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Merkel cell carcinoma associated with HIV: review of 14 patients

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Merkel cell carcinoma (MCC) is a rare, aggressive neuroendocrine tumor that has a high propensity for early metastases and high rates of local recurrence after surgical excision. Most cases of MCC are associated with human polyomavirus (HPyV) infection, and immunosuppression is a known risk factor [1,2]. Indeed, the risk of developing MCC is 13 times greater in HIV patients compared with the general population [1–3].

We evaluated the demographic and clinical aspects of HIV-associated MCC (HIV-MCC) in three patients seen at a tertiary care specialty hospital and 11 other patients previously described in the medical literature, and compared these with the clinical aspects of MCC in immunocompetent patients (IC-MCC). All methods were previously approved by the Institutional Review Board of the Fred Hutchinson Cancer Research Center (FHCRC). A total of 14 HIV-MCC patients were identified for review, including 11 patients from the English language literature (references [4–14]) and three patients from the FHCRC database '*Repository of Data and Specimens for MCC*' (W10, W137, and W162). We analyzed the average age at diagnosis, lesion location, duration of HIV diagnosis prior to MCC diagnosis, the relationship between CD4 cell counts and MCC diagnosis, and the average duration of survival after MCC diagnosis.

The demographic and clinical characteristics of 14 patients with HIV-MCC are summarized in Table 1. This group comprises 11 men and three women. The average age at the time of diagnosis was 49 years. Five patients had head and neck lesions, whereas the remaining nine patients had lesions on other sites. In the six patients whose HIV was clearly diagnosed prior to their MCC diagnosis, the average duration from the time of HIV diagnosis to MCC diagnosis was 9.5 years. The average CD4 cell count was 256 cells/μl (normal range 500–1500 cells/μl) in nine patients at the time of MCC diagnosis.

Ten patients with HIV-MCC were treated with wide local excision (WLE), and six of these also received additional radiation therapy or chemotherapy. Chemotherapeutic agents included etoposide, cisplatinum, adriamycin, vincristine, cyclophosphamide, and doxorubicin. Two patients were treated with Mohs surgery, and one of these received additional radiation therapy. Two patients were treated with radiation therapy or chemotherapy alone. Five of the ten patients treated with WLE or Mohs surgery, either alone or in combination with radiation, survived for longer than 23 months. Two patients treated with chemotherapy or radiation alone had survival of at least 9 and 11 months, respectively.

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Eleven patients were also treated for their HIV with highly active antiretroviral therapy (medications included azidothymidine, indinavir, nelfinavir, stuavudine, lamivudine, abacavir, nevirapine, saquinavir, efavirenz, lopinavir, and ritonavir). Five of these began antiretroviral therapy after their diagnosis of MCC.

The average survival of HIV-MCC after MCC diagnosis was approximately 18 months.

This demographic and clinical analysis included the largest number of HIV-MCC patients reviewed to date in the English language literature. Similar to IC-MCC, HIV-MCC had a male predominance. However, the average age at diagnosis for HIV-MCC was 49 years, which is significantly younger when compared with 70 years for IC-MCC [1,2]. As most MCC is associated with HPyV infection [15], it is possible that virally induced oncogenesis may be more rapid and extensive in the setting of HIV-induced immunosuppression. This might account for the increased risk and earlier age of MCC onset in patients with HIV.

In contrast to IC-MCC, the majority of tumors in HIV-MCC occurred on nonhead and neck skin. This indicates that ultraviolet radiation might not represent the most important etiopathologic factor for the development of MCC in HIV patients.

The average period from the time of HIV diagnosis to the time of MCC diagnosis was 9.5 years. This is significantly longer than the 5.6-year period for other AIDS-defining cancers, or the 6-year period for a non-AIDS-defining malignancy [16]. Notably, there was no clear relationship between CD4 cell counts or the duration of HIV diagnosis with MCC diagnosis or the duration of survival.

The markedly increased risk for MCC, as well as much earlier age of onset and nonclassical locations of MCC in HIV patients, should alert clinicians to the possibility of this aggressive and rare malignancy in patients with HIV and other endogenous or exogenous immunosuppression.

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N.C.Z., E.N., J.G.I., and P.N. designed and performed the study.

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Table 1

Patient characteristics in HIV-associated Merkel cell carcinoma

Case (reference)	Sex	Race	Age at MCC diagnosis (years)	MCC site	HIV diagnosis to MCC (years)	CD4 cell count (cells/μl)	Viral load (copies/ml)	Treatment of MCC	on HAART?	Survival (months)
1 [5]	M	NA	47	Right buttock	HIV after MCC	625	NA	Chemotherapy	No	Recurrence at 11
2 [4]	M	NA	60	Nose	NA	329 (2 years after diagnosis)	NA	Mohs radiation therapy	Yes	24
3 [7]	M	NA	63	Forehead	12	232	Undetectable	Mohs	Yes	NA
4 [8]	M	W	54	Left upper extremity	HIV after MCC	82	250000	WLE	Yes (after diagnosis)	25
5 [6]	M	NA	51	Right buttock	6	122	32000	Local radiation therapy (refused surgery)	Yes (×5 months)	9
6 [9]	M	NA	57	Right dorsal middle finger	14	357–573 (last 3 years)	Undetectable	WLE	NA	>40
7 [10]	F	African black	36	Left ear	NA	63	24000	WLE	Yes	>9
8 [11]	M	NA	48	Buttock	10	267	>750000	WLE, radiation therapy	Yes (after diagnosis)	>11
9 [12]	M	Italian	40	Left inguinal lymph node (no known skin primary)	3	160	11000	WLE	Yes	>42
10 [13]	F	African black albino	25	Right cheek	NA	332	187000	Chemotherapy, radiation therapy, WLE	Yes (after diagnosis)	12
11 [14]	M	W	48	Scalp	12	Normal	Undetectable	WLE, radiation therapy	Yes	>12
12*	M	W	46	Right buttock	HIV after MCC	74 (21 months after diagnosis)	<75000	WLE, radiation therapy	Yes (after diagnosis)	23
13*	F	W	52	Right buttock	NA	NA	NA	WLE, radiation therapy	NA	12
14*	M	W	58	Left forearm	HIV after MCC	421	40000	WLE, lymphadenectomy, chemotherapy, radiation therapy	Yes (after diagnosis)	18

F, female; HAART, highly active antiretroviral therapy; M, male; MCC, Merkel cell carcinoma; NA, not available; W, whites; WLE, wide local excision.

*Cases obtained from the data and specimen repository at the Fred Hutchinson Cancer Research Center.