

POSTER 44

Metastases in patients with Merkel cell carcinoma: Management and survival - A SEER population-based cohort study

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Abstract:

Introduction: Merkel cell carcinoma (MCC) is a rare cutaneous cancer with a highly aggressive behavior. Lymph node (LN) involvement and distant metastases have been associated with worse prognosis. For localized disease, surgery is the mainstay of treatment; however, there is no clear consensus on the management of MCC metastases. To date, in depth data on MCC metastatic pattern, management and survival is scarce and consists mainly of case studies.

Objectives: The purpose of this large population study was to: 1) describe demographic and clinical characteristics of patients with MCC, 2) analyze risk factors for regional LN and distant metastases, 3) analyze risk factors for overall and disease-specific death in patients with metastatic disease, and 4) evaluate the impact of LN involvement and metastatic disease on overall and disease-specific survival.

Materials and Methods: Patients diagnosed with MCC from 2000 to 2018 were identified in the Surveillance, Epidemiology and End Results (SEER) database. All patients included in the analysis had histopathological confirmation of MCC. Demographic (age, gender, race), clinical (primary location, tumor size, LN involvement, metastatic status, AJCC stage, history of previous malignancy, current status, cause of death) and treatment variables (surgery to primary site or distant site, LN surgery, radiotherapy, chemotherapy) were included. Overall 5-year survival was calculated using the Kaplan-Meier method, and the survival difference was assessed using the log-rank test. Multivariate analysis was performed using Cox proportional hazard regression to determine significant risk factors.

Results: We included 2010 patients with MCC in our analysis, out of which 288 had metastases at diagnosis (14.3%). Regarding **1) patient characteristics** in metastatic disease, median age was 76 years, 72.9% were male, and 96.03% were white. About 33% of primary tumors in patients with metastases were located in the face, head, or neck, followed by the limbs (26%) and trunk (12%). Tumor size was greater in patients with metastases, with 18.5% of the sample having tumors >50 mm; only 5.7% of patients without metastases had tumors >50 mm. The most common sites of metastasis were the distant lymph nodes (38.3%), liver (39.3%), bone (27.7%) and the lungs (21.9%). On **2) risk factors for regional LN and distant metastases**, multivariate analysis showed that males were 1.33 times more likely to have regional LN involvement (OR=1.33, p<0.001). Primary tumor location in the trunk was a risk factor for LN involvement (OR=1.27, p=0.017), while location in the limbs was a protective factor for distant metastases (OR=0.6, p=0.011). **Tumors >10 mm showed risk for LN involvement**

being higher when size was >20 mm (OR=2.76, p<0.001); similarly, risk for distant metastases was higher when tumor size was >20 mm (OR=8.88, p<0.001). Bone, liver, distant LN, and other distant metastases were also associated with increased risk for regional LN compromise. Among these, patients with distant LN compromise had the highest risk of showing regional LN involvement (OR=3.89, p=0.001). Patients with surgery to the primary site were less likely to develop regional LN or distant metastases (OR=0.77, p=0.024 and OR=0.16, p<0.001, respectively). Similarly, patients who underwent LN surgery had a 0.58 times lesser risk of presenting metastases at diagnosis (OR=0.421, p=0.037). In terms of **3) risk factors for overall and disease-specific death in metastatic disease**, primary location in the trunk was a protective factor for overall death (OR=0.27, p=0.011); surgery to another site and radiotherapy were also associated with decreased risk of overall death (OR=0.27, p=0.011 and OR=0.32, p=0.004, respectively). Finally, on **4) the impact of LN involvement and metastatic disease on overall and disease-specific survival**, one-year overall survival was 79.6% and 40.5% for patients with only regional LN disease and distant metastases, respectively. Patients without regional LN involvement had a statistically significant higher disease-specific survival than those with regional LN compromise (p < 0.001, Log rank test).

Conclusion: Although rare, regional LN involvement or metastatic MCC severely affects the patient's prognosis. Male gender, location of the tumor in the trunk, and increased tumor dimensions are risk factors for LN compromise and/or distant metastases. Tumor location in the limbs is a protective factor against metastatic MCC. Patients without regional LN involvement have a significantly higher disease-specific survival.

Level of evidence: Level III, management and prognostic study.

Table 1. Demographic characteristics of patients with MCC by metastatic status. Group *Mets* includes patients with any combination of distant lymph nodes, liver, bone, brain, and/or liver metastases, with the exception of **only** having bone metastases. *IQR*: interquartile range, *Mets*: metastases, *LN*: lymph nodes.

*Data displayed in Age, Follow-up and Overall survival refers to the median and data between brackets refers to the interquartile range. For the remaining variables, data between brackets refers to the percentage of patients.

