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Total remission of Merkel cell carcinoma after coronavirus infection: a case report

Remissão total do carcinoma de células de Merkel após infecção por coronavírus: relato de caso

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ABSTRACT

A 65-years old Peruvian woman was admitted to the Brazilian National Cancer Institute, with a diagnosis of Merkel cell carcinoma in the left shoulder. A PET-CT confirmed the locally advanced disease, with the involvement of lymph nodes in the axillary region. At the time of the proposed surgical procedure, the patient tested positive for COVID-19 without symptoms. She returned for an appointment one month later recovering from COVID-19, reporting a significant decrease in the lesion. One month later, no lesion was clinically found on the left shoulder. Due to the possible remission of the disease, a new PET CT was requested, revealing no metabolic findings suggestive of active neoplastic tissue.

Keywords: Merkel cells; COVID-19; Remission, Spontaneous.

RESUMO

Uma mulher peruana de 65 anos foi admitida no Instituto Nacional do Câncer com diagnóstico de carcinoma de células de Merkel no ombro esquerdo. A PET-CT confirmou a doença localmente avançada, com envolvimento de gânglios linfáticos da região axilar. No momento do procedimento cirúrgico proposto, a paciente testou positivo para COVID-19 sem sintomas. Retornou à consulta um mês depois, recuperando-se da COVID-19, relatando diminuição significativa da lesão. Um mês depois, nenhuma lesão foi encontrada clinicamente no ombro esquerdo. Devido à possível remissão da doença, foi solicitada nova PET-CT, não revelando achados metabólicos sugestivos de tecido neoplásico ativo.

Descritores: Células de Merkel; COVID-19; Remissão espontânea.

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INTRODUCTION

Merkel cell carcinoma (MCC) is a rare, aggressive, cutaneous malignancy that has a high propensity for recurrence and metastases.[1] Traditionally, it was believed to arise from Merkel cells located at the basal layer of the epidermis and hair follicles and are associated with sensory neurites in the dermal papillae, the skin mechanoreceptors.[2] However, there are other alternatives hypothesis that these tumors originate from an immature totipotent stem cell that acquires neuroendocrine features during malignant transformation.[3]

The incidence is higher in men than in women,[4] and MCC is more frequent in older people[4] and individuals with conditions causing immunosuppression, such as patients with hematological malignancies[5] or HIV infection[6] and solid organ transplantation recipients.[7]

MCC incidence increases exponentially with advancing age. In the USA the incidence was 0.1, 1, and 9.8 per 100,000 person-years among individuals aged 40-44, 60-64 and >85 years, respectively.[8] In Brazil the incidence seems to present tendency,[9] due to ethnicity/skin color distribution across the country most of the cases are in the Southeast/South states, where white color is predominant compared with other areas.

The Merkel cell polyomavirus can be detected in approximately 80% of all MCCs by real-time polymerase chain reaction (PCR).[10] In a locoregional disease, an extensive excision of the primary tumor achieving widely negative margins is the initial standard management whenever possible. The immune system plays an important defensive role against MCC, based on increased incidence in immunosuppressed patients, association with Merkel cell polyomavirus (MCPyV), and some reports of spontaneous regression.[11,12]

In patients with advanced or metastatic MCC, the standard initial treatment options are the checkpoint inhibitors – anti PD-L1 (avelumab)[13-15] or anti PD-1 (pembrolizumab, nivolumab).[16-18]

This case presentation was approved by the ethics in human research committee of the Brazilian National Cancer Institute, Rio de Janeiro, Brazil - CAAE 55545822.6.0000.5274 and all the related procedures were conducted following the good clinical practice guidelines. Written informed consent was provided by the patient.

CASE REPORT

A 62 years-old female was referred to INCA, in January 2021, reporting a nodular lesion in her left shoulder, with hyperpigmentation and rapid growth since November 2020. The lesion was biopsied and a diagnosis of MCC was made on 01/19/2021, without satellitosis. The immunohistochemistry demonstrated positivity for enolase, chromogranin A and CK20 and negativity for TTF1, LCA and CD68.

