G Chir Vol. 36 - n. 5 - pp. 231-235
September-October 2015

clinical practice

Unexpected histopathologic result of a wide surgical excision of a bleeding lesion of the skin: a case of Merkel cell carcinoma of the leg

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SUMMARY: **Unexpected histopathologic result of a wide surgical excision of a bleeding lesion of the skin: a case of Merkel cell carcinoma of the leg.**

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Background. *Merkel cell Carcinoma is a very rare primary cutaneous tumor that often looks like an innocuous and asymptomatic nodule or plaque of the skin, but with a very fast growing. It is also called neuroendocrine carcinoma of the skin or trabecular cancer. The main treatment is based on a local excision followed by radiotherapy or chemotherapy. The most common site of presentation of this lesion is head and neck (40-60%.) and it often occur in older men with immunological system dysfunction like HIV patients, cancer, severe infections and immunosuppression for transplantation.*

Methods. *The authors report a case of a bleeding Merkel Cell Carcinoma of the right leg in a 83 years old man with HCV infection, chronic kidney disease and diabetes mellitus type 2 that required local excision.*

Results. *Lesion was entirely removed and then patient was sent to oncologists. After two months from surgical excision, healing process is regular and without complications.*

Conclusions. *This type of tumor can be misdiagnosed and, if bleeding, it can represent a serious surgical emergency.*

KEY WORDS: Merkel cell carcinoma - Surgical excision - Bleeding lesion.

Introduction

Merkel Cell Carcinoma is a rare potentially fatal neuroendocrine tumour of the skin, first described by Toker in 1972. It was defined as a "trabecular carcinoma of the skin" for its microscopic features (1). It occurs mainly in elderly people and in patients with immunosuppression (2). The most frequent localizations are head and neck (40-60%), followed by the trunk (33%) and more rarely by the extremities (10-20%) (3), whereas the small intestine, and particularly the ileum, is the most common site of all neuroendocrine tumours in the human body (4). Controversies still exist about the best treatment for this rare disease. Nowadays therapeutic options are surgical excision, radiotherapy, chemotherapy (5) and new biological agents (6). Hereby we report a case of a Merkel cell carcinoma localized on the lower limb, that is rarely reported in literature (7).

Case report

A male patient, 83 years old, was admitted at our Department for a bleeding cutaneous lesion localized on anterior part of right leg. At physical examination this lesion presented following features: quick growth during last year, very painful and hard texture (Figures 1 and 2). All laboratory data are within normal values. Chest radiography revealed no anomalies. The patient was affected by chronic kidney disease (CKD) in treatment with hemodialysis, high grade hypertension, diabetes mellitus type 2 and hepatitis virus C (HCV) chronic infection. US - scan wasn't helpful for evaluation of clinical aspects of the lesion. Therefore we prescribed a Computer Tomography (CT) of right lower limb that revealed no evidence of muscle and bone infiltration. An accurate informed consent was obtained by patient for surgical procedure. Thus a wide surgical excision of the lesion was made. Post-operative course was regular and any complications were observed. The patient was discharged two days after the procedure. Diagnosis of Merkel Cell Carcinoma was the result of histologic examination of the specimen. Consequently, the patient was sent to oncologists to plan an adequate therapeutic strategy. Total body CT didn't reveal distant metastases. Therefo-

