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Neuroendocrine Skin Carcinoma: Merkel Cell Carcinoma Literature Review for a Case Study

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Abstract

Merkel cell carcinoma, also called neuroendocrine skin of the skin, is a very rare type of skin cancer that generally appears as a bluish meat or red color nodule, more frequently in the facial, head, and neck region. Merkel cell carcinoma develops mainly in older people since long-term exposure or a weak immune system can increase the risk of developing it. Merkel cells are at the base of the outermost layer of the skin (epidermis) and are connected to nerve endings that are responsible for the sense of touch. It tends to grow quickly and spread to other parts of the body. Therefore, the treatment options for Merkel cell carcinoma depend on whether the cancer has spread beyond the skin.

Keywords: Neuroendocrine skin carcinoma; Merkel cell carcinoma

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Introduction

Merkel cell carcinoma is a rare cutaneous malignant neoplasia, first described in 1972. It originates from the neural crest cells, which generate the round Merkel cells, located in the basal stratum of the epidermis. Its etiology is not fully understood, there are several risk factors related to their pathogenesis, which include exposure to ultraviolet light, a history of squamous cell carcinoma or basal cell carcinoma, immunosuppression (patients with HIV AIDS stadium), or hematological neoplasia's. Recently, a Merkel cell polyomavirus virus has been described that could explain viral oncogenesis since up to 80% integration of the virus to neoplastic cells has been found. It is a very rare disease since around 2000 cases have been documented, since the first description in 1972. The incidence is 0.01 - 0.23 per 100,000 thousand inhabitants, being more common in white leather people. 78% occurs in over 59 years. It affects both genres more frequently in men (Figure 1). It is mostly produced in areas exposed to the sun such as the head and neck in 50.8% of cases, although also in very low proportions they could appear in non-exposed regions, such as the vulva, penis, pharynx, or mucous membranes. It has an aggressive character from the beginning and according to the published series, lymphatic dissemination is observed in diagnosis by up to 27 - 32% of patients. In fact, the Ganglione stadium is the main prognostic factor, with survival rates at 5 years of 51% diagnosis in localized tumors and <14% in the case of distance metastasis.

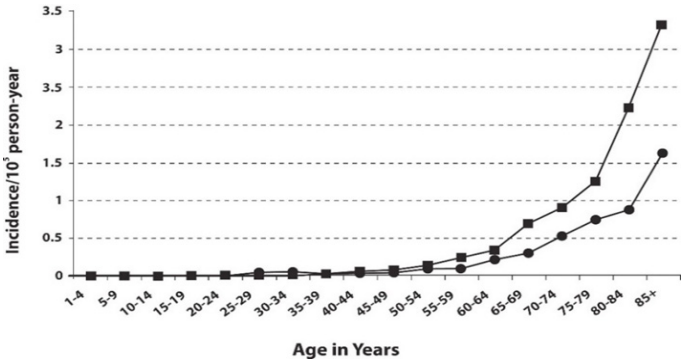

Figure 1: CCM frequency by age and sex in men (square) and women (circle).

Case Presentation

70 -year -old female patient concurs to the hospital for presenting stony tumor in the left buttock region of 1 year of evolution, associated with slight intensity pain, loss of 5 kg of weight in that period, asthenia, and adinamia. The physical examination observed extensive skin and

soft tumor, with loss of continuity solution of approximately 15 x 15 cm, erythematous with necrotic areas, of irregular edges, over suits with purulent debit and foul smell, slightly painful to palpation, in the buttock region left. Associated with left inguinal adenopathy impressing to be an adenomegallic conglomerate palpable, painless, and unchanged in skin coloration (Figure 2). A biopsy of the injury sent to pathological anatomy is requested cutaneous fragment of 2.8 x 1.4 cm shows in the dermis a proliferation of neoplastic cells with rounded nuclei.

Hyperchromatic and scarce cytoplasm, in diffuse pattern with intratumoral lymphocytes. The infiltrate hypodermis lesion with a depth not less than 12 mm and contacts the resection margins. Immunohistochemical techniques with antibodies were performed to observe positivity in neoplastic cells with cytokeratin 20, chromogranin, and synaptophysin. The proliferation index measured by KI-67 was 20% with a definitive neuroendocrine carcinoma/ leather Merkel cells diagnosis. For its correct stratification, and with the suspicion already in this instance of dissemination ganglion Rounded mass of lobed, heterogeneous edges, which measures 54 x 52 x 51 mm and associate trabeculation of adjacent fatty planes. The lesion is hypermetabolic with a Max of 8.5, with possibly necrotic hypocaptant areas (Figure 3, Figure 4, and Figure 5). Three hypermetabolic inguinal adenomegalias of 18 mm, 22 mm, and 14 mm in diameter are identified on its short axis with a max of 3.8, 7.5, and 2.5, respectively (Figure 6). It is also performed, thinking about the possibility of ganglion emptying, an ultrasound of skin and soft tissue of the left inguinal region for the assessment of the augmented ganglia of the size where several ovoid images of contours are evidenced mostly defined in shape in the shape of conglomerate, those of larger size with loss of its center of greatest ecogenicity and the cortical-medullary ratio measured from 29 x 24 mm and that is 9 mm from the surface plane of the skin.

