Case Report

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Merkel cell carcinoma in a patient with basal cell carcinoma: a case of localized disease with negative sentinel node biopsy

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Introduction: Merkel cell carcinoma (MCC) is a rare but aggressive neuroendocrine skin cancer with a high risk of recurrence and metastasis. It typically affects sun-exposed areas in elderly or immunocompromised individuals. Early diagnosis and management are essential due to its rapid progression and potential for early metastasis.

Case presentation: We report the case of a 65-year-old male with a history of diabetes mellitus and basal cell carcinoma who developed MCC on his left upper extremity. Initial imaging, including a sentinel lymph node biopsy (SLNB) and magnetic resonance imaging (MRI), localized the tumor and assessed lymph node involvement. The SLNB was negative for metastasis, and a wide excision confirmed no residual MCC. Further imaging with positron emission tomography (PET) and computed tomography (CT) scans showed no distant metastasis, indicating localized disease. The patient underwent wide excision followed by radiation therapy (RT) (50 Gy in 25 fractions), experiencing mild post-radiation effects such as swelling and erythema.

Clinical discussion: MCC poses significant diagnostic and therapeutic challenges due to its nonspecific presentation and rapid progression. In this case, early detection and appropriate imaging allowed for timely intervention. Negative SLNB results and localized disease justified the use of wide excision and MC. Multimodal treatment, including surgery and radiation, is crucial in managing localized MCC.

Conclusion: This case emphasizes the importance of early detection, comprehensive imaging, and multimodal therapy in the management of MCC. Close follow-up remains essential, especially in cases with negative SLNB, to monitor for recurrence or metastasis.

Keywords: basal cell carcinoma, Merkel cell carcinoma, positron emission tomography, radiation therapy, sentinel lymph node biopsy

Introduction

Merkel cell carcinoma (MCC) is an aggressive neuroendocrine skin cancer with a high risk of recurrence and metastasis[1]. It typically presents as a fast-growing, firm, reddish nodule with a smooth surface, although it may also appear as a plaque or ulcer[2]. Named by Rywlin in 1982, its cells resemble Merkel cells and share similar immunophenotypical features[3]. MCC development is linked to the integration of Merkel cell polyomavirus (MCPyV) DNA into the host genome or UV-induced mutations, particularly in sun-exposed skin of fair-skinned

HIGHLIGHTS

- Merkel cell carcinoma (MCC) is a neuroendocrine skin cancer with a high risk of recurrence and metastasis, often affecting elderly or immunosuppressed individuals.
- A 65-year-old male with a history of basal cell carcinoma developed MCC on his left upper extremity. Imaging revealed localized disease with no metastasis, confirmed by a negative sentinel lymph node biopsy (SLNB).
- The patient underwent wide excision followed by radiation therapy. Negative SLNB results helped establish a favorable prognosis, emphasizing its role in guiding management of localized MCC.
- Early diagnosis and comprehensive imaging allowed for timely intervention, underscoring the need for vigilant follow-up, particularly in patients with prior skin cancers.

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individuals[1,2]. The risk is higher in immunosuppressed populations[2].

To aid diagnosis, the acronym AEIOU describes common MCC features: asymptomatic, expanding rapidly, immune suppression, age of 50 years, and ultraviolet-exposed site on fair skin[2]. Microscopically, MCC infiltrates the dermis and subcutaneous tissue, often bypassing the epidermis. It has distinct cellular features like a high nucleocytoplasmic ratio and scant cytoplasm[2]. Early lymphatic and vascular invasion is common, and detecting MCPyV through immunohistochemistry or PCR is crucial for confirming the diagnosis, especially in lymph node cases where the primary skin tumor is undetectable[4]. Surgery is the main treatment[5], though there is debate about optimal excision margins, adjuvant radiotherapy, and systemic therapy for advanced stages[2,5]. While MCC represents a small portion of skin cancers, the 5-year survival rate is 76% for localized disease, dropping to 19% for distant metastasis[2].

