Merkel cell carcinoma - a clinical case report

Clinical Case

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Abstract

Aim: To report a case of Merkel cell carcinoma in a patient who presented with a rapidly growing cervical mass.
Background: Merkel cell carcinoma is a rare and aggressive cutaneous malignant tumor, with a high recurrence rate and propensity for metastasis. Our goal is to alert and raise awareness among otorhinolaryngologists about this entity, especially in the differential diagnosis of neck masses.
Case description: A 77-year-old woman presented to the clinic due to rapidly growing left cervical swelling. Following fine-needle aspiration cytology and incisional biopsy, Merkel cell carcinoma was diagnosed. The patient died 6 months after the initial presentation.
Conclusion: Merkel cell carcinoma is a rare entity with a rapid and aggressive evolution which normally manifests as a cutaneous lesion of the head and neck but should be included in the differential diagnosis of cervical masses.

Keywords: Merkel cell carcinoma, cervical mass, cutaneous lesion

Introduction

Merkel cell carcinoma (MCC) is a rare and aggressive neuroendocrine skin cancer, characterized by a high recurrence rate and strong tendency to metastasize. The tumor cells resemble Merkel cells, which are specialized neuroendocrine cells located in the basal layer of the epidermis and share the expression of markers such as chromogranin A, synaptophysin, and cytokeratin 20 (CK20).
The incidence of MCC increases exponentially with age. The identified risk factors include fair skin phototypes, older age, male sex, immunosuppression, coexisting neoplasms (particularly hematologic malignancies), and some genetic variants (*MAGT1*, *ATM*, *BRCA1*, *BRCA2,* and *TP53). MCC may be associated with both ultraviolet (UV) radiation exposure and Merkel cell polyomavirus (*MCPyV)

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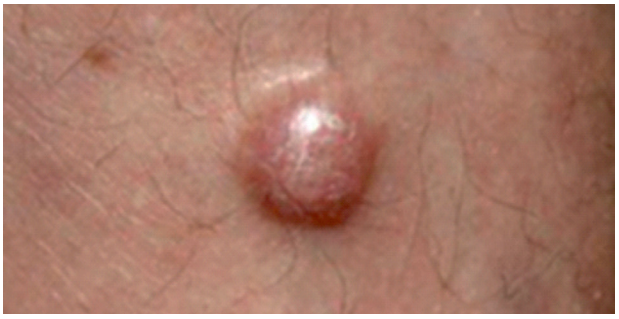
infection, which is detected in 60–80% of cases. MCPyV infection typically occurs in children and is usually asymptomatic.[1-3]

Clinically, MCC most often presents as a solid, firm, skin-colored or violaceous nodule that grows rapidly in sun-exposed areas. The head and neck are affected in 40–60% of cases. MCC is frequently misdiagnosed as a benign lesion, such as a cyst, lipoma, pyogenic granuloma (Figure 1). A rapidly growing lesion (developing in ≤3 months), particularly one that is firm and located in a sun-exposed area in older, fair-skinned individuals should prompt further investigation, including histopathological examination.[4] This study aimed to raise awareness among otorhinolaryngologists regarding this entity, especially in the differential diagnosis of cervical masses.

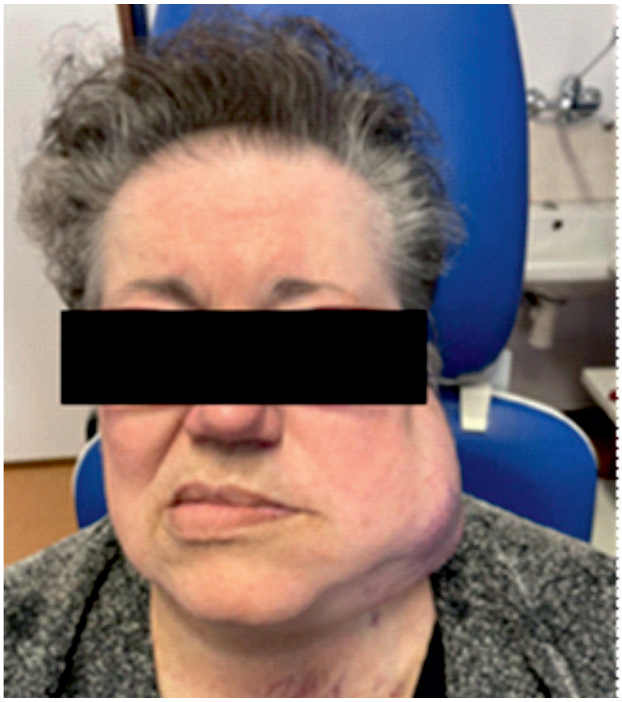
Figure 1
Typical clinical presentation of Merkel cell carcinoma

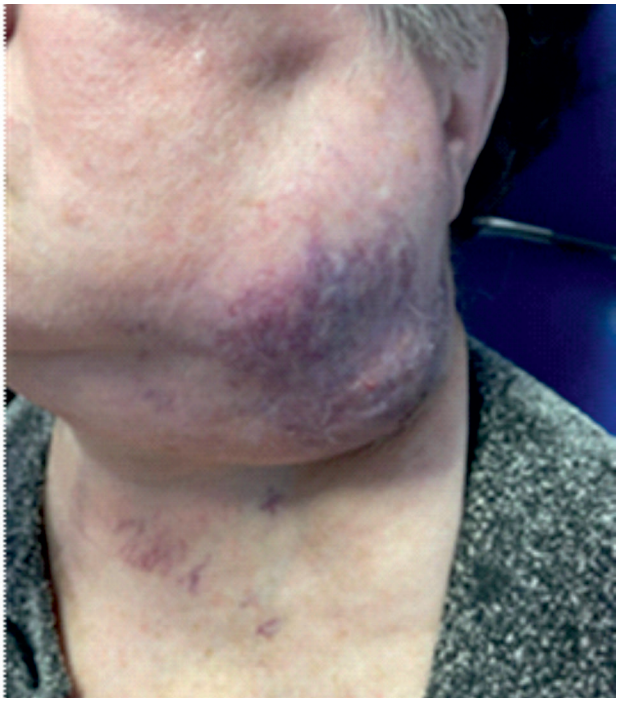


Case report

A 77-year-old woman presented to the otolaryngology clinic with a 2-month history of a rapidly growing, mildly painful swelling in the left cervical region. Although she was experiencing some difficulty in chewing, she reported no dysphonia, dyspnea, or dysphagia. She also reported weight loss of approximately 7 kg over the same period. Her medical history included type 2 diabetes mellitus, hypertension, dyslipidemia, and obesity. She denied smoking and alcohol use. Physical examination revealed a firm, ill-defined mass measuring approximately 7 cm in the left lateral cervical region, adherent to the deep structures and slightly painful on palpation. Additionally, she exhibited grade III peripheral facial paralysis on the left side, according to the House–Brackmann scale (Figures 2 and 3). Fine-needle aspiration cytology was performed, and the findings described a lesion "*consistent with neuroendocrine carcinoma, possibly MCC, although a metastatic neuroendocrine tumor from another primary*

Figures 2 and 3
Initial appearance of the cervical mass





site could not be excluded." A contrast-free cervical computed tomography (CT) scan was performed due to a reported allergy to contrast media and revealed a "*solid mass measuring 92 × 75 × 46 mm, with no distinct cleavage plane separating it