		No mets (n = 1724)	Mets (n = 277)	Only bone mets (n = 9)	p value
Age*		76 (67-84)	76 (67-83)	76 (74-87)	0.5663
Follow-up* (months)		13 (6-22)	7 (3-13)	4 (2-14)	0.0001
Gender	Male	1089 (63.17)	202 (72.92)	8 (88.89)	0.002
	Female	635 (36.83)	75 (27.08)	1 (11.11)	
Race	White	1629 (94.49)	266 (96.03)	9 (100)	0.732
	African American	28 (1.62)	6 (2.17)	4 (4.71)	
	American Indian / Alaska Native	11 (0.64)	0 (0)	0 (0)	
	Asian or Pacific Islander	44 (2.55)	5 (1.81)	0 (0)	
	Unknown	12 (0.7)	0 (0)	0 (0)	
Primary location	Face/Head/Neck	735 (42.63)	91 (32.85)	4 (44.44)	<0.001
	Trunk	150 (8.7)	34 (12.27)	0 (0)	
	Limbs	761 (44.14)	73 (26.35)	2 (22.22)	
	Unknown	78 (4.52)	79 (28.52)	3 (33.33)	
Tumor size (mm)	No tumor found	29 (2.18)	26 (14.61)	0 (0)	<0.001
	<1mm	13 (0.98)	0 (0)	0 (0)	
	1-10 mm	452 (33.91)	13 (7.3)	0 (0)	
	11-20	364 (27.31)	32 (17.98)	0 (0)	
	21-30	229 (17.18)	34 (19.10)	1 (16.67)	
	31-40	112 (8.4)	22 (12.36)	1 (16.67)	
	41-50	58 (4.35)	18 (10.11)	1 (16.67)	
	> 50	76 (5.7)	33 (18.54)	3 (50)	
Regional LN	N0	1177 (76.58)	102 (37.23)	6 (66.67)	<0.001
	N+	309 (20.1)	130 (47.45)	2 (22.22)	
	NX	51 (3.32)	42 (15.33)	1 (11.1)	
Metastatic status	No mets	1724 (100)	0 (0)	0 (0)	<0.001
	Bone	0 (0)	76 (27.74)	9 (100)	<0.001
	Liver	0 (0)	108 (39.27)	0 (0)	<0.001
	Lungs	0 (0)	60 (21.9)	0 (0)	<0.001
	Brain	0 (0)	11 (4.03)	0 (0)	<0.001
	Distant LN	0 (0)	54 (38.3)	0 (0)	<0.001
	Other places	0 (0)	65 (44.52)	0 (0)	<0.001
Stage	0	10 (0.64)	0 (0)	0 (0)	<0.001
	I	577 (36.78)	0 (0)	0 (0)	
	II (IIA or IIB)	303 (19.31)	0 (0)	(0)	

	III	309 (19.69)	0 (0)	(0)	
	IV	0 (0)	277 (100)	9 (100)	
	Unknown	370 (23.58)	0 (0)	(0)	
Previous malignancy	No	1126 (65.31)	170 (61.37)	4 (44.44)	0.198
	Yes	598 (34.69)	107 (38.63)	5 (55.56)	
Current status	Alive	1352 (78.36)	79 (28.52)	4 (44.44)	<0.001
	Dead	373 (21.64)	198 (71.48)	5 (55.56)	
Cause of death	Disease-related	157 (42.09)	126 (63.64)	3 (60)	<0.001
	Other cause	216 (57.91)	72 (36.36)	2 (40)	

	Yes	0.52	0.46 - 0.58	<0.001	0.77	0.62 - 0.97	0.024	0.13	0.099 - 0.17	<0.001	0.16	0.1 - 0.25	<0.001
LN surgery	No	-	-	-	-	-	-	-	-	-	-	-	-
	Yes	-	-	-	-	-	-	0.322	0.15 - 0.69	0.003	0.421	0.19 - 0.95	0.037
Qx to another site	No	-	-	-	-	-	-	-	-	-	-	-	-
	Yes	3.96	2.396 - 4.75	<0.001	5.61	4.16 - 7.59	<0.001	3.67	2.47 - 5.47	<0.001	3.74	1.81 - 7.74	<0.001
RT	No	-	-	-	-	-	-	-	-	-	-	-	-
	Yes	2.71	2.46 - 2.99	<0.001	2.21	1.95 - 2.51	<0.001	0.74	0.58 - 0.96	0.021	0.56	0.39 - 0.8	0.001
QT	No	-	-	-	-	-	-	-	-	-	-	-	-
	Yes	5.05	4.43 - 5.74	<0.001	4.43	3.67 - 5.34	<0.001	11.22	8.12 - 15.5	<0.001	11.24	7.05 - 17.93	<0.001