have a wide range of presentations; it can present as a slowly growing firm nodule mimicking other benign dermatological lesions or it can present similar to benign blepharoconjunctivitis, or it may manifest with widespread local and distant metastases. Given the wide range of presentations, patients often have delayed diagnosis of sebaceous adenocarcinomas, which may contribute to worsening prognosis.[4,5]

Surgical treatment of sebaceous adenocarcinomas can involve either wide local excision (WLE) with standardized margins or Mohs micrographic surgery (MMS). A surgical margin of 5–6 mm has been recommended for the WLE approach.[9] The MMS approach offers potential advantages of definitive marginal excision as well as tissue preservation, particularly in the periorbital region, where anatomy and function should ideally be preserved.

Given the rarity of sebaceous adenocarcinomas, there are limited available data comparing the surgical outcomes and survival following MMS versus WLE treatment for eyelid sebaceous adenocarcinomas. The majority of available evidence in the literature is limited to small case series or case reports. Therefore, to address current limitations in the literature, we analyzed a nationwide database to compare survival outcomes of WLE versus MMS techniques for sebaceous adenocarcinomas of the eyelid.

Methods

Data source

Retrospective analysis was conducted using data obtained from the Surveillance, Epidemiology, and End Results (SEER) cancer registry database.[10] The SEER database, which is sponsored by the National Cancer Institute, consists of 18 population-based cancer registries and accounts for approximately 28% of the United States population. No institutional review board approval was required for this study, as the database uses publicly available information without personal identifiers.

Patient selection

Cases in the SEER database have histology and involved anatomic site recorded by the morphology and topography codes of the International Classification of Diseases for Oncology – Third Edition.[11] We analyzed case diagnoses between 1998 and 2015 from the database, which includes parameters such as demographics, tumor histology, tumor morphology, cancer stage at diagnosis, treatment regimen, and survival. Patients diagnosed with sebaceous adenocarcinoma were identified using ICD codes 8410/3. Cases that underwent MMS were identified using SEER surgery codes 34, 35, and 36, whereas cases that underwent WLE were identified using codes 45, 46, and 47. Cases were limited to first primary sebaceous adenocarcinomas involving specifically the eyelid region (ICD-O-3 topography code C44.1 eyelid). Cases that were not included in this analysis were those of patients for whom the primary site of disease was ambiguous or unknown, those for whom sebaceous adenocarcinoma was not the first primary malignancy, and those who did not undergo MMS or WLE for surgical treatment.

Data collection

Demographic data including age at diagnosis, sex, race, and ethnicity were collected. Tumor and treatment characteristics collected included diagnosis type, laterality, grade, stage, radiation use, and chemotherapy use. Outcomes assessed included overall survival and cancer-specific survival.

Statistical analysis

Pearson's chi-square test was used to compare demographic, tumor, and treatment variables between MMS and WLE groups. Kaplan–Meier (KM) survival was evaluated at 5- and 10-year follow-up and compared using logrank analysis. Bivariable and multivariable Cox proportional regression models were used to calculate the hazard ratios (HR) with 95% confidence interval (CI) for cancer-specific survival and overall survival. Covariates included in the adjusted model were age at diagnosis, race, sex, ethnicity, stage, grade, radiation treatment, and chemotherapy treatment. All statistical analysis was performed using SPSS statistical software (version 25, IBM Corp., Armonk, NY, USA). *P*-value of less than 0.05 was used to determine statistical significance.

Table 1 Demographic, tumor, treatment, and survival characteristics of patients with sebaceous adenocarcinoma.

		Surgery type				
		MMS		WLE		Chi-square
		N	%	N	%	*p*-value
Age group	0–59 years	19	28.4%	16	14.0%	0.062
	60–74 years	21	31.3%	44	38.6%	
	75 + years	27	40.3%	54	47.4%	
Race	White	54	80.6%	92	80.7%	0.568
	Black	2	3.0%	7	6.1%	
	Other	9	13.4%	14	12.3%	
	Unknown	2	3.0%	1	0.9%	
Sex	Female	43	64.2%	55	48.2%	0.038
	Male	24	35.8%	59	51.8%	
Ethnicity	Nonhispanic	65	97.0%	106	93.0%	0.252
	Hispanic	2	3.0%	8	7.0%	
Stage	Stage I/II	31	46.3%	13	11.4%	<0.001
	Stage III/IV	0	0.0%	2	1.8%	
	Unknown stage	36	53.7%	99	86.8%	
Grade	Grade I/II	4	6.0%	15	13.2%	0.019
	Grade III/IV	12	17.9%	36	31.6%	
	Unknown	51	76.1%	63	55.3%	
Laterality	Unilateral	67	100.0%	114	100.0%	-
Diagnosis type	Positive histology	67	100.0%	114	100.0%	-
Radiation	No/unknown	66	98.5%	103	90.4%	0.033
treatment	Yes	1	1.5%	11	9.6%	
Chemotherapy	No/unknown	64	95.5%	113	99.1%	0.112
treatment	Yes	3	4.5%	1	0.9%	
Vital status	Alive	54	80.6%	51	44.7%	-
	Dead	13	19.4%	63	55.3%	
Cause-specific	Alive or dead of other cause	64	95.5%	104	91.2%	-
vital status	Dead attributable to cancer diagnosis	2	3.0%	10	8.8%	
	Unknown/NA	1	1.5%	0	0.0%	

MMS, Mohs micrographic surgery; WLE, wide local excision; -, not available.

