Merkel cell carcinoma of the upper extremity. A case report.

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Case Report

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Abstract: Merkel cell carcinoma (MCC) is a rare form of neuroendocrine carcinoma first described by Toker (1) as trabecular carcinoma in 1972, The name was changed to Merkel Cell carcinoma because the tumor cells resemble Merkel cells, which are present in the basal layer of the epidermis, in particular around hair follicles (2), These cells tend to express neuroendocrine markers such as chromogranin-A, synaptophysin and cytokeratin 20 (CK20). In this case we report a 64 year-old Hispanic woman with a history of left breast cancer 38 years previously managed with RT (Radiation therapy) and chemotherapy was referred to our hospital for surgical evaluation of disseminated Merkel cell carcinoma in the upper limb, we manage the patients with intravenous antibiotics and surgical management with upper limb amputation.

Key words: Merkel cell carcinoma; MCC, Neuroendocrine carcinoma.

Introduction

Merkel cell carcinoma is an aggressive neuroendocrine carcinoma primary to skin and occurs most commonly in association clonally integrated Merkel cell polyomavirus with related retinoblastoma protein sequestration or in association with UV radiation-induced alterations involving the TP53 gene and mutations (3), MCC presents as solitary cutaneous nodule, most frequently in sun-exposed areas, ultraviolet light (UV) exposure is probably involved in both viral-mediated and non-viral-mediated carcinogenesis, by contributing to immunoppresion or DNA damage, respectively. Diagnosis of MCC is rarely clinically suspected because the primary tumor lacks distinguishing characteristic features and is often asymptomatic(4). In previous study Albores (5) reported 3870 cases recorded at SEER (Surveillance, Epidemiology, and End Results) program from 1973 to 2006 report skin of upper limb and shoulder as second most common site of presentation .

MCC tumors visualized by hematoxylin and eosin (H&E) typically contain small round blue cells with salt-and-pepper chromatin, MCC practically defines patter recognition. Most frequently, the tumor cells are uniform, with round to oval nuclei, finely dispersed chromatin, inconspicuous nucleoli, distinct nuclear membranes, scant cytoplasm, and numerous mitosis with nuclear fragmentation (3). A majority of MCC express cytokeratins, most characteristically CK20 in 95% of cases or Cam5.2 in a paranuclear dot-like and/or cytoplasmic pattern, neuroendocrine markers (most commonly synaptophysin, immunohistochemical staining for cytokeratin 20 is a pathognomonic marker for MCC, allowing differentiate from other cancers, such as melanoma (6). Although imaging such as computed tomography (CT) or magnetic resonance imaging (MRI) must be performed for staging and identifying distant metastases. The gold standard treatment consists in surgical resection, excise with histological negative margins, NCCN guides recommend wide excision with 1- to 2- cm margins to investing fascia of muscle when clinically feasible (7), Sentinel lymph node biopsy (SLNB) should be performed if possible, is SLNB is positive observation of nodal basin or RT should be consider, chemotherapy is only recommended in patients with disseminated disease and only recommended if curative surgery or RT is not feasible in regional disease (7).

Case report

A 64 year-old Hispanic woman with a history of left breast cancer 38 years previously managed with RT and chemotherapy was referred to our hospital for surgical evaluation of disseminated Merkel cell carcinoma in the upper limb (**Figure 1A and B**) with myiasis, we proposed surgical treatment, however patient refused at this hospitalization, we managed with tobacco tar to remove larvae successfully, intravenous antibiotics for 3 days with decrease in white blood cells from 13.2 K/uL at hospitalization to 10.9 K/uL, we decided to discharge patient with oral antibiotics and send patient with the oncologist who