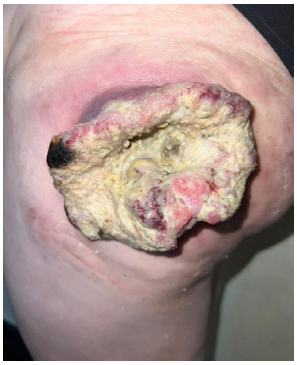

Figure 2: Skin and soft tissue injury in the left butt of 1 year of evolution, exophitic, irregular edges, and necrotic areas.

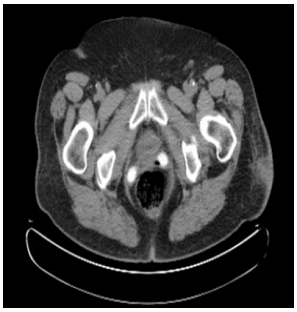

Figure 3: Pelvis tomography: In the thickness of the subcutaneous cell tissue at the level of the lateral face of the left hip, there is a rounded mass of lobed, heterogeneous edges, which measures 54 x 52 x 51 mm and associate trabeculation of the adjacent fatty plans.

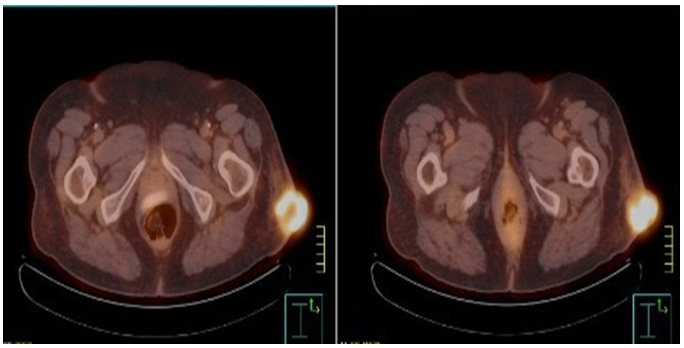

Figure 4: PET, axial cut: hypermetabolic lesion with Max of 8.5, with possibly necrotic hypocaptant areas.

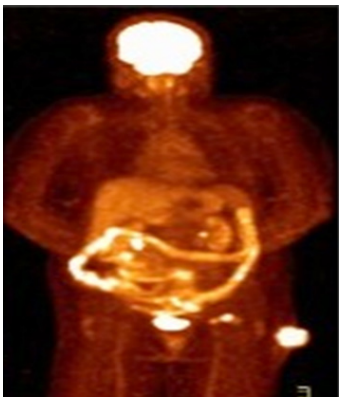

Figure 5: PET, coronal cut: hypermetabolic lesion with Max of 8.5, with possibly necrotic hypocaptant areas.

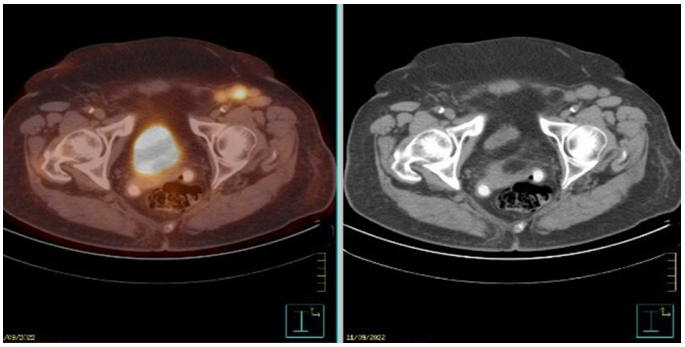

Figure 6: Three 18 mm, 22 mm, and 14 mm diameter hypermetabolic inguinal adenomegalias on its short axis with a max of 3.8, 7.5, and 2.5, respectively.

