Ulcerative Variant of Merkel Cell Carcinoma in an Immunocompetent Individual: An Unusual Presentation

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Sir,

Merkel cell carcinoma (MCC) also called as cutaneous neuroendocrine carcinoma generally presents as rapidly growing solitary firm red to violaceous nodule with a smooth shiny surface with the involvement of photo exposed areas of face and neck in 50% cases, extremities in 40% of cases, and trunk and mucosa in less than 10% of cases.[1] Ulceration is rarely observed in advanced cases. Risk factors for MCC include advanced age with mean age of diagnosis at 70 years, UV radiation, immunosuppressed states like organ transplant recipients, HIV infection, or malignancies.[2] Merkel cell polyoma virus (MCPyV) has been recently postulated in the pathogenesis of MCC with MCPyV found to be clonally integrated in the genome of MCC tumor cells in 80% cases.[3] It is an aggressive tumor with poor prognosis, with a 5-year mortality of 40% and shows a tendency for local recurrence, lymph node involvement, and distant metastasis.[4] MCC is a very rare skin cancer with an incidence of 0.44/1,00,000 in US[3] and has been rarely reported in Indian population.[4] We report a case of MCC in an elderly male with two unusual clinical features–arising on photo protected site on lower back as an ulcerated growth mimicking squamous cell carcinoma and developing de novo without any underlying immunosuppression.

An 85-year-old male patient presented with asymptomatic gradually progressive growth over the lower back of 4 years duration, rapidly progressing since 4 months with ulceration. There was no history of weight loss or any other systemic complaints. Before presenting to our center patient had consulted a few other clinicians; however, the lesion was not subjected to histopathology examination. Examination revealed the involvement of left lower back in the form of solitary fungating growth with ulceration measuring 5 cm × 4 cm × 3.5 cm. Few sub-centimetric, discrete, hyperpigmented to erythematous satellite plaques were present in the vicinity of growth [Figure 1a and b]. Patient was investigated with the differentials of squamous cell carcinoma, amelanotic melanoma, cutaneous lymphoma, and chronic granulomatous diseases like cutaneous leishmaniasis. Hematological and biochemical investigations were normal. Enzyme-linked immunosorbent assay for HIV was negative.

Skin biopsy for histopathology showed ulcerated tissue infiltrated by nests and trabeculae of round blue cells on low power, with high nucleocytoplasmic ratio, scant cytoplasm, dispersed powdery chromatin, inconspicuous nucleoli, and brisk mitotic activity seen on higher power [Figure 2a-c]. Immunohistochemistry was done to differentiate small round blue cell tumors of skin which showed positive CK20 [Figure 3a], synaptophysin [Figure 3b], chromogranin [Figure 3c], CD56, EMA, and CD117 along with negative p40, CK7, vimentin, LCA, CD3, CD20, BEREP4, and CD138. MIB1 labelling index was high both in tumor cells and underlying squamous epithelium. Lympho-vascular invasion was seen at tumor margins. Final diagnosis was given as MCC with carcinoma *in situ* changes in lining squamous epithelium. Diagnosis of *in situ* carcinoma changes in the underlying squamous epithelium was made on the basis of histopathological features of high-grade dysplasia along with findings of high MIB-1 index with no unequivocal invasion by dysplastic squamous cells.

Positron Emission Tomography-Computed Tomography (PET-CT) scan for tumor

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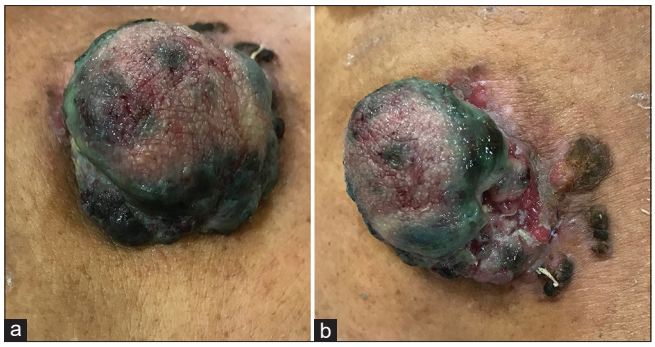

Figur e 1: (a) Fungating growth with ulceration. (b) Hyperpigmented to erythematous satellite plaques present in the vicinity of growth

