



CASE REPORT

# Description of a case: merkel cell carcinoma in a male nipple after a kidney and liver transplant



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Received 2 May 2024; accepted 28 May 2024

Available online xxxx

**KEYWORDS**

nipple;  
breast;  
merkel cell carcinoma;  
immunosuppression

**Abstract** Primary Merkel cell carcinoma (MCC) is rare primary neuroendocrine skin carcinoma that arises most commonly on sun-damaged skin of elderly or immunosuppressed patients. Breast involvement is even rarer with incidence under 0.1% of all breast carcinomas. To our knowledge, only eight cases of primary MCC of the breast have been reported in the literature and seven of them were in female patients. We present the second case of primary MCC described in a male breast so far. A 61-year-old male presented for evaluation of a mass in the left nipple. He presented a double kidney and liver transplant in 2014 due to an hepatocarcinoma. The patient was definitively diagnosed as unresectable locally advanced MCC. MCC risk is sharply elevated after solid organ transplant, likely resulting from long-term immunosuppression. MCC should be suspected in the presence of a rapidly amelanotic growing mass in the breast.

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**PALABRAS CLAVE**

pezón;  
mama;  
carcinoma de células  
de Merkel;  
inmunosupresión

**Descripción de un caso: carcinoma de células de merkel sobre el pezón de un hombre tras un trasplante de hígado y riñón**

**Resumen** El carcinoma de células de Merkel primario (CCM) es un carcinoma cutáneo neuroendocrino primario infrecuente que se presenta más comúnmente en la piel dañada por el sol de pacientes ancianos o inmunosuprimidos. La afectación mamaria es aún más rara, con una incidencia inferior al 0,1% de todos los carcinomas de mama. Hasta donde sabemos, solo se han reportado ocho casos de CCM de mama en la literatura y siete de ellos fueron en mujeres. Presentamos el segundo caso de CCM descrito en una mama masculina hasta ahora. Un hombre de 61 años consultó por una masa en el pezón izquierdo. Había recibido un trasplante doble de riñón e hígado en 2014 debido a un hepatocarcinoma. El paciente fue diagnosticado

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definitivamente como CCM localmente avanzado no resecable. El riesgo de CCM se eleva considerablemente después de un trasplante de órgano sólido, probablemente como resultado de la inmunosupresión a largo plazo. Se debe sospechar de CCM en presencia de una masa amelanótica en la mama que crece rápidamente.

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## Introduction

Primary Merkel cell carcinoma (MCC) is an unusual neuroendocrine skin carcinoma that most commonly arises on sun-damaged skin of elderly or immunosuppressed patients.<sup>1</sup> Nipple involvement is exceptionally uncommon, with an incidence of less than 0.1% among all cases of breast carcinomas.<sup>2</sup> It usually presents a very aggressive evolutionary course, which often causes locoregional recurrence and metastasis.<sup>1</sup> The ultraviolet radiation and the presence of the Merkel cell polyomavirus in the genome of MCC cells are essentials in the etiopathogenesis of this tumor.<sup>1</sup>

To our knowledge, only eight cases of primary MCC of the breast have been reported in the literature and seven of them were in female patients.<sup>2-9</sup> We present the second case of primary MCC described in a male breast. The patient's consent has been obtained for the publication of this article.

## Case report

A 61-year-old male presented for evaluation of a mass in the left nipple, which he had felt for a few months.

He had undergone a double kidney and liver transplant in 2014 due to an hepatocarcinoma after an alcoholic liver disease. He had been under tacrolimus and mycophenolate mofetil treatment with good evolution since then.