Case Management

Due to the presentation of the painting, with a single affected ganglion station, confirmed by imageological study, surgical behavior is decided together with the plastic surgery service that will resection the primary leather and general surgery tumor that will be responsible for performing the left inguinal ganglion emptying, without prior neoadjuvant treatment. In this case, 5 months after the diagnosis, an incision of the Rangers was carried out following prior dialing to 2 cm per side. Exeresis in injury block. It is sent to pathological anatomy by freezing that reports a deep margin at 0.5 cm from it so that resection is extended covering the fascia orototic fascia of the entire surgical bed (Figure 7, Figure 8, and Figure 9). Subsequently, the inguinal emptying is carried out left with a left vertical inguinal incision. Ganglionic and vascular package conglomerate is verified, 6 x 4 cm necrotic appearance

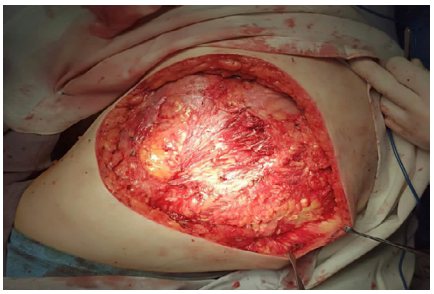

Figure 7: Intraoperative image of the post-resection surgical bed, with image expansion.

Figure 8: Macroscopic piece by deferred of the leather drying with lateral safety margins.

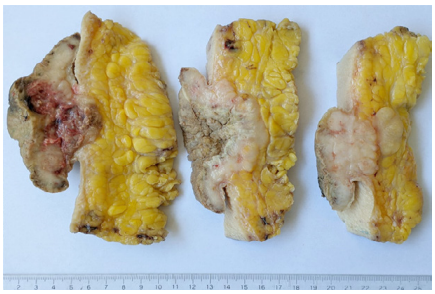

Figure 9: Sagittal cut of the macroscopic piece. On the right, the deep margin is identified at 0.5 cm from the injury.

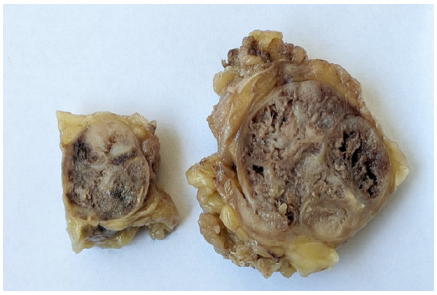

Figure 10: Lymphadenectomy. Macroscopically positive ganglia of left inguinal region.

plus adenopathies period femoral vein that are resected (Figure 10). The approach of the surgical wound defect in thigh skin is performed with eight seals for deferred progressive advance. (Figure 11). The result of the pathological anatomy reported by Merkel cell carcinoma (Figure 12 and Figure 13) whose immunohistochemistry gives positive for synaptophysin and CD56, that is, markers of neuroendocrine differentiation (Figure 14), and cytokeratin 20 with Dot Paranuclear (Figure 15), being negative for ACL.

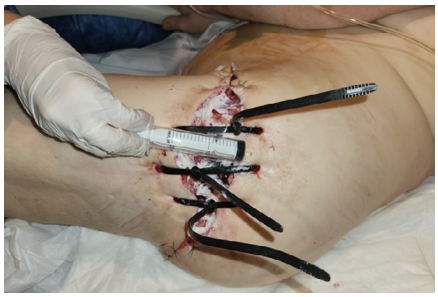

Figure 11: Immediate postoperative. Plastic seals for progressive injury.

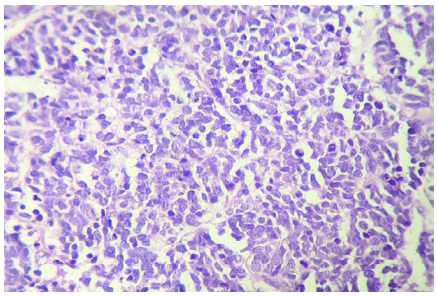

Figure 12: Microscopy: Hye 400x technique. The neoplastic proliferation of monomorphic epithelial cells with a high cytoplasm nucleus ratio, round nuclei with granular distribution chromatin in salt and pepper, arranged in beaches.

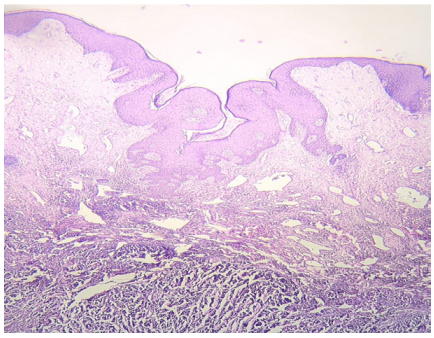

Figure 13: Microscopy: HYE technique, 40x. Merkel cell carcinoma. Epidermis without alterations. At the dermal level neoplastic proliferation of epithelial cells with infiltrative growth pattern.