She was submitted to PET-CT on February 5, 2021, showing an expansive lesion with soft tissue density and lobulated borders in the cutaneous/subcutaneous region of the left shoulder, posterior to the humeral head, measuring about 5.0x5.1cm and with a maximum SUV (standard uptake value) of 6.7, associated with other similar nodules adjacent to the described lesion, arranged in subcutaneous tissue of different sizes, including one measuring about 1.8x1.6cm with (SUV 3.1). Prominent lymph nodes in the left axillary region, with a slight increase in the glycolytic metabolism (SUV 1.9) (Figure 1A) were also detected.

Prior to the prescribed surgical procedure, the result of a SARS-CoV-2 screening swab performed on 03/02/2021 was positive and continued positive on 03/30/2021. She returned for an appointment on 04/01/2021, reporting significant decrease of the lesion, no longer prominent and nodular, being evaluated with residual hyper-pigmented macule. She was submitted to primary tumor resection and sentinel lymph node biopsy on 04/09/2021, with a subsequent histopathological diagnosis of chronic inflammatory process with foreign body-like gigantocellular reaction and lymphoid follicles in the dermis. No residual neoplasm was identified (Figures 2C and 2D).

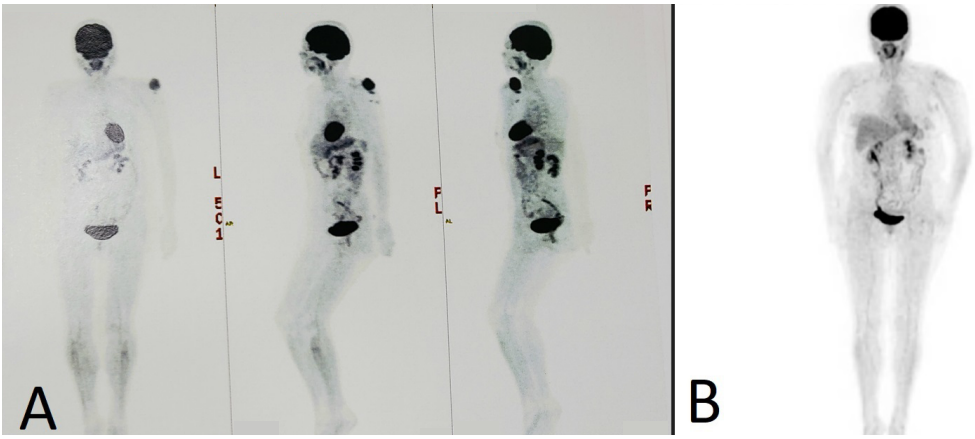

Figure 1. A. Initial PET CT in March 2021 demonstrating left shoulder showing an expansive formation with soft tissue density and lobulated borders in the cutaneous/subcutaneous region of the left shoulder, posterior to the humeral head; **B.** Final PET in August 2021 at the same local, without capitating lesions.