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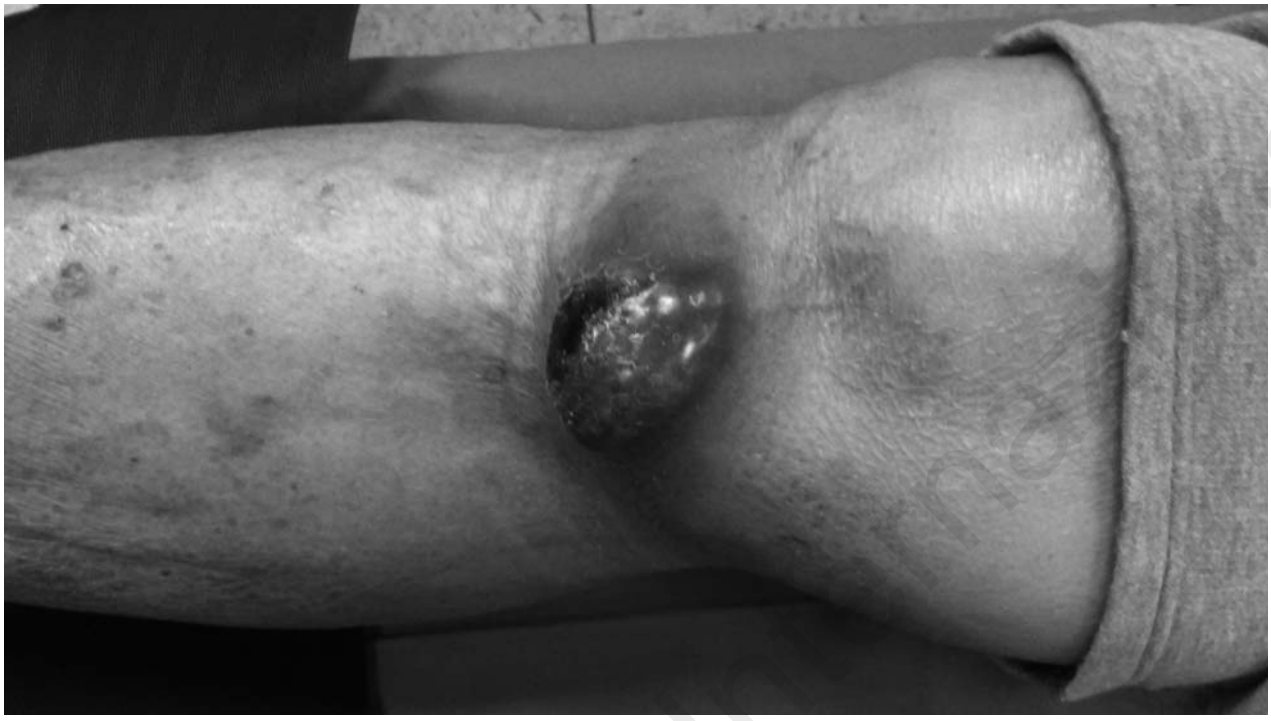

Fig. 1 - Anterior view of the leg lesion.

