



An Unusual Presentation of Merkel Cell Carcinoma of the Gluteal Region with Brain Metastases: A Rare Case Report

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Abstract

Merkel cell carcinoma (MCC) is a small cell rare and aggressive neuroendocrine carcinoma arising in the skin. It usually arises in sun-exposed regions. It is associated with advanced age, ultraviolet (UV) radiation and polyomavirus infection. This paper reports a case of a 39-year-old male patient who underwent wide local excision of the left gluteal lesion. The biopsy report of the excised specimen showed features consistent with Merkel cell carcinoma. The patient had received adjuvant chemotherapy and palliative radiotherapy to the brain for brain metastasis. In view of poor general condition, the patient was kept on supportive care and he expired eight months after the start of treatment.

Keywords: brain metastasis, gluteal, merkel cell carcinoma, neuroendocrine.

Introduction

Merkel cell carcinoma (MCC) is a rare, aggressive, highly malignant cutaneous neuroendocrine cancer of the skin that commonly affects sun-exposed regions in elderly and/or immunosuppressed males.¹ It produces neuron-specific enolase and contains membrane bound neurosecretory granules within the tumor cell. It is also known as primary small cell carcinoma of skin, primary undifferentiated carcinoma of skin, primary neuroendocrine carcinoma of skin, trabecular carcinoma of skin, anaplastic carcinoma of skin and cutaneous amine precursor uptake and decarboxylation tumor (APU Doma).² Its incidence is 0.15 to 0.79 cases per 1,00,000 population with local infiltration of lymph nodes

and distant metastasis present in 50% of cases.³ Due to its rarity, no official treatment guideline is available. In this paper, we report a case of a male patient hailing from North-East India with chronic hepatitis B and C, having MCC of the left gluteal region with brain metastasis and review the clinical, macroscopic, and microscopic findings with the treatment options available.

Case Presentation

A 39-year-old male patient attended the OPD at the Department of Radiation Oncology, Regional Institute of Medical Sciences (RIMS) with complain of headache, vomiting, generalized weakness and occasional seizures for the past 10 days.

The patient gave history of a painless swelling about 5cm × 5cm in size, with redness of the skin on the left buttock which was gradually increasing in size for the last one month. He underwent wide local excision (WLE) of the left gluteal region mass on 23/09/2021, at PGI, Chandigarh. The excised specimen was sent for histological (HPE) analysis which showed features consistent with Merkel Cell Carcinoma.

There is no history of trauma to the area. There is no history of similar illness in the past or family history of cancer or any communicable disease. There is no history of diabetes, hypertension, tuberculosis or any known drug allergy. The patient is on oral antivirals for both Hepatitis C and Hepatitis B for the past 2 years. There is no history of smoking, alcohol consumption or pan/tobacco chewing.

Histopathological (HPE) analysis of the excised left gluteal mass showed a tumor in the upper dermis extending up to muscle and ulcerating overlying epidermis, with infiltration of dermis by the tumor arranged in sheets, island, nests and scattered populations. The tumor extends till the subcutaneous tissue with vascular invasion. Tumor is reaching up to muscle plane with external iliac lymph node metastasis (5/5) (Fig. A).

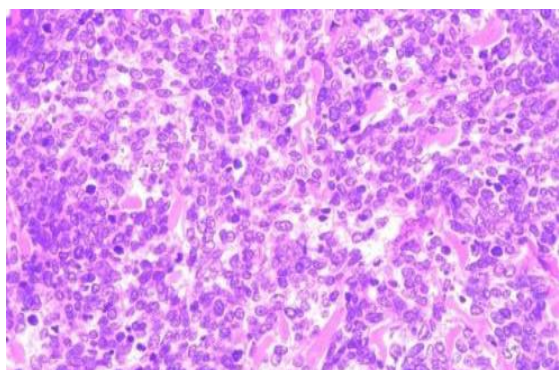


Fig. A: HPE report of the excised gluteal mass showing multiple small round cells with high mitoses.

On immunohistochemical (IHC) analysis, the cells were positive for CD99, CD38 and CD138; with CK7 and CK20 having dot-like positivity. The cells also have high proliferative index (Ki67) of 90%. On the basis of HPE and IHC analysis a diagnosis of Merkel Cell Carcinoma (MCC) of the

left gluteal region was made. MRI of the brain showed no space occupying lesion, but CSF analysis was positive for malignant cells.

The patient gave history of treatment with 6 cycles of adjuvant chemotherapy with Injection Carboplatin and Injection Etoposide, 3 weekly cycles, following operation, along with palliative whole brain radiotherapy for brain metastases at PGI, Chandigarh up to 25/03/2022, following which the patient came back to his hometown, Imphal, for further treatment.