Case presentation

A 65-year-old male patient came to our OPD with a history of diabetes mellitus and previously treated basal cell carcinoma (BCC) 2 years ago. The BCC was present on his left forearm that was treated surgically. Now, the patient presented with a knot-like swelling on the left upper extremity for the past 6 months, for which the swelling increased in size and pain intensity enhanced in the past 2 weeks. Following clinical evaluation and imaging, the patient underwent further diagnostic procedures and diagnosis of MCC was made.

A sentinel lymph node (SLN) localization scan was performed using nuclear medicine techniques. Specifically, 0.55 mCi of technetium-99 m filtered sulfur colloid was injected intradermally at four sites on the left wrist and forearm. Imaging of the thorax and left upper extremity revealed focal radiotracer uptake, identifying a single SLN in the left axillary region. No abnormal uptake or lymphatic channels were observed in the epitrochlear area. The findings localized the lymph node, supporting subsequent excision. Histopathological analysis of the excised SLN from the left axilla showed no evidence of metastasis, as determined by hematoxylin and eosin staining and immunohistochemical analysis using cytokeratin markers (CAM 5.2 and CK20). Additionally, the wide excision of the soft tissue from the left arm and its deeper margins revealed no residual neoplasm or tumor involvement.

MRI of the left forearm, performed with and without contrast, showed a lobulated enhancing mass in the subcutaneous fat of the distal ulnar aspect of the forearm, measuring 1.6 × 1.4 × 2.6 cm. The lesion was separate from underlying musculature, neurovascular bundles, and bone, and appeared T1 isointense and T2 hyperintense. Differential considerations included both benign and malignant etiologies, such as a possible hemangioma. There was no evidence of fracture, stress fracture, or avascular necrosis. A positron emission tomography/computed tomography (PET/CT) scan from the skull base to mid-thigh using 15.9 mCi of fluorodeoxyglucose (FDG) further confirmed the absence of distant metastasis. The results established a diagnosis of localized disease without systemic involvement or metastatic spread.

The patient was treated with wide surgical excision followed by radiation therapy (RT). RT was initiated on 3 June 2024, and completed on 10 July 2024. The patient received a total dose of 50 Gy delivered in 25 daily fractions using 3D conformal RT and image-guided RT, with a 5 mm bolus applied daily. The patient experienced mild post-radiation effects, including localized swelling, erythema, and stable numbness near the surgical site.

Post-treatment care instructions included keeping the wound sites clean and dry, avoiding unnecessary medication application, and promptly reporting signs of infection such as redness or warmth at the incision sites. Follow-up was scheduled 30 days post-treatment, with ongoing monitoring by medical oncology.

The patient expressed significant concerns about future malignancies and recurrence, given his history of BCC and the aggressive nature of MCC. Although the negative SLNB and absence of distant metastasis provided some reassurance, he remained anxious about the need for vigilant follow-up and the potential for additional skin cancers. He also noted the emotional and physical challenges of undergoing RT and emphasized the importance of clear communication and support from the healthcare team throughout his treatment.

Discussion

MCC is a rare skin cancer, often triggered by excessive sun exposure or immune factors[1,6]. The annual incidence of MCC is 0.6 cases per 100 000 population and is increasing, with projections suggesting up to 3000 cases by 2025[7]. A report indicates that men are more likely to develop MCC before the age of 65, while women have a higher likelihood of developing it after the age of 80. Research also shows a higher risk of death associated with MCC[8]. This case underscores the importance of early diagnosis and comprehensive imaging in managing localized MCC in a patient with a history of BCC. Studies suggest a stronger-than-expected association between squamous cell carcinoma and cutaneous neuroendocrine carcinoma, although no morphologic evidence supports a shared cellular origin for these two tumors[9]. Our case highlights MCC following BCC, an area warranting further investigation.

Histological analysis reveals that MCC cells form nests, cords, and sheets of undifferentiated neuroendocrine-type cells (Meckel) with focal areas displaying distinct squamous features[10]. This supports the hypothesis that a single precursor cell may differentiate into either squamous or Merkel cell types. Additionally, the coexistence of neuroendocrine and squamous properties within individual cells may explain the mixed or simultaneous occurrence of squamous cell carcinoma and MCC. The observed symptoms and patterns of MCC further suggest an etiological role for ultraviolet radiation[10]. This neuroendocrine malignancy primarily affects sun-exposed skin, particularly in the head and neck region[7]. Immunosuppressed individuals are at higher risk, comprising about 10% of cases[1,11].Other risk factors include arsenic exposure, a history of cancer, and chronic diseases[1].