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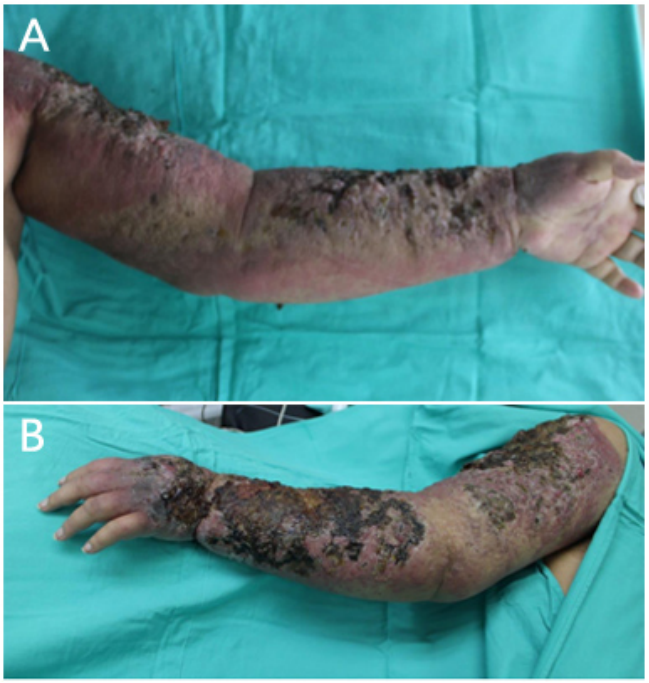

Figure 1. A. Volar view. B. Dorsal view.

referred back 7 days for surgical treatment, oncologist surgeon evaluated patient and proposed surgical treatment with forequarter amputation , at surgery we found macroscopic axillar nodes, tumor and nodules were macroscopically completely removed (**Figure 2**), patient was discharged 5 days after amputation. The histopathological findings revealed an MCC without resection margins in soft tissue, negative margins in skin, and bone tissue. Follow-up showed good wound healing and absence of complications at one month, patient was sent to oncologist to evaluate chemotherapy or RT.

Discussion

MCC are rare tumors of the skin. According to SEER, the estimated annual incidence in 2006 was 0.6 per 100,000 persons (5). Merkel cell carcinomas have been reported to occur in areas of the body exposed to the sun such as the head and neck (50%), the upper and lower limbs (35%–40%), and the trunk (<10%) (8). MCC presents more often in males than females with incidence rates of 0.41 for males and 0.18 cases in females per 100,000 person-year. The Mean age of diagnosis for MCC is 76.2 years for women and 73.6 for men (5). The etiology remains uncertain, though there is some evidence that UV radiation and immune system depression are important risk factors, some studies have shown the role of the Merkel cell polyomavirus (MCV) in development of this tumor (9).

MCC usually presents as painless, purple lesions on the skins, most patients (73%) present with localized disease (stages I-II); 23% have regional

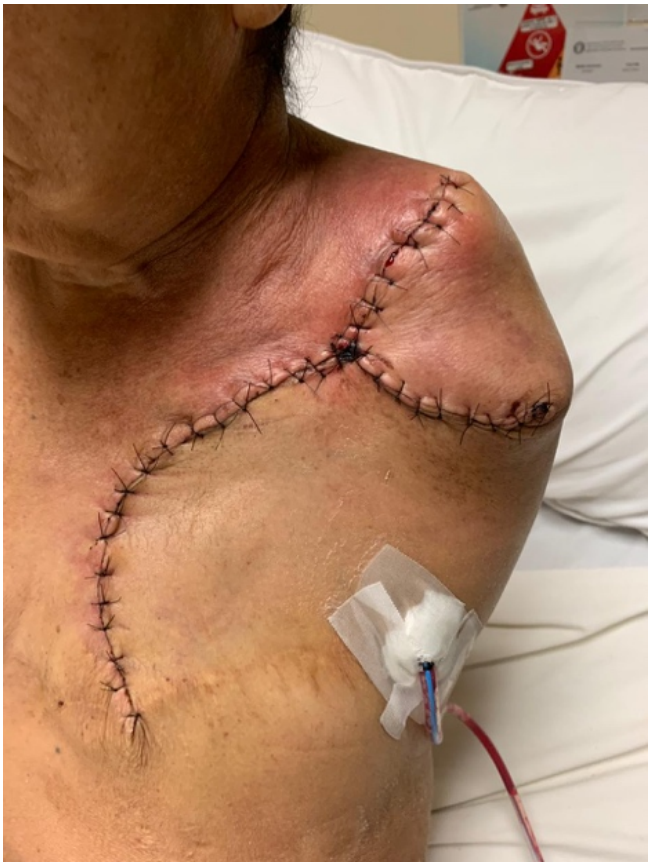

Figure 2. Patient after amputation.

disease (stage III), and 4% have stage IV metastatic disease (10). MCC presents as a rapidly growing, cutaneous or subcutaneous tumour that is located in sun exposed areas, more often in head and neck and upper extremities (11). MCC typically presents as a rapidly growing, asymptomatic lesion, ulceration more frequent presents on late scenarios (12). The most common site of metastases are regional nodal basins, distant skin, lung, bone and brain (12), There is a group of patients who presents with nodal disease without an identifiable primary, with only few case reports over the years (13), review of 9387 cases reported 4% patients with positive nodal disease and unknow primaries and known primaries, compared overall survival at 5 years was 26.6% for know primary vs 42.2% unknown primary (14).