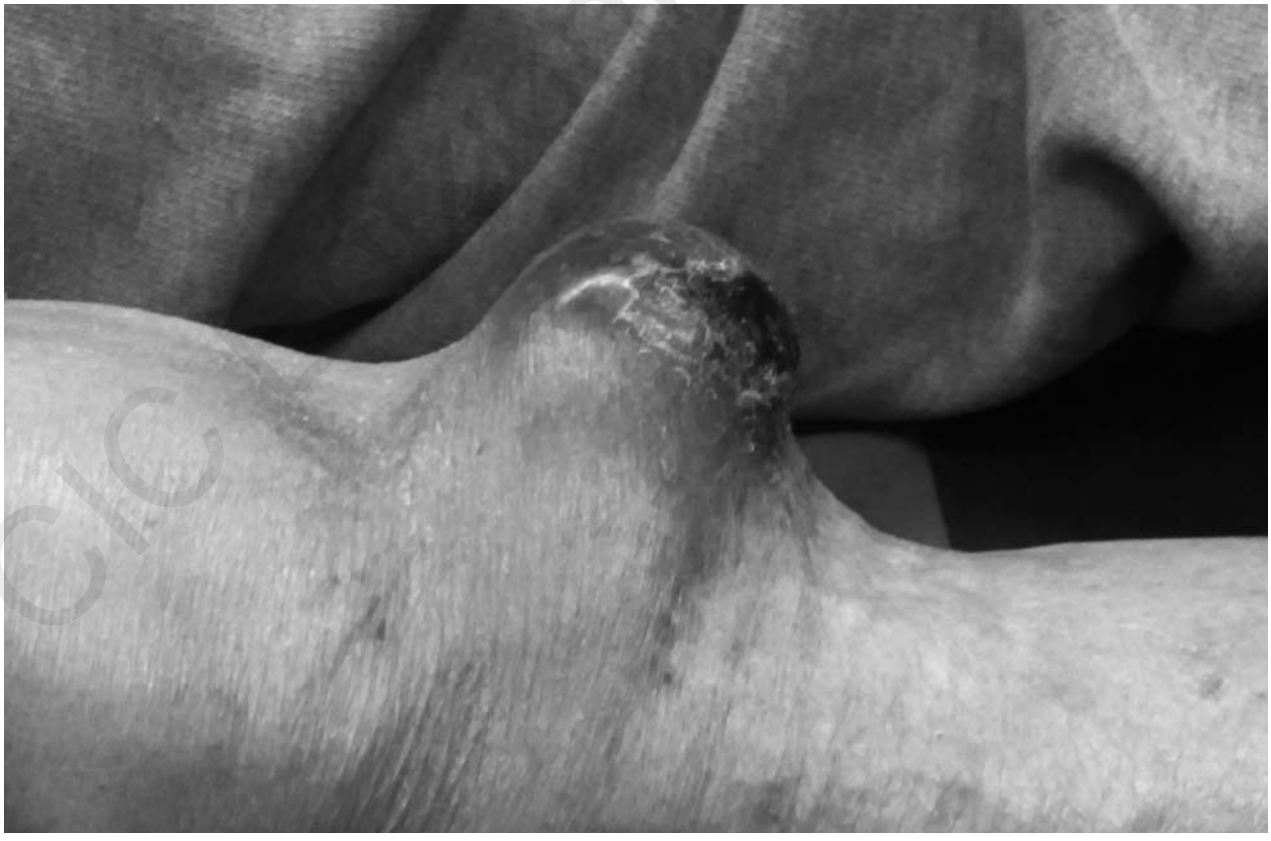

Fig. 2 - Lateral view of the leg lesion.

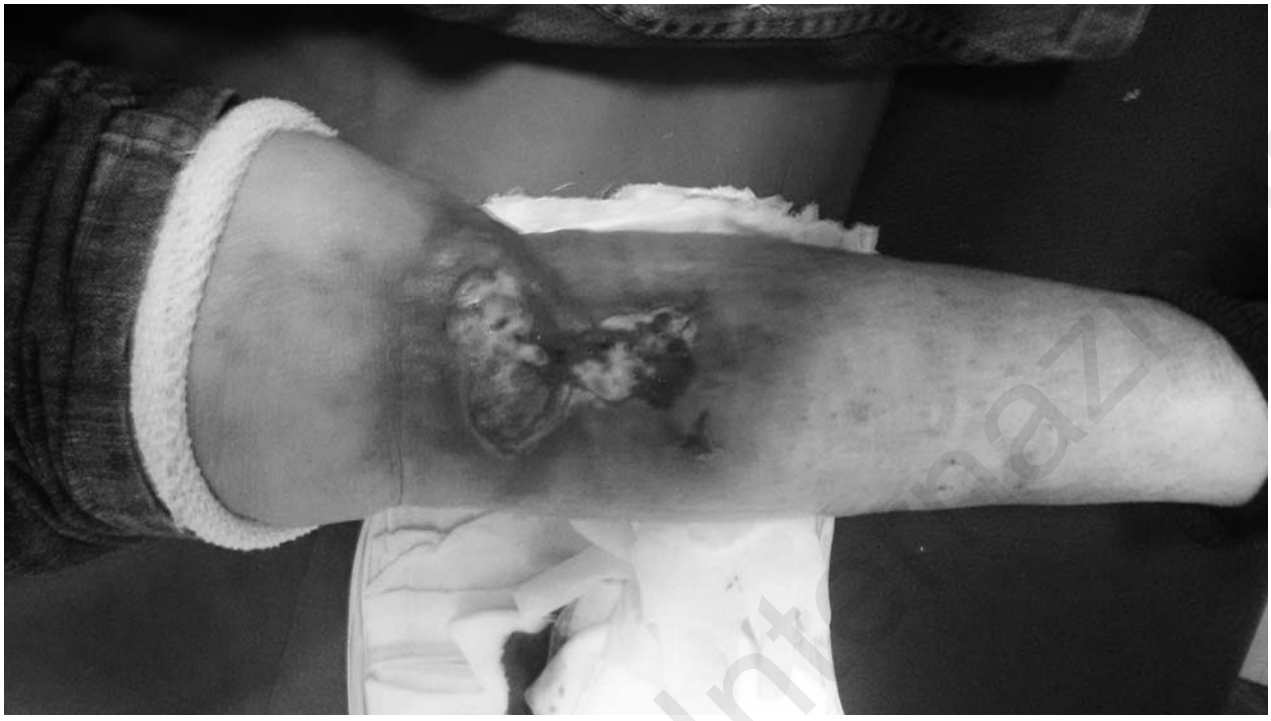

Fig. 3 - Scar healing two months after the surgical procedure.

re, the oncologists decided to treat the affected region of the lower limb by radiotherapy. At our follow up control, two months after the surgery, the scar healing proceeded regularly (Figure 3).