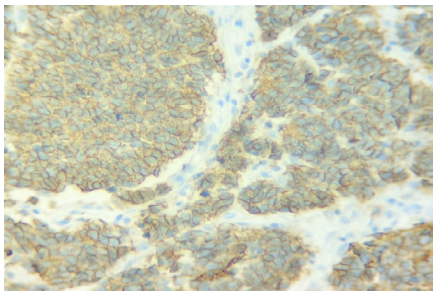

Figure 14: Immunohistochemistry: positive for neuroendocrine differentiation markers CD 56.

Discussion

Merkel cell carcinoma consists of a rare, very aggressive neoplasm, which is more frequently diagnosed in advanced stages, with a poor prognosis (five-year survival from 0% to 68%). The factors that affect survival are the ganglionic state, distance disease, recurrence, and tumor size, as well as narrow margins in surgery. The diagnosis will

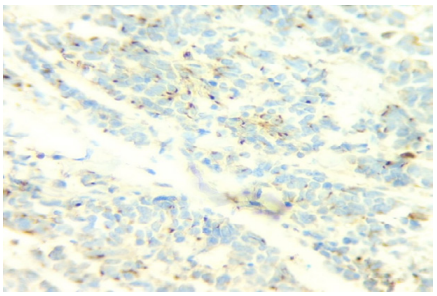

Figure 15: Immunohistochemistry: positive for cytoqueratin 20 with a pattern in Dot Paranuclear.

be made histologically with a sample of the lesion. Microscopically, neoplastic proliferation is observed that grows below the epidermis which is respected, and diffuse the dermis diffuse, being able to extend to the subcutaneous cellular tissue. Within differential diagnoses, lymphoma, neuroendocrine carcinomas metastasis, small cell sarcomas, and melanoma, among others, should be included. In most cases, morphological characteristics, positive staining for CK20 with pattern in Dot Paranuclear and neuroendocrine markers such as synaptophysin, chromogranin, and CD56 together with negative staining for TTF1, CK7, and lymphoid markers are sufficient to confirm the diagnosis.

There is no consensus on the most appropriate image techniques for the extension study in patients with Merkel cell carcinoma. Tomography is considered. By positron emission tomography/computed tomography (PET/CT) of the full body such as a choice image test when evaluating the tumor extension.

As for the therapeutic management of Merkel cell carcinoma, it will depend on the stage of the disease and its distance dissemination. Surgery is the main treatment of this pathology in the initial stadium (I, II, N1). Within its approach are the extension of margins, biopsy of the sentinel ganglion, as well as ganglional dissection.

Recommend 3 cm margins and depth when possible 2 cm. Mohs surgery followed by radiotherapy is used in small injuries, reducing persistent metastasis. If the physical examination or image study does not reveal the affectation of the lymph nodes, the surgical removal must be accompanied by a biopsy of the sentinel ganglion, and it must be studied in serial cuts with routine technique and with an immunohistochemical study for CK20. In case of positivity, the corresponding ganglion emptying must be performed. If that is not possible, the patient must perform neoadjuvant radiotherapy both to the initial primary and the ganglional region.

In addition, if high-risk factors are present (tumor >1cm, affected or insufficient surgical margins, lymphovascular affectation, head, and neck location), current guides recommend administering radiotherapy at 50 - 66 gy to the tumor bed. Radiotherapy has documented complete tumor response in 96% and 4% partial response (100% global response rate). Improvement of local recurrence and medium survival compared to patients who have only been intervened with resection surgery. As for chemotherapy, it has not shown the same benefits because its impact on global survival has been little or almost nil. Although there are several simple or combined chemotherapy schemes (cisplatin with etoposido, doxorubicin, vincristine with cyclophosphamide) there is no standard treatment scheme. Global survival is 10 months in metastatic disease.

In the case of our patient, the possibility of performing neoadjuvant and ganglion therapy was dismissed by the clear diagnosis of unique ganglion metastasis by PET. Due to the patient's clinical status, evolution will be awaited for surgical leather wound resolution, so the approach with seals that reduces, although not completely, the wound gap, reduces the risk of infection, which reduces the risk of infection is decided in the first instance, which reduces the risk of infection and complications in the immediate postoperative period. To make the diagnosis of Merkel cell carcinoma, one must complete the corresponding cancer treatment and monitoring.

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