Results

Patient and tumor characteristics

From the SEER database, 67 cases of MMS were compared with 114 cases of WLE for eyelid sebaceous carcinoma across a mean (±SD) follow-up period of 76.3 (±55.8) months. There was a significantly higher proportion of elderly patients ≥75 years in the WLE group than in the MMS group (47.4% vs. 40.3%, $P = 0.062$). There was no significant difference in the distribution of race between MMS and WLE ($P = 0.568$). There was a higher proportion of females in the MMS group than in the WLE group (64.2% vs. 48.2%, $P = 0.038$). The proportion of Stage I/II sebaceous adenocarcinomas was significantly higher for the MMS cohort than for the WLE cohort (46.3% vs. 11.4%, $P < 0.001$). In terms of grading of tumor, Grade I/II was significantly lower in the MMS group than in the WLE group (6% vs. 13.2%, $P = 0.019$). All sebaceous adenocarcinomas of the eyelid studied were unilateral and diagnosed histologically (Table 1).

Survival outcomes

Overall KM survival for MMS compared to WLE survival at 5-year (75.6% vs. 70.3%) and 10-year follow-up (69.2% vs. 46.9%) did not show significant difference by logrank ($P = 0.062$). Similarly, after adjusting for demographic, tumor, and treatment characteristics, there was no significant difference in cancer-specific survival (HR 0.45, 95% CI 0.03-6.92, $P = 0.57$) and overall survival (HR 0.94, 95% CI 0.50-1.74, $P = 0.83$) when MMS surgical technique was compared with WLE techniques (Table 2).

Discussion

Multiple surgical techniques are used for the excision of sebaceous adenocarcinomas. A significant proportion of this rare and potentially aggressive tumor is located in the periocular region, especially the eyelids. For tumors of this location, MMS is an emerging technique with advantages

Table 2 Unadjusted and adjusted cox regression analysis.

		Overall survival		Cause-specific survival	
		HR (95% CI)	*p*-value	HR (95% CI)	*p*-value
Unadjusted analysis	WLE	Ref	Ref	Ref	Ref
	MMS	0.568 (0.31, 1.039)	0.066	0.446 (0.097, 2.047)	0.299
Adjusted analysis	WLE	Ref	Ref	Ref	Ref
	MMS	0.936 (0.504, 1.736)	0.833	0.447 (0.029, 6.921)	0.565

MMS, Mohs micrographic surgery; WLE, wide local excision.

of preservation of anatomical function and cosmesis. Few studies have directly compared outcomes of MMS versus traditional WLE for sebaceous adenocarcinomas of the eyelid. Using a large nationwide database, we performed a retrospective analysis to compare 67 cases of MMS with 114 cases of WLE for eyelid sebaceous carcinoma. We found that patients who underwent MMS had similar overall and cancer-specific survival as those of WLE for sebaceous adenocarcinoma.

Traditionally, WLE with 5–6 mm margins has been the surgical treatment of choice for sebaceous carcinomas.[1,12] Wide margin excision for sebaceous carcinomas is associated with high recurrence rates of 36% and 5-year mortality rates of 18%.[13] Nevertheless, in areas such as the periocular region, which are functionally and anatomically sensitive, it may not be ideal to pursue 5–6 mm excision margins. As a result, alternative surgical approaches with greater tissue preservation should be considered. Some reports have suggested that the MMS technique is associated with lower recurrence rates[7,12] and maximal tissue preservation.[12] However, few studies have directly compared WLE and MMS techniques for sebaceous carcinomas. Hou et al.[14] compared 35 cases of sebaceous carcinomas treated with MMS with 26 cases treated with WLE. Of cases with documented follow-up, the authors found one case of recurrence in the MMS group compared with one case of recurrence in the WLE group and concluded that both techniques were effective for sebaceous carcinoma treatment.

The disadvantage of the MMS technique for sebaceous carcinoma treatment is that it may be multifocal and challenging to interpret pagetoid spread in frozen sections.[15,16] The advantage of the MMS approach compared to those of the WLE approach is that it involves definitive marginal excision, with minimal loss to the surrounding normal tissues. This point is particularly pertinent considering the anatomical eyelid location, which is the close vicinity of multiple important structures.

The present study is constrained by several limitations. The nature of this study is a retrospective analysis from a national registry and therefore is susceptible to selection bias. Another limitation is that the potential for miscoding cannot be completely excluded, given that cases were identified using ICD codes.

In summary, our adjusted analyses demonstrated no differences in overall survival or cancer-adjusted survival for patients with eyelid sebaceous adenocarcinomas treated with MMS compared with WLE. In areas requiring preservation of tissue due to cosmetic or functional purposes, MMS is a reasonable surgical approach.

Author contributions

Dr. Phan, Loya, had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Phan, Loya. Acquisition, analysis, and interpretation of data: Phan, Loya. Drafting of the manuscript: Phan, Loya. Critical revision of the manuscript for important intellectual content: Phan, Loya. Statistical analysis: Loya. Obtained funding: No funding. Administrative, technical, or material support: Phan, Loya. Study supervision: Phan, Loya.

(I) Conception and design: Kevin Phan, Asad Loya; (II) Administrative support: Kevin Phan, Asad Loya; (III) Provision of study materials or patients: Kevin Phan, Asad Loya; (IV) Literature search: Kevin Phan, Asad Loya; (V) Collection and assembly of data: Kevin Phan, Asad Loya; (VI) Data analysis and interpretation: Kevin Phan, Asad Loya; (VII) Manuscript writing: Kevin Phan, Asad Loya; (VIII) Final approval of manuscript: Kevin Phan, Asad Loya.

Conflicts of interest

None.

Ethical approval

This is not required for this study, as neither humans nor animals were used.

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