Discussion

Merkel cell carcinoma is a rare malignant neuroendocrine tumour. This term was used prior to the 1980s (8). In mammals, Merkel cells are localized in the basal layer of the skin and mucosa either as single cells or in clusters. These contain about 50 cells and they are in close neighbourhood to nerve terminals forming mechanoreceptors. Considering the most recent studies, the origin of this type of cells is not clear: they probably originate from the neural crest (9). The carcinoma has an incidence of around 5 cases per 1 million population and it is extremely rare in children (10). It occurs mainly in people older than 65 years old, more in men and those with immunological system dysfunction due to cancer, HIV and other severe infections or immunosuppression post-transplantation (11). The tumour growth pattern was trabecular and column – like infiltrating between dermal bundles. Immunohistochemically, this type of tumor is characterized by various specific markers such as cytokeratin 20 (CK – 20), that is part of low molecular weight cytokeratins. CK – 20 helps to distinguish between Merkel cell carcinoma and small - cell lung carcinoma since both tumours are morphologically similar (12). Moreover, thyroid transcription factor 1 [TTF – 1] is a very reliable and accurate diagnostic marker for small – cell lung carcinoma but it is not expressed by Merkel cell carcinoma (13). Other important markers are neuron-specific enolase [NSE] and neurofilament protein [NFP], typically present in neuroendocrine tumours (14). The macroscopically seemingly enclosed form of the cancer contrasts with its tendency to microscopic spread to distant sites. Most of the nodules are localized carcinomas in the dermis. The cytological picture is characterized by dull, monotonous medium size nuclei with numerous mitoses. Histologically there are three types of tumour: the trabecular type, the intermediate type and a variant based on small cells occurs more frequently and is much more malignant (15, 16). For patients with Merkel cell carcinomas, imaging and subsequently staging of the disease are of great importance. Among whole body imaging techniques, TC scanning and FDG – PET showed highly reliable and accurate images in patients with metastatic disease (17, 18). In regard to treatment, wide surgical resection of the primary lesion and adjuvant radiotherapy is the best treatment for controlling loco-regional disease (19). Indeed this neuroendocrine tumour is highly radio-sensitive (20). The radicality of the treatment is proportional to the stage of the disease. In the first and second sta-

ges without nodal or distant metastasis, radical excision is possible, followed in patients at high risk by radiotherapy. In the third stage, where loco – regional metastases have occurred, surgical excision with a radical dissection of draining lymph nodes, followed by radiotherapy is done. In the fourth stage (presence of distant organ metastases), the treatment is palliative involving chemotherapy, supplemented by radiotherapy (21). The tumour frequently metastasizes to the lungs, liver and bones (22). The chemotherapeutic agents most commonly used are etoposide and carboplatin (23). The most recent treatment for Merkel Cell Carcinoma is biological and it is related to the finding of Merkel Cell Carcinoma Polyomavirus (MCPyV). In 2008, Feng and coworkers found novel viral sequences in four Merkel Cell Carcinoma tumour tissues (24). In particular, polyomaviruses encode for large and small T-antigens which bind to host proteins facilitating viral replication and inactivation of tumour suppressor proteins p53 and pocket retinoblastoma (pRb). The MCPyV large T - protein was highly expressed in primary as well as metastatic lesions (25). This observation is highly and clinically relevant in two points: firstly MCPyV large T - protein can be easily and cost – effectively detected by CM2B4, a highly sensitive and specific mouse monoclonal antibody, in specimens that lack CK – 20 immunoreactivity (26). Secondly, since the expression of MCPyV large T – protein is homogeneously over - expressed in primary and, more important, in metastatic lymph nodes, it can be used as a target protein for systemic therapy in patients with disseminated disease with very poor outcome (27).

Conclusions

Merkel cell carcinoma is a rare malignancy with an uncertain prognosis. This kind of tumour has only recently been included in the international classification of tumours (NCCN). However, the management of patients with Merkel Cell Carcinoma is a tremendous challenge for the clinician as well as the patients and their families. The first step for optimal treatment is clinical investigation and proper diagnostic work – up of the patient including determination of the histology, imaging of the tumour and any metastatic disease, and finally determination of the therapeutic plan within a multidisciplinary setting. Because its rarity and lack of randomized studies, there is no agreement on optimal treatment. Future perspectives are interesting, especially about looking for new strategies to target the Merkel cell polyomavirus either to prevent infection or to inhibit viral – induced carcinogenesis.

Conflict of interests

Authors have any conflict of interests.

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