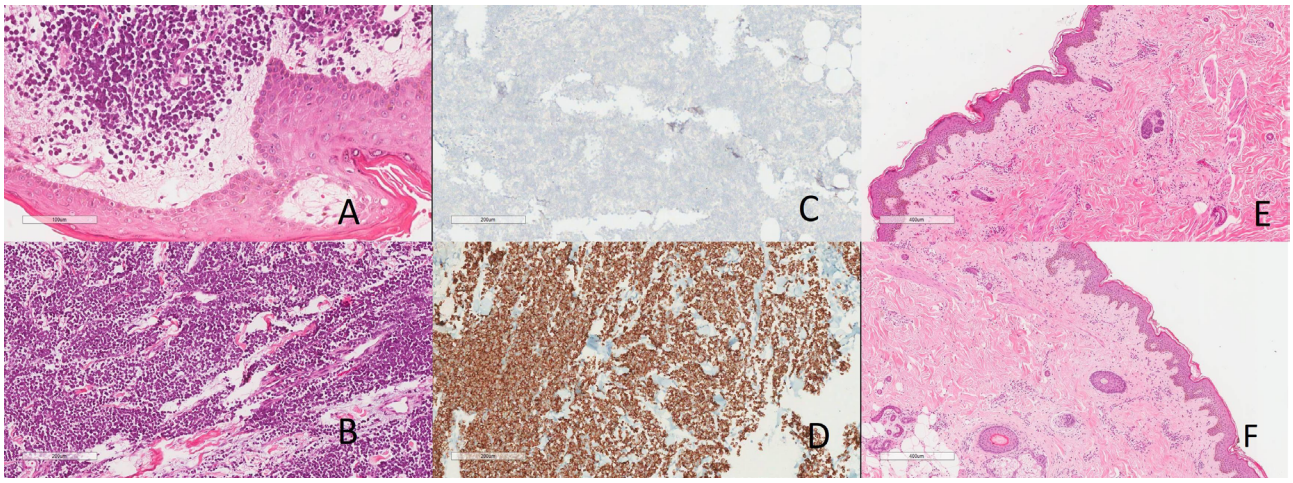

Figure 2. A-B. Initial Biopsy in HE with immunochemistry demonstrating (C) Negative TTF-1 and (D) Positive CK20; **E-F.** Biopsy of Residual lesion in 04/2021 demonstrating chronicle inflammatory process. At 200x magnification.

On 05/18/2021 the patient was evaluated and only the surgical scar was clinically detected. Due to the possible disease remission, a new PET-CT was performed on 06/08/2021, showing level IIA bilateral cervical lymph nodes (SUV 1.6) with inflammatory aspect.

Discrete radiopaque uptake in the area of densification of subcutaneous cellular tissue in the region posterior to the left humeroscapular joint and axillary joint on the same side (SUV 1.6), probably corresponding to post-surgical alterations, absence of other hyper-metabolic findings suggestive of active neoplastic tissue (Figure 1B). No systemic treatment was proposed at that time. After 24 months follow-up, no disease was detected.

DISCUSSION

Spontaneous remission after bacterial or viral infection in patients with lymphoma has been reported.[19,20] While an antitumor immune response has been thought responsible for this spontaneous remission, the exact mechanism has not been elucidated. Additionally, rare cases of tumor response related to SARS-CoV-2 infection can be found in the literature.[21] Infectious diseases are known to trigger the innate immune system and may even induce tumor responses.[22] The implication of the immune system, modulated by infectious agents via innate immune receptors such as Toll-like receptors (TLRs), was determined to be the mechanism of tumor response.[23] Indeed, SARS-CoV-2 infection activates innate immune responses via TLRs and induces production of multiple proinflammatory cytokines and chemokines including interferon-alpha, tumor necrosis factor alpha, interleukin (IL)-1, and IL-6.[24,25]

The physiopathology of SARS-CoV-2 (COVID-19) is similar to other respiratory viral diseases, such as influenza, profound lymphopenia may occur in individuals with COVID-19 when SARS-CoV-2 infects and kills T-lymphocyte cells. In addition, the viral inflammatory response, consisting of both the innate and the adaptive immune response, impairs lymphopoiesis and increases lymphocyte apoptotosis.[26] ACE-2 has been identified as a functional receptor for SARS-CoV-2 and is highly expressed on the pulmonary epithelial cells.[27] It is through this host receptor that the S protein binds initially to start the host cell invasion by the virus.[28,29] The target of SARS-CoV-2 ACE2 binding can be found em skin cells showing trophism to this.[30]

The authors of this paper did not find any other articles that correlate the interaction between SARS-CoV-2 and MCC.

CONFLICT OF INTEREST

There is no conflict of interest.

AUTHORS' CONTRIBUTIONS

LHRV	Manuscript writing
CLCM	Manuscript writing
ACM	Manuscript writing

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