SKIN

RESEARCH LETTER

Merkel Cell Carcinoma Primary Sites and Overall Survival: The Prognostic Indications of Head and Neck Tumors

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Merkel cell carcinoma (MCC) is a rare cutaneous neuroendocrine tumor. Primarily affecting the elderly, the incidence of MCC is 0.10 to 1.6 cases per 100,000 people per year.[1] MCC has a low overall survival (OS), ranging between 37 and 74% at 5 years.[1–5] The majority of lesions occur on the head and neck followed by the trunk and extremities.[2,3] In a trial of high-risk MCC, patients treated with chemoradiotherapy, tumor site and positive nodes were predictive of worse local control and survival.[3] Other reported poor prognostic factors include age >60 years, male sex, primary lesion size >2 cm, and absence of radiotherapy treatment.[3] Still, there is limited literature describing the influence of primary tumor site as a prognostic factor for MCC. This study aims to compare OS between head and neck MCC (hnMCC) and other MCC body regions (oMCC). This study also specifically examines outcomes of scalp and neck MCC (snMCC) compared to other head regions (ohMCC).

A retrospective cohort study was performed for patients with cutaneous stage I-IV MCC between 2004-2017 reported to the National Cancer Database (NCDB). NCDB is a US oncology database of hospital registry data from >1,500 Commission on Cancer (CoC)-accredited facilities. The following cases were excluded: non-primary tumors, follow-up time of 0 months, palliative care, diagnosis date after facility's reference date, age at diagnosis <18 years, and cases diagnosed at different reporting and treatment facilities. Outcomes were analyzed via Kaplan-Meier survival plots with log-rank testing and Cox proportional-hazards modeling—controlling for: age, sex, race, Charlson-Deyo Comorbidity score, insurance status, stage, surgical margins, radiation, chemotherapy, and facility location.

A total of 11,579 cases were analyzed—4,808 hnMCC and 5,790 oMCC cases, with 981 missing primary site information. About 80% of hnMCC were specifically snMCC cases (3,809 cases). Univariate analysis revealed statistically significant differences in OS for oMCC (1-year:86.9%; 5-year:47.3%) and hnMCC (1-year:82.7%; 5-year:38.7%) (log rank $p<0.001$ and $p<0.001$, respectively). (**Table 1**) On Cox regression analysis, hnMCC showed significantly increased risk of death compared to oMCC (Hazard Ratio [HR]=1.091; 95% Confidence interval [95%CI] 1.017-1.169; p=0.014). Among hnMCC, snMCC showed lower OS (1-year:76.6%; 5-year:29.7%) compared to ohMCC (1-year:84.4%; 5-year:41.3%) (log

Table 1. Overall survival in Merkel cell carcinoma patients, 2004-2017.

Overall survival (95% CI)	Primary Site		p-value
	Body (n= 5,790)	**Head (n= 4,808)**	
1-Year	86.9%	82.7%	<0.001
3-Year	63.6%	56.2%	<0.001
5-Year	47.3%	38.7%	<0.001
	Scalp and Neck (n=999)	**Other Head (n= 3,809)**	
1-Year	76.6%	84.4%	<0.001
2-Year	45.1%	58.3%	<0.001
5-Year	29.7%	41.3%	<0.001

rank p<0.001). Multivariable regression demonstrated an independent association between snMCC primary site and an increased risk of death when compared to ohMCC (HR=1.297; 95% CI 1.153-1.457; p<0.001).

There is limited data on tumor location as a prognostic factor for MCC. Our findings show the scalp and neck are locations of greatest incidence, which is consistent with prior evidence that MCC occurs more commonly on sun-exposed regions of the body.[1] With regards to prognosis, OS for hnMCC at 1 and 5-years was significantly lower than oMCC. Other literature has also reported hnMCC as a negative prognostic indicator.[1] More specifically, snMCC had the lowest survival rates and highest risk of death, which suggests that location of primary tumor has substantial impact on prognosis. Previous studies determined that age, tumor stage, and immunocompromised status are predictive of overall mortality.[4] As one of the largest studies of MCC patients, our results provide evidence that tumor location is a vital factor for prognostic indication when evaluating patients. Our results may be utilized by patients and physicians to assess risk and prognosis, which also influences treatment modality decision-making. Limitations include inability to record MCC patients who were not treated at health systems within the database.

Our findings demonstrate that patients with head and neck MCC are at an increased risk of poorer survival outcomes compared to other body primary sites. Specifically, among head and neck primary tumors, those with scalp and neck MCC involvement appear to have an even greater mortality risk.

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