Merkel cell carcinoma-A rare primary neuroendocrine skin tumor: Case report and discussion

ABSTRACT

Merkel cell carcinoma (MCC) is a rare but aggressive cutaneous primary small cell carcinoma with an unfavorable prognosis. It is a disease of the sun exposed skin of the elderly commonly involving the head, neck, and extremities. Though most cases present as localized disease, treatment should be definitive with wide excision of the primary lesion (2-3 cm margin) and prophylactic lymphadenectomy followed by irradiation to the primary site. Even when locoregional control is achieved, close surveillance is required due to high rates of local and systemic relapses. Chemotherapy is preserved for systemic disease, though the success of this treatment is limited and no chemotherapy protocol has been shown to improve survival.

KEY WORDS: Carcinoma, merkel, neuroendocrine, skin

INTRODUCTION

Merkel cell carcinoma (MCC) is a rare neuroendocrine malignancy of the skin with an annual incidence of 0.2-0.45 per 1 lakh (100 times as rare as melanoma).[1] It was first described by Toker in 1972 as trabecular carcinoma. MCC begins in the merkel cells found in the base of epidermis of skin.[2] It is an aggressive disease with overall five-year survival of 50-68%.[3] It has a propensity for local recurrence, lymph node involvement, and systemic spread. Management of MCC is still a challenging problem. We report a case of this rare disease with discussion regarding management modalities.

CASE REPORT

A 79-year-old man with no preexisting comorbidities presented with a soft tissue lesion on the right ala of nose, recent onset, and gradually progressive. The patient underwent wide local excision of the same. While awaiting the histopathology of the primary lesion, the patient developed a right-sided preauricular swelling. The histopathology of the primary lesion showed malignant neuroendocrine carcinoma of skin [Figures 1 and 2] with all resection margins free from tumor infiltration. Immunohistochemistry showed tumor cells strongly positive for neuron-specific enulase (NSE), synaptophysin, weakly positive for CK and negative for HMB-45 and leucocyte common antigen (LCA). Fine needle aspiration cytology (FNAC) from the pre-auricular swelling showed round blue cell tumor deposit consistent with metastatic tumor deposit. The patient was then taken up for radical neck dissection with parotid removal. Histological examination showed tumor cell deposits in 13/19 lymph nodes removed and the adjoining parotid was infiltrated by the tumor. The patient was then planned for postoperative adjuvant radiation therapy to the primary and bilateral neck with a dose of 60 Gy/30 fractions over 6 weeks with the Intensity modulated radiation therapy (IMRT) technique. Presently, six months after radiation, the patient has no signs of local or systemic relapse.

DISCUSSION

MCC was first described in 1972.[2] Since then, most of the reports concern single cases or epidemiological studies. MCC begins in the Merkel cells found at the base of the outermost layer of the skin (epidermis). Merkel cells are connected to the nerve endings in the skin that are responsible for the sense of touch. In close association with primary nerve endings in the skin, they form the MC-axon complex.[1]

Although the etiology is not fully understood, there are several risk factors that contribute to its pathogenesis. These include UV light, sun-related skin malignancies (squamous cell carcinoma, basal cell carcinoma), psoriasis treatment with methoxsalen, and arsenic exposure. Patients on immunosuppressive agents or those with diagnosis...
of AIDS, chronic lymphocytic leukemia, congenital dysplasia syndrome, and organ recipients carry a higher risk as well. MCC most commonly occurs in the head and neck (50%), upper and lower limbs (35-40%), and less than 10% in the trunk. Similarly, our patient also had MCC in the head and neck region. The epidemiological studies have revealed that large tumor size, male sex, truncal site, nodal/distant disease at presentation, and duration of disease before presentation are poor prognostic factors.

Clinically, MCC appears as a painless, firm, non-tender, ulcerated skin lesion commonly measuring less than 2 cm at the time of presentation. The typical clinical course of the disease is rapid progression of the primary tumor with early and frequent metastasis to the regional lymph nodes (40-70%) and distant metastasis (30-50%). Involvement of parotid gland is considered to be by direct extension rather than by metastases. Likewise, our patient developed lymph node metastasis while awaiting the histopathology report of primary lesion and intraoperatively, parotid was also infiltrated by the disease. Metastatic potential of neuroendocrine cancer mandates that an early and accurate diagnosis be made by the clinician and the pathologist. Confirmation of diagnosis is made by excisional biopsy on typical histology and immunohistochemistry.

Because of the rarity of the tumor, there is a multitude of treatment protocols. However, the surgical treatment seems to be the cornerstone of the different treatment protocols. It is widely accepted that patients with regional node metastases should undergo excision of the primary lesion and lymph node dissection. Patients with midline head and neck primary tumors should undergo bilateral radical neck dissection which may be staged. Sentinel lymph node biopsy (SLNB) is strongly advocated in the treatment and staging of individual tumors. Especially for the MCC cases occurring in the head and neck region. Mohs micrographic surgery has been recommended as an advanced technique for local control, especially in areas calling for excellent cosmetic results (ie, head and neck region) without compromising the principles of cancer surgery.

Adjuvant radiation therapy to the primary site and regional nodes is generally recommended in addition to lymph node dissection. Postoperative radiotherapy (RT) (40-60 Gy) is associated with a reduced risk of local recurrence and increased median survival up to 63 months compared with 45 months without radiation therapy. RT alone can be used as a palliative treatment with good control of primary and LN mets. Chemotherapy has been performed with protocols based largely on agents active in small cell lung carcinoma. No chemotherapeutic protocol has, however, been able to achieve a significant increase in survival rate. Multiple agents have been used with different response rates. Those include cyclophosphamide, doxorubicin, etoposide, cisplatin, vincristine, methotrexate, 5-fluorouracil, and carboplatin. Biologic agents such as interferon, tumor necrosis factor (TNF), and imatinib mesylate promise better results on local or systemic control of MCC.

Depending on the length of the follow-up period, up to 45-91% of the patients develop regional lymph node metastasis. Distant dissemination is not infrequent, with about 40-50% of the patients developing visceral metastasis, particularly to the lungs, liver, and bone. The mean time to locoregional recurrence is eight months. The mean time to develop distant metastases is 18 months. Considering the aggressive disease course, treatment should be definite with close follow-up.

CONCLUSION

MCC is an unusual but fatal disease, with patients having a poor chance of survival. Early diagnosis, optimal resection, and postoperative radiotherapy achieve locoregional control of the tumor. Research on MCC has produced prognostic markers and molecular pathways, which when translated into clinical practice, will lead to discovery of new treatments such as the role of anti-angiogenic medications and improved survival.
REFERENCES


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