Treatment for MCC remains controversial, however excision margins of 1-2cm should be the mainstay of treatment when possible (15). Adjuvant radiotherapy play a role in treatment in MCC, reports have shown that it may improve outcomes in terms of minimizing the risk of local and regional recurrence, however there is not data to suggest that overall survival is improved (16).

Conclusion

MCC is a rare tumor that requires a high index of suspicion since most patients presents with early

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localized disease and prognosis may change with treatment options, currently the best treatment is surgery and radiotherapy on some scenarios, in this case disease was limited at upper extremity and we perform amputation, node dissection and adjuvant radiotherapy with good evolution at 6 months.

Conflicts of interests

The authors have no conflicts of interests to declare.

References

1. Toker C. Trabecular carcinoma of the skin. An ultrastructural study. Cancer. 1978;42(5):2311–21.
2. Becker, J. C., Stang, A., DeCaprio, J. A., Cerroni, L., Lebbé, C., Veness, M., & Nghiem P. HHS Public Access. 2018;1–41.
3. Pulitzer Melissa. Merkel Cell Carcinoma Melissa. Surgical Pathology Clinics. 2017;10(2):399–408.
3. Anita Engh, Hammond L, Daniels GA, DiMaio D, Buffett Cancer Center Jeffrey Farma PM, Fisher K, et al. NCCN Guidelines 2019. 2019.
5. Albores-saavedra J, Chable-montero F, Sagy N, Schwartz AM, Henson DE. Merkel cell carcinoma demographics , morphology , and survival based on 3870 cases : a population based study. 2010;20–7.
6. Leroux-Kozal V, Lévêque N, Brodard V, Lesage C, Dudez O, Makeieff M, et al. Merkel cell carcinoma: Histopathologic and prognostic features according to the immunohistochemical expression of Merkel cell polyomavirus large T antigen correlated with viral load. Human Pathology. 2015;46(3):443–53.
7. Anita Engh, Hammond L, Daniels GA, DiMaio D, Buffett Cancer Center Jeffrey Farma PM, Fisher K, et al. NCCN Guidelines 2019. 2019.
8. Min HJ, Kim JH, Kim YW, Cheon YW. Merkel Cell Carcinoma of the Wrist: A Case Report. Annals of Plastic Surgery. 2018;81(2):244–7.
9. Prewett SL, Ajithkumar T. Merkel Cell Carcinoma: Current Management and Controversies. Clinical Oncology. 2015;27(8):436–44.
10. Medina-Franco H, Urist MM, Fiveash J, Heslin MJ, Bland KI, Beenken SW. Multimodality treatment of merkel cell carcinoma: Case series and literature review of 1024 cases. Annals of Surgical Oncology. 2001;8(3):204–8.
11. Becker, J. C., Stang, A., DeCaprio, J. A., Cerroni, L., Lebbé, C., Veness, M., & Nghiem P. HHS Public Access. 2018;1–41.
12. Xue Y. Merkel Cell Carcinoma Review. Hematology/Oncology Clinics of NA. 2019;33(1):39–52.
13. Tarantola TI, Vallow LA, Halyard MY, Weenig RH, Warschaw KE, Weaver AL, et al. Unknown primary Merkel cell carcinoma: 23 new cases and a review. Journal of the American Academy of Dermatology. 2013;68(3):433–40.
14. Harms KL, Healy MA, Nghiem P, Sober AJ, Johnson TM, Bichakjian CK, et al. Analysis of Prognostic Factors from 9387 Merkel Cell Carcinoma Cases Forms the Basis for the New 8th Edition AJCC Staging System. Annals of Surgical Oncology. 2016;23(11):3564–71.
15. Saini AT, Miles BA. Merkel cell carcinoma of the head and neck: Pathogenesis, current and emerging treatment options. OncoTargets and Therapy. 2015;8:2157–67.
16. Hasan S, Liu L, Triplet J, Li Z, Mansur D. The role of postoperative radiation and chemoradiation in Merkel cell carcinoma: A systematic review of the literature. Frontiers in Oncology. 2013;3(10):1–10.

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