The general condition of the patient was poor at the time of presentation in our OPD on 04/04/2022 and was managed conservatively. On examination, the patient has an average built with a Body Surface Area (BSA) of 1.4 m² and Karnofsky Performance Score (KPS) of 70%. On physical examination, a field defect of 15.0 cm × 15.0 cm size was seen of the left buttock region, with irregular margins and an ulceroproliferative mass on the left side of field defect with irregular surface and margins (Fig B). No other mass or any lymph node were clinically palpable.



Fig. B: Photo of the left gluteal mass at the time of presentation at the Department of Radiation Oncology, RIMS.

Routine baseline investigations (complete blood count, biochemistry, ECG and chest x-ray) were done and were found to be uneventful. PET-CT scan showed a metabolically active ill-defined soft tissue thickening in the cutaneous and subcutaneous planes of left gluteal region with loss of intervening fat planes (suggestive of residual disease) with metastatic left external iliac and inguinal lymph nodes.

The patient received 2 more cycles of adjuvant palliative chemotherapy with the same regimen at our department from 10/04/2022 to 07/05/2022. The patient general condition deteriorated during the course of treatment, due to progressive disease and was kept on supportive care. Poor prognosis of the patient was explained to the patient party and was discharged on request. He succumbed to the disease and expired 10 days after discharge from the hospital.

Discussion

Merkel Cell Carcinoma (MCC) was described first as trabecular carcinoma of the skin by Dr. Toker in 1972. MCC is a rare highly malignant locally aggressive neuroendocrine cutaneous tumor characterized by small cells with round monomorphic basophilic nucleus, and minimum cytoplasm with high mitosis number and apoptotic bodies.⁴ It is generally seen on sun-exposed areas such as head and neck (40.6%), extremities (33%) and trunk (23%).⁵ Regional lymph node metastasis rate, distant organ metastasis rate and local recurrence rate is 45-91%, 18-52% and 27-60% respectively.⁶ The 5 year survival rate is 13-55% on the basis of size and depth of the initial lesion, presence of regional lymph nodes metastases and distant metastases (worst prognosis).⁷

Its differential diagnosis includes amelanotic melanoma, Ewing's sarcoma, basal cell carcinoma, metastatic neuroendocrine tumor, squamous cell lung cancer and cutaneous lymphoma.⁸ Clinically MCC presents as a firm, painless, non-tender, bluish red, rapidly growing nodule. Overlying skin at the site of exposure may exhibit ulcerative, telangiectasia or acneiform characteristics.⁹

Diagnosis of MCC is usually made with a combination of history; physical, skin and nodal examination; histopathological and immunohistochemical (IHC) analysis. IHC is very crucial in the diagnosis of MCC. It is CK 8, 18 and 20 positives, with characteristic paranuclear dot pattern. It is also neuron specific enolase

positive, S-100 weak positive and stain for CD117.¹⁰ Unfavorable prognostic factors includes male gender, age more than 65 years, distant metastatic disease, tumor more than 2 cm in diameter, presence of vascular invasion, high Ki67 index and tumor with more than 10 mitoses per high power field, with stage of the disease at the time of presentation being the most consistent prognostic factor.¹⁰

The Memorial Sloan Kettering Cancer Center in 1999 proposed a size-based four-tiered grading system and correlated it with survival: Stage I (primary tumor <2 cm in diameter), Stage II (primary tumor >2 cm), Stage III (regional disease), and Stage IV (distant metastasis). The 5-year survival rates for each stage are [Stage I - 81%, Stage II - 67%, Stage III - 52%, and Stage IV - 11%].¹¹

Extra cranial metastases to lungs, liver, bones and skin itself is common; with intracranial metastases being quite rare, and the exact mechanism for brain metastases is still unclear.¹² After a diagnosis of MCC is made, further workup is required to identify and quantify regional and distant metastases, which includes CT scan, MRI scan or PET-CT scan. MRI brain being the best imaging modality to detect brain metastases.

Due to its aggressive behavior the treatment of choice is wide local excision of the primary tumor with adjuvant radiotherapy to control the local disease.¹³ Surgery alone has a very high local recurrence rate, with post-operative radiotherapy increasing the survival, as MCC is very radiosensitive. Radiotherapy plays a crucial role in case of large primary tumor or negative surgical margins.¹⁴ The treatment for metastatic disease includes palliative radiotherapy and chemotherapy with cisplatin, carboplatin, etoposide, cyclophosphamide, doxorubicin, vincristine or methotrexate.¹⁵ Immunotherapy in the form of Pembrolizumab, Nivolumab and Avelumab can also be used.

Due to the rarity of brain metastases of MCC, there is no proper treatment guideline, with evidence suggesting that aggressive treatment

with resection, radiotherapy and chemotherapy increases survival.¹⁶

Conclusion

Merkel Cell Carcinoma (MCC) of the gluteal region is quite uncommon, with brain metastases being extremely rare. Proper history, thorough physical examination, HPE and IHC analysis is required for accurate diagnosis, with IHC playing an important role in differentiating MCC from other tumors.

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