Physical examination (Fig. 1a) revealed mild erythema and a 6 cm mameloned and indurated mass on the left nipple

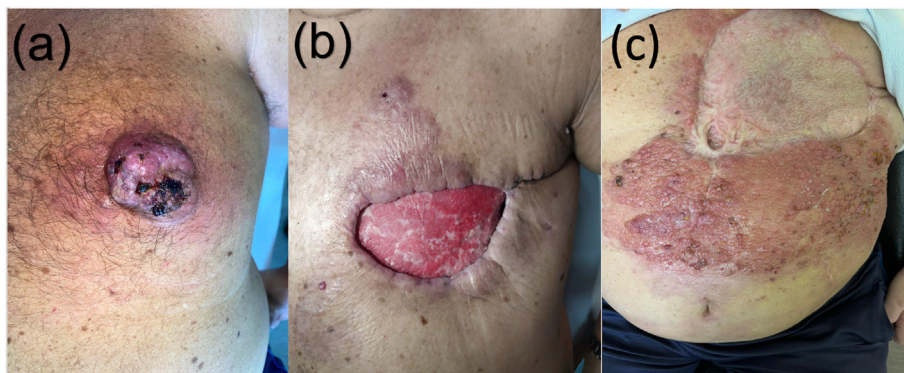
with ulceration and scabs. Several 2–3 mm infiltrated nodules with significant edema were palpated in the internal part of the chest.

Skin biopsy, mammography-ultrasound with lymph node biopsy and a chest-abdominal PET-CT scan were performed. An hypermetabolic mass on the left nipple with infiltration of the subcutaneous cellular tissue with ipsilateral axillary lymphadenopathies were observed. No signs of hematogenous metastatic spread were detected.

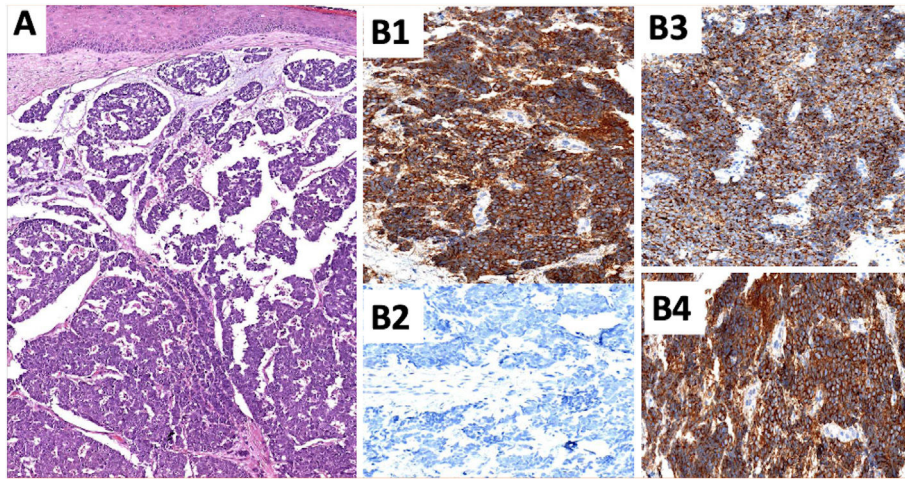
The histopathological analyses of the skin and lymph node biopsies established the identification of a skin neuroendocrine carcinoma, exhibiting an immunohistochemical profile in accordance with MCC (Fig. 2). Other immunohistochemical determinations were also performed to exclude melanoma and others neuroendocrine carcinomas of the breast (NECBs).

The patient was definitively diagnosed as unresectable locally advanced MCC. It was decided to start neoadjuvant chemotherapy with carboplatin-etoposide. After a mild breast response, a mastectomy and left axillary lymphadenectomy were performed. Following the histopathological analysis, a diagnosis of MCC was confirmed on the areola-nipple complex skin. The tumor exhibited a poor response to neoadjuvant treatment, with 4 out of 10 lymph nodes found to be affected. The tumor was classified as stage IIIB (ypT3N3M0) according to the AJCC/UICC TNM 8th Edition.<sup>10</sup>

During the postoperative period, the patient presented a suture deficiency with exposure of the pectoralis major muscle (Fig. 1b) that was covered with a graft. Two months



**Figure 1** Physical examination of the left breast. A. Basal examination: a 6 cm indurated mass on the nipple with ulceration and scabs over mild erythema. B. Dehiscence suture with peripheral nodules that suggested tumor recurrence. C. Cutaneous progression: nodular lesions throughout the left hemiabdomen.



