

Introduction

- Merkel cell carcinoma (MCC) is a rare cutaneous malignancy of neuroendocrine origin with an incidence of 0.7 per 100,000 persons
- 40-50% of patients go to have distant dissemination, of which 13% will have CNS involvement
- Historically, the treatment of metastatic MCC has been chemotherapy (CT) and radiotherapy (RT) to nodal or metastatic disease
- While the treatment of MCC is evolving, the role for surgical resection of BM remains not well established

Methods

- Survey of institutional databases (BWH & MGH) to identify patients with MCC BMs.
- Systematic review of the literature to identify cases reporting on neurometastatic MCC
- Pooled analysis to assess factors affecting overall survival in patients with MCC BM
- Survival analysis in R (ver 3.4.0) was done with K-M curves with Log Rank statistic (risk unadjusted) and Cox proportional hazard ratio (risk adjusted)

Results

Institutional series

- A total of 13 patients between 2004-2017 were identified, of which seven patients underwent resection of 1 or more BM

Literature review

- 27 cases of MCC BM were identified in the literature, describing operative (7) and non-operative (20) management

Pooled patient characteristics

- Age at MCC diagnosis and time to CNS involvement was similar between the groups
- Patients managed non-operatively had more extensive intracranial burden of disease (BoD) but similar systemic BoD, compared to those managed operatively
- Non-operative and adjuvant therapy included radiotherapy, CT and/or immunotherapy

Table 1 - Baseline Patient Characteristics

Age at diagnosis, yr (mean ± SD)	65.1 ± 10.1
Sex, n female (%)	11 (27.5)
Location of primary, n (%)	
Head and neck	12 (42.5)
Torso	4 (10.0)
Upper extremities	2 (5.0)
Lower extremities	3 (7.5)
Unknown	14 (35.0)
Chemotherapy before CNS spread, n (%)	23 (57.5)
Regional RT to primary site and/or LN disease, n (%)	24 (60.0)
Time to CNS involvement, mts (median, IQR)	17.0 (10.5–26.5)
Systemic BoD, n (%)	
Only CNS	17 (42.5)
Extensive	23 (57.5)
Intracranial BoD, n (%)	
Single BM	25 (62.5)
Extensive	15 (37.5)
Resection of ≥ 1 BM, n (%)	14 (35.0)
Brain-directed RT, n (%)	
None	7 (17.5)
SRS	12 (30.0)
WBRT	26 (65.0)
Systemic therapy after CNS spread, n (%)	
None	15 (40.5)
Chemotherapy	11 (29.7)
Immunotherapy	6 (16.2)
Other ^a	7 (18.9)

Results

Predictors of overall survival (OS)

- Median survival was 73- and 25-months (95% CI 31-115, 14-36) in the operative group and non-operative group, respectively (Fig1)
- Bivariate analysis showed an OS benefit to neurosurgical resection of BM, lower intracranial disease burden and brain-directed RT
- On risk-adjusted analysis only surgical resection conferred a survival benefit compared to non-operative management (HR 0.12, 95%CI 0.03-0.049, p=0.003)

Figure 1 - Effect of neurosurgical resection on OS

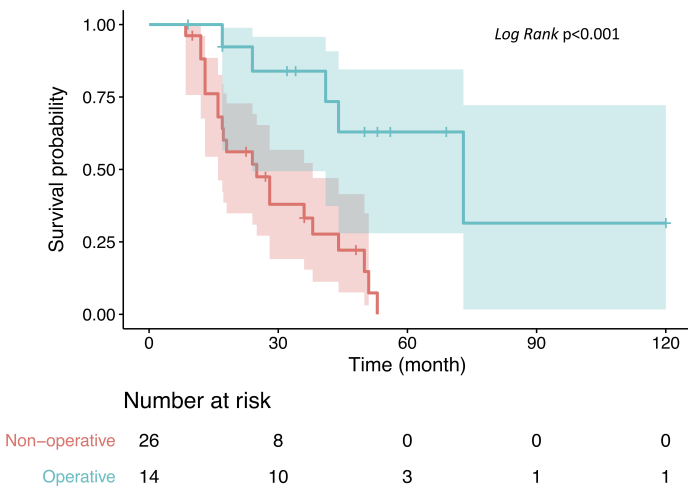


Table 2 - Predictors of Overall Survival

	Bivariate Cox Regression			Multivariable cox regression		
	HR	95%CI	p-value	HR	95%CI	p-value
Surgical resection (ref non-op)	0.18	0.06-0.54	0.002	0.12	0.03-0.49	0.003
Age	1.00	0.96-1.03	0.86			
Sex (ref male)	0.62	0.25-1.54	0.30	2.02	0.66-6.20	0.22
Location of primary						
Head & Neck	Ref					
Torso	0.68	0.15-3.03	0.61			
Upper Extremities	0.36	0.04-3.05	0.35			
Lower Extremities	0.00	NA	1			
Unknown	0.99	0.42-2.34	0.97			
Intracranial BoD (ref single BM)	2.51	1.12-5.6	0.03	1.10	0.43-2.78	0.85
Systemic BoD (ref only CNS)	1.69	0.73-3.90	0.22	1.17	0.44-3.11	0.75
Therapy prior to CNS involvement (ref none)	0.77	0.31-1.94	0.58			
Systemic therapy after CNS involvement (ref none)	1.52	0.65-3.57	0.33			
Brain-directed RT (ref none)	0.37	0.14-0.93	0.04	0.40	0.14-1.14	0.09

BM = Brain metastasis, BoD = Burden of disease, CNS = Central nervous system, RT = radiotherapy

Conclusions

- In patients who are candidates for surgery, resection of MCC BM is associated with an OS benefit relative to non-operative management and should therefore be considered
- Further investigation of multimodal therapy for neurometastatic MCC is warranted