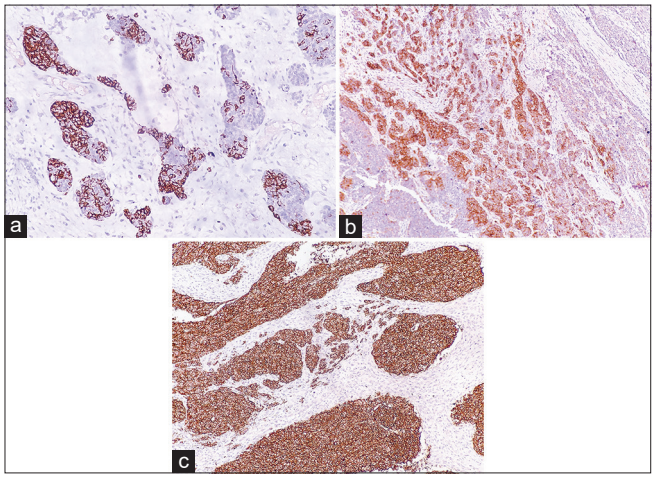

Figure 3: (a) Tumor cells positive for cytokeratin 20. (b) Tumor cells positive for synaptophysin. (c) Tumor cells positive for chromogranin

and metastasis revealed FDG avid exophytic lesion in posterior abdominal wall, FDG avid nodular lesions in abdomen abutting left internal oblique muscle, and subcutaneous nodular lesions in Rt inguinal region suggesting metastasis [Figure 4a-d]. Patient was managed with wide local excision of tumor with 1 cm margin. Gross section of the excised specimen revealed an encapsulated nodular ulcerative tumor measuring 5 cm × 4 cm × 3.5 cm. Cut surface was gray pink, soft with areas of punctate hemorrhages and necrosis. Patient was started on radiotherapy and was offered chemotherapy which he declined, and subsequently succumbed to his illness within 2 months of diagnosis of the disease.

The first description of MCC was given by Toker who called it Trabecular carcinoma of the skin.[5] MCC has a varied clinical presentation although rapid growth of an asymptomatic red violaceous papule or nodule is classically noted. In the absence of underlying immunodeficiency syndromes and diseases, age-related decline of immune function and cumulative doses of UV rays are implicated as risk factors.[6] In our reported case, advanced age of 85 years was a contributing factor, but the photo protected site of lower back is a rare site for origin of MCC.

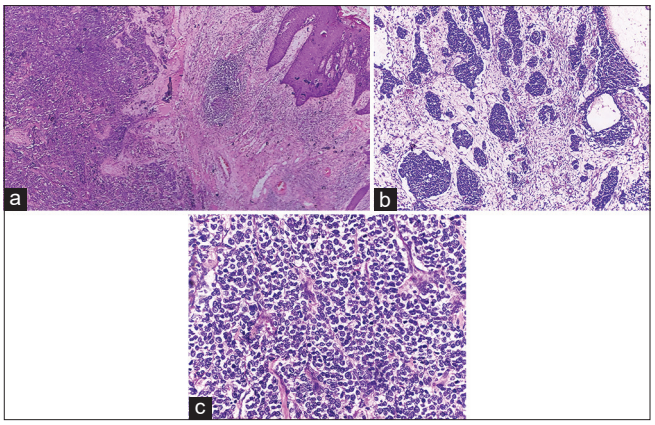

Figure 2: (a) Haematoxylin and eosin stain-5×: Ulcerated tissue infiltrated by nests and trabeculae of round blue cells. (b) Haematoxylin and eosin stain-10×: Ulcerated tissue infiltrated by nests and trabeculae of round blue cells. (c) Haematoxylin and eosin stain-20× High nucleocytoplasmic ratio, scant cytoplasm, inconspicuous nucleoli, and brisk mitotic activity

