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Primary retroperitoneal Merkel cell carcinoma: Case report and literature review

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ABSTRACT

BACKGROUND: Merkel cell carcinoma (MCC) is an aggressive cutaneous neuroendocrine carcinoma that affects elderly patients and typically arises in sun-exposed skin. The disease is very rare and only few cases present with no apparent skin lesion. In the retroperitoneum there are only two cases reported in the literature.
CASE PRESENTATION: We report a case of a 54-year-old Mexican male with MCC, which presented as a large retroperitoneal mass. Pathological and immunohistochemical analysis of the transabdominal CT-guided biopsy specimen revealed a MCC. The patient underwent preoperative chemotherapy followed by a laparotomy and the mass was successfully excised.
DISCUSSION: There are two possible explanations for what occurred in our patient. The most plausible theory is the retroperitoneal mass could be a massively enlarged lymph node where precursor cells became neoplastic. This would be consistent with a presumptive diagnosis of primary nodal disease. Moreover, metastasis to the retroperitoneal lymph nodes has been reported as relatively common when compared to other sites such as liver, bone, brain and skin. The less probable theory is the non-described "regression" phenomena of a cutaneous MCC, but we are not found a primary skin lesion.
CONCLUSION: Preoperative chemotherapy and excision of the primary tumor is the surgical treatment of choice for retroperitoneal MCC. We propose that further studies are needed to elucidate the true efficacy of chemotherapy in conventional and unconventional patients with MCC.

1. Introduction

This report examines the unusual case of a patient with Merkel cell carcinoma (MCC) of retroperitoneal origin without evidence of disease in another site in the body. In the current literature, there are a very few cases worldwide of MCC cases originated out of the skin.

MCC is a rare skin tumor that was first described by Toker in 1972. The cells arise from the amine precursor uptake and decarboxylation cell system, and recent studies suggest that they develop from an epidermal cell lineage. With an incidence of 0.18–0.41/100,000, they represent a fraction of skin cell tumors, and UV light is a known risk factor [1]. Primary extracutaneous cases are very rare, with only a few cases reported in the literature; most present in the lymph nodes without a cutaneous tumor [2]. To the best of our knowledge and after a broad review, through July 2015 we identified only three cases of primary retroperitoneal MCC in the literature [3–5]. Furthermore, whereas MCC shows a propensity for local spread and metastasis to regional lymph nodes, and although distant metastasis has been reported in multiple sites including intra-abdominal, thoracic, and the central nervous system [6,7], retroperitoneal or pancreatic metastasis is very rare. An extensive literature search identified only 10 cases of MCC metastasizing to the retroperitoneum [8–17]. We present the case of a primary retroperitoneal MCC and review the literature, concentrating in particular on the clinical presentation of this rare disease.

2. Case report

A 54 year old man, without significant personal or familial history of cancer, presented in our institution with vague and diffuse abdominal pain in September of 2011. Physical examination showed a palpable mass in the right flank and right iliac fosse

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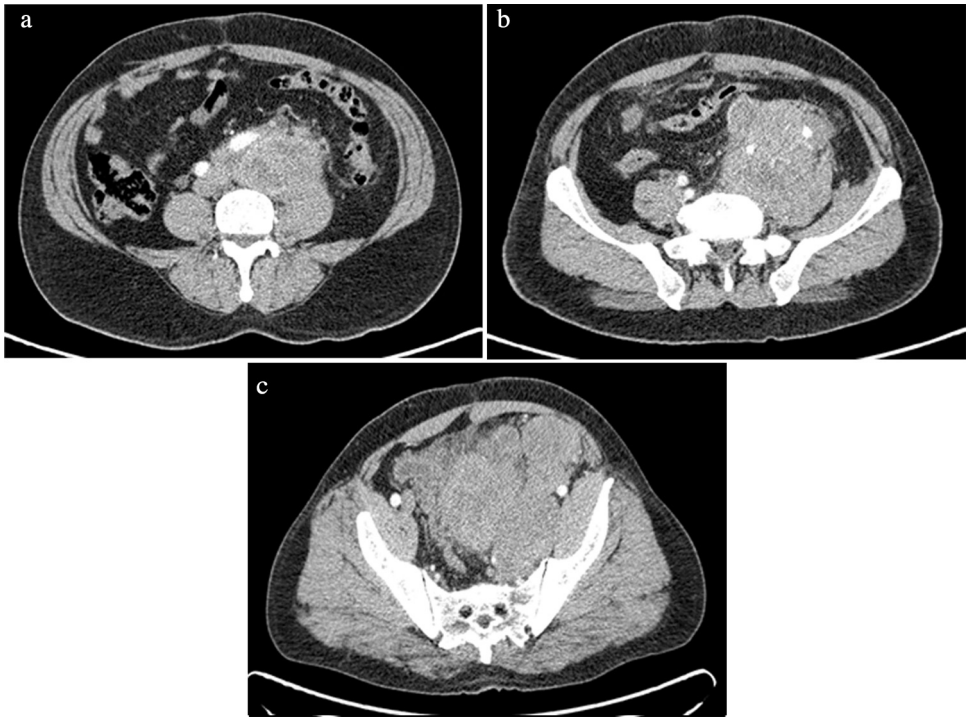