Clinically, MCC presents as a firm, painless, purple nodule that may become hyperkeratotic when enlarged[6]. Early presentations may resemble cysts, acne scars, or vascular lesions[2,12]. Less common findings include red plaques or ruptured blood vessels[13]. Biopsy is crucial due to MCC's nonspecific clinical features[6]. Approximately 89% of cases display at least three AEIOU symptoms[12]. A thorough head and neck examination, including palpation of the parotid gland and cervical lymph nodes, is important[7]. A punch or excisional biopsy of suspicious skin is preferred to assess lesion depth accurately.

Immunohistochemical staining is essential for diagnosing MCC, which typically shows dense blue cells and granular "salt-and-pepper" chromatin[14]. MCC is often positive for cytokeratin 20 (CK20), neurofilaments, and MCPyV[15].

According to the 8th edition of the American Joint Committee on Cancer (AJCC) Cancer Staging Manual, the staging of MCC determined by tumor size (T), lymph node involvement (N), and the extent of metastasis to other organs (M), are used to classify the disease into stage 1 to stage 4[16]. SLNB is the most important method for lymph node diagnosis in MCC. It can detect lymph nodes that are not cancerous in approximately 1% of patients[17]. Complete lymph node dissection is recommended for patients with sentinel-positive disease or confirmed MCC[17]. Reports indicate that treating only the primary site of MCC often results in a poor prognosis, primarily due to regional lymph node metastasis[18]. MCC distal metastases frequently involve the liver, lungs, brain, bone, and regional lymph nodes[19]. In this case, a negative SLNB provided valuable prognostic information, aligning with studies showing a significantly lower recurrence rate (7.5%) in cases with negative SLNB compared to those with positive SLNB (18.7%)[18]. The absence of metastasis was confirmed through PET/CT imaging, supporting a localized disease classification.

However, the development of MCC in adults often leads to surgical intervention. Radical RT can be used as an alternative treatment when surgery is not possible[20]. Avelumab, a monoclonal antibody directed against death ligand-1, is the first approved treatment for patients with metastatic MCC[17].

Despite the favorable outcome in this case, several limitations must be acknowledged. First, the follow-up duration was relatively short, limiting conclusions about long-term outcomes. Additionally, the lack of molecular studies precludes insights into potential viral associations or genetic mutations that might have contributed to MCC in this patient. Further research is needed to explore the links between MCC and prior skin cancers, such as BCC.

The case highlights the critical importance of early diagnosis, comprehensive imaging, and a multimodal treatment approach, including surgery and RT, in the management of localized MCC. Negative SLNB results provide valuable prognostic information, offering reassurance about the potential for favorable outcomes with vigilant follow-up. This report also emphasizes the need to consider MCC in patients with a history of prior skin cancers, such as BCC, contributing to a better understanding of its management and prognosis in similar clinical contexts.

Conclusion

This case underscores the importance of vigilant monitoring and early intervention in patients with a history of skin cancers, such as BCC, who develop MCC. The negative SLNB highlights the potential for localized disease, allowing for effective treatment through wide excision and RT. It also emphasizes the need for continued surveillance in patients with multiple primary skin cancers, as early detection and comprehensive management can significantly improve prognosis.

Ethical approval

Patient anonymity is maintained throughout this manuscript, and consent was obtained for publication from the patient. Ethical approval from an institutional review board or ethics committee is not required as this is a case report.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request

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Author's contribution

S.J., I.B.: validation; visualization; formal analysis and writing – original draft. M.H.A.: project administration; supervision and writing – original draft. M.A.: conceptualization; project administration; supervision; validation; visualization; writing – original draft; writing – review and editing. H.S.: data curation; project administration; supervision and writing – review and editing. U.A.: Validation; visualization and writing – review and editing. H.A.S.: data curation; resources, validation and visualization. A.S.: resources; validation and data curation.

Conflicts of interest disclosure

The authors have no conflict of interest to declare.

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