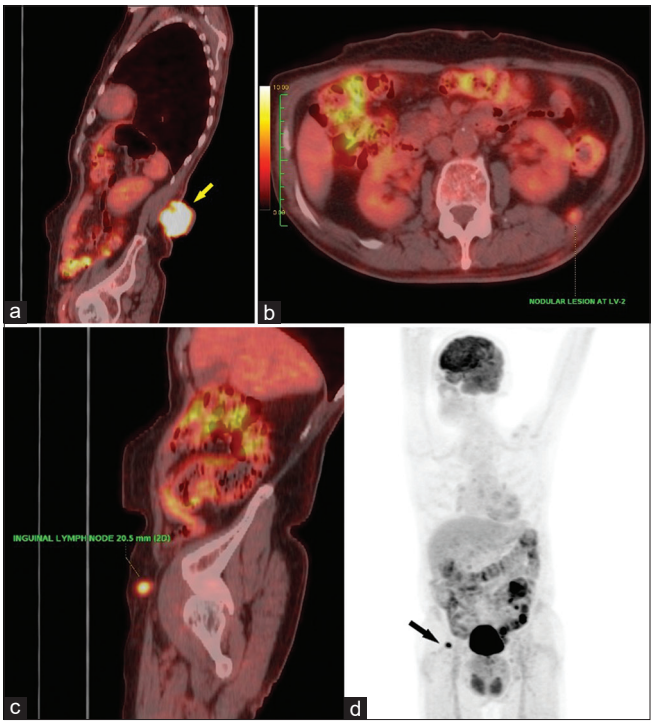

Figure 4: (a) FDG avid exophytic lesion in posterior abdominal wall. (b) FDG avid nodular lesions in abdomen abutting left internal oblique muscle. (c) FDG avid subcutaneous nodular lesions in right inguinal region. (d) MIP images in coronal section showing metastatic metabolically active right inguinal lymph node

Clinical differentials of squamous cell carcinoma, cutaneous lymphoma, and amelanotic melanoma were given initially owing to the atypical ulcerative and fungating morphology and slow growth of tumor for 4 years. Histopathology and immunohistochemistry are of paramount importance in clinching the diagnosis as was seen in our case. Three histopathological patterns have been described: (1) Trabecular type with connective tissue separating interconnecting cellular trabeculae, (2) Intermediate cell type, which is commonest, with solid nests and trabeculae

at periphery, and (3) Small cell type consisting of sheets of small cells with a diffusely infiltrative pattern.[3] In the present case, the predominant pattern was of sheets of small round cells. The tumor cells in MCC are rounded, monomorphic, small to medium sized with scanty cytoplasm, round nuclei with inconspicuous nucleoli (blue cells). The nuclei have finely granular chromatin and may show the typical salt and pepper appearance.[7]

MCC is histologically indistinguishable from metastasis of small cell lung cancer, hematological malignancy, and other skin tumors with neuroendocrine differentiation, thereby highlighting the importance of immunohistochemistry. CK20 positivity, in a distinctive peri-nuclear dot-like pattern, is strongly specific staining 80%–90% of MCC. The dense core granules of MCC show immunoreactivity for neuroendocrine markers, chromogranin, synaptophysin, and neuron-specific enolase.[8] IHC for MCPyV antigen is also specific, however, could not be done in our case due to nonavailability. Histological features associated with poor outcome include tumor size (≥5 mm), extension into the subcutaneous tissue, diffuse growth pattern, absence of an intratumoural T-cell infiltrate, and high mitotic rate.[9]

MCC is a very aggressive tumor and, hence, the need for early diagnosis and staging. The most frequent sites of metastasis are skin, lymphatics, and liver although potentially any organ including CNS can be affected. PET-CT scans have been widely used in MCC for detecting locoregional nodal and distant metastatic disease and staging work up. It is a noninvasive imaging technique that has the potential to detect occult lesions bigger than 5–8 mm in minimal diameter that are not detectable by other imaging techniques.[10] As PET-CT scanning is a whole-body scan, it helped us in delineating the metastatic metabolically active lesions and lymph nodes, as well as the high metabolic activity of primary lesion suggesting its aggressiveness.

Management of MCC is dependent on tumor staging at presentation, with curative intent for locoregional disease and palliative intent for distant disease. Optimal management of MCC includes surgical excision of primary tumor with wide margins, and adjuvant radiotherapy, chemotherapy, immunotherapy, and molecular-targeted therapy in the case of metastasis.[11] Our patient was managed with wide local excision of the tumor with the histopathological margins being free of tumor and was started on radiotherapy for subcutaneous and intraabdominal metastasis. Patient was offered chemotherapy which he declined, and succumbed to his illness within two months of diagnosis of MCC.

Our case highlights an unusual variant of MCC presenting as an insidious onset ulcerated growth over lower back in an elderly male without any underlying immunosuppression. A high index of suspicion is of paramount importance on the part of the treating dermatologist, for prompt and early diagnosis of MCC to arrest the disease in its incipient stages.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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