Fig. 1. (a) Computer tomography scan shows a lobulated paraaortic retroperitoneal mass. (b) The neoplasm extends through the left primitive iliac vein until the bifurcation, encasing the external left iliac vein. (c) The neoplasm compresses pelvic structures.

that was mobile and of irregular contour. The computer tomography (CT) showed a retroperitoneal mass of $11 \times 9 \times 7$ cm with extrinsecal compression of the sigmoid colon and urinary bladder (Fig. 1a). In addition, there were multiple para-aortic and left iliac lymphadenopathies measuring up to 50 mm of diameter (Fig. 1b and c). This adenopathies caused functional exclusion of the left kidney. In October 2011 a CT-guided biopsy was taken from the tumor that confirmed the diagnosis.

A PET-CT scan was performed with 68Ga-DOTATOC in November 2011 and showed bilateral cervical lymphadenopathies with SUVmax of 7.4, and a right pharyngeal nodule of 1.7 cm with SUVmax of 5.3. The patient was treated with systemic chemotherapy with six cycles of Carboplatin (570 mg) and Etoposid (190 g) from November 2011 to March 2012, and disease progression was documented with a PET-CT scan in April 2012 (i.e., increased of size of the retroperitoneal mass).

A surgery was performed in June 2012 found a 12×8 cm retroperitoneal tumor that was hardly attached to the left external iliac vein with extension to cava vein. The duration of the surgery was 210 min and the postoperative stay was of three days, without complications. The final diagnosis of the surgical specimen was MCC. The patient was taken to adjuvant radiotherapy with 50.4 Gy from September 2012 to October 2012. During a follow-up visit in May 2013, a PET-CT scan showed disease progression with a right lung nodule of 4 mm and an 18 mm hepatic nodule. Palliative chemotherapy was offered to the patient; however, the patient declined treatment and was attended for the last time in September 2013, with stable disease. The patient was lost in the follow-up.

2.1. Pathologic findings

Pathologically, the mass was a white grayish retroperitoneal mass 12 cm in diameter, histologically composed of small to medium round cells, and with a high nuclear-to-cytoplasmic ratio with an area of vague trabeculae that was highly suggestive of MCC (Fig. 2). Immunohistochemistry confirmed this finding, as the mass

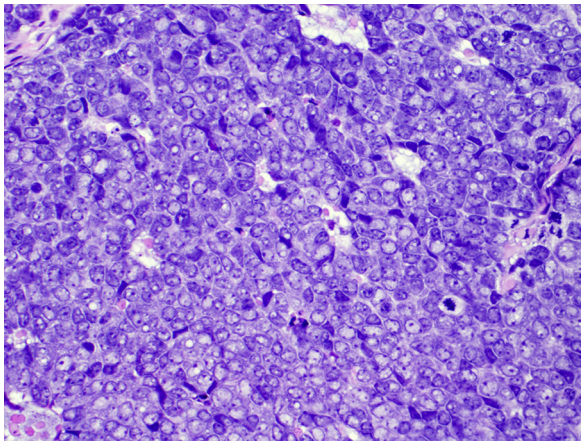

Fig. 2. Microscopic details of the neoplasm showing the characteristic "merkeloid" open dusty chromatin with eccentric nucleoli and a solid and trabecular growth pattern. There are multiple abnormal mitotic figures.

was positive for CD56, synaptophysin, CKAE/AE3, and a characteristic paranuclear cytokeratin (CK) 20 staining (Fig. 3). The neoplasm was negative for CD 138, CD 45, CD 99, HMB-45, desmin, myeloperoxidase, S-100, and vimentin.

3. Discussion

MCC is a cutaneous neuroendocrine carcinoma, and an aggressive neoplasm with a high propensity for metastasis. The tumor mainly affects elderly Caucasians. The disease is rare with an annual incidence ranging from 0.2 to 0.45 cases per 100,000 [18,19]. In a review of 661 cases conducted in 2000, only 2% presented with no apparent primary lesion [20].