**Figure 2** Cutaneous biopsy results. A. H-E (x10): Diffuse dermal infiltration by small and uniform cells with scant cytoplasm and “salt and pepper” chromatin. Numerous mitotic figures are identified. B. IHC (x20): B1. CK 20 +, B2. CK7-, B3. cromogranin +, B4. synaptophysin +.

later, peripheral nodules were detected around the area of the dehiscence whose biopsy confirmed the tumor recurrence.

After several cycles of chemotherapy with carboplatin-etoposide, the cutaneous lesions spread locally (Fig. 1c). Finally, the patient suffered a massive left pleural effusion due to metastatic pleurisy and died.

## Discussion

MCC of the nipple is an unusual and aggressive type of neuroendocrine skin carcinoma. Prognosis is poor with a 2-year survival rate of 30–50%.<sup>1</sup> MCC risk is sharply elevated after solid organ transplant, likely resulting from long-term immunosuppression.<sup>1</sup> Clarke et al.,<sup>11</sup> in 2015, carried out a review of 89,498 solid organ transplant recipients from 1987 to 2009 and observed that the overall risk of MCC was increased 23.8% (95% CI) after solid organ transplantation. Adjusted risks were highest among older recipients, increased with time since transplantation, and varied by organ type (all  $P \leq .007$ ). Azathioprine, cyclosporine, and mTOR inhibitors given for maintenance immunosuppression increased risk. Immunosuppressive medications may act synergistically with ultraviolet radiation to increase risk.<sup>1</sup>

MCC should be suspected in the presence of a rapidly amelanotic growing mass in immunosuppressed subjects. The differential diagnosis should include amelanotic melanomas and others neuroendocrine carcinomas of the breast (NECBs).<sup>1</sup> Imaging features of MCC may be similar to others NECBs. They typically appear as oval circumscribed masses on mammography and as irregular masses with increased vascularity on sonography.<sup>9</sup> While both MCC and primary NECBs demonstrate positive immunostaining for synaptophysin, MCC originates from dermal-epidermal junction of skin whereas NECB arises from the mammary gland.<sup>9</sup> Moreover, obtaining immunohistochemical stains for specific markers, such as CK7 and CK20 is imperative to confirm the diagnosis of MCC. Around 90% MCC have a CK20

positive and CK7 negative keratin profile.<sup>1</sup> The main difference with amelanotic melanomas is histological, with cells originating from melanocytes. This can be confirmed using immunohistochemical markers such as S100, HMB-45, and melan-A.<sup>12</sup>

Surgical excision remains the primary treatment option for MCC, with recommended margins of 2–5 cm to ensure better local control. This is typically accompanied by prophylactic lymphadenectomy in all patients, followed by radiotherapy to the primary site and regional lymph nodes. Radiation therapy may also be utilized for patients who are not suitable candidates for surgery. Chemotherapy is generally reserved for cases with distant metastases, although no standardized protocol has been established for this treatment.<sup>1</sup>

In conclusion, MCC should be suspected in the presence of a rapidly amelanotic growing mass in immunosuppressed subjects even in the nipple. Correlation with clinical history and judicious use of immunohistochemistry is essential in distinguishing MCC from amelanotic melanomas and other NECBs, which has obvious implications for patient therapy and prognosis.

## Funding

None.

## Ethical disclosure

The work described was undertaken in accordance with the Code of Ethics of the World Medical Association. Approval has also been obtained from the local ethics committee.

## Patients consent

The authors declare that the patient's consent has been obtained for the publication of this article.

## Conflicts of interest

None of the authors have any conflict of interests to declare.

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