Merkel cells reside in the basal layer and hair follicles of the skin's epidermis and are associated with mechanoreceptors in the dermal papillae. It has been proposed that neuroendocrine

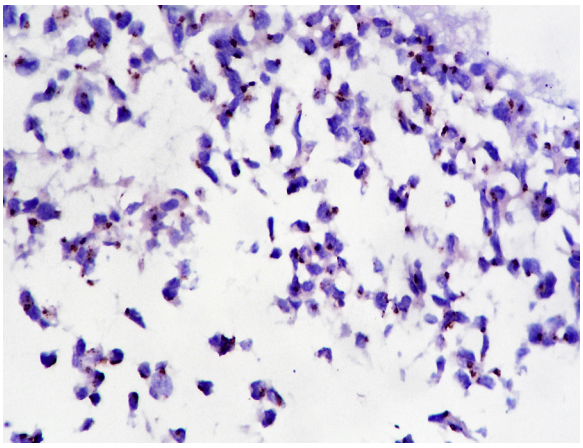

Fig. 3. The neoplasm shows paranuclear CK20 staining.

carcinoma of the skin arises from these cells. However, since MCC is mainly a dermal tumor, an alternative hypothesis that they originate from immature pluripotential stem cells and acquire neuroendocrine characteristics upon malignant transformation [21] is perhaps more plausible. The occasional presence of squamous or eccrine differentiation in these tumors also suggests stem cell origin [22].

It is estimated that 97.6% of MCC cases occur in the skin and 0.4% occur in other locations [23]. MCC has been reported in the lips and oral cavity [24], parotid gland [25], and lymph nodes [26–29]. Only 2% of all cases present without a primary site [20].

We think that our case and the two reported cases in the retroperitoneal space represent a lymph node primary MCC. There are several possible theories for the origin of the MCC. The first is that the retroperitoneal mass could be a massively enlarged lymph node where nodal Merkel cells became neoplastic. Alternatively, an initial skin lesion could have spontaneously regressed, and the retroperitoneal mass represents a single site of metastasis. Since Merkel cell precursors have never been identified within lymph nodes the latter theory seems more convincing, and is supported by the fact that metastasis to the retroperitoneal lymph nodes has been reported as relatively common when compared to other sites such as liver, bone, brain, and skin [30]. A third explanation is that the tumor might have arisen in subcutaneous soft tissues and metastasized to the draining lymph nodes [31]. Finally, another theory that could explain the lymph node as the primary site is that it arose from primitive neuroectodermal (pluripotential) rests in the lymph node [3].

Pathologically, is difficult to accurately diagnose neuroendocrine carcinoma due to its similarity to other poorly differentiated "small blue cell tumors" like small cell carcinoma of the lung. Immunohistochemistry and molecular techniques are necessary for a definitive diagnosis. When found, perinuclear keratin filaments on an electron microscope and a dot-like pattern with CK 20 and CK 7 staining aid in diagnosis [32,33].

Regarding prognosis, MCC of the skin is aggressive and has a high rate of metastasis and recurrence. Survival rates for patients where the disease has progressed beyond the primary lesion are comparable to those of patients with malignant melanoma, where nodal spread is the best predictor of distant metastasis or death [34]. Primary nodal neuroendocrine carcinoma follows a less aggressive course than the metastatic form of nodal involvement [35]. Thus, follow-up of patients may provide insight into whether the nodal disease was primary or metastatic.

The aggressive nature of this disease necessitates frequent follow-up. The presence of risk factors including tumors larger than 2 cm, trunk location, male sex, age over 65, nodal or distant disease at presentation, and duration of disease before presentation should determine the appropriate frequency [36]. During examination, the clinician should focus on the lymphatic and integumentary systems. When symptoms lead to suspicion of recurrence, appropriate imaging studies should be performed.

Preoperative chemotherapy and excision of the primary tumor is the surgical treatment of choice for retroperitoneal MCC. We propose that further studies are needed to elucidate the true efficacy of chemotherapy in conventional as well as unconventional patients with MCC.

Conflicts of interest

None to declare.

Funding

None to declare.

Ethical approval

The Instituto Nacional de Cancerología de México's ethics committee approved our work.

Consent

We have obtained written consent from the patient and that we can provide this to the Editor if necessary.

Author contribution

Osvaldo A Quiroz-Sandoval—study concept, data collection, data analysis or interpretation.

Mario Cuellar-Hubbe—study concept, data collection, data analysis or interpretation.

Leonardo S. Lino-Silva—study concept, data analysis or interpretation and writing.

Rosa A. Salcedo-Hernández—study concept, data collection, writing, data analysis or interpretation.

Horacio N. López-Basave—study concept, data collection, data analysis or interpretation.

Alejandro E. Padilla-Rosciano—study concept, data collection, data analysis or interpretation.

Alberto M. León-Takahashi—study concept, data collection, data analysis or interpretation.

Ángel Herrera-Gómez—study concept, data collection, data analysis or interpretation.

Guarantor

Dr. Leonardo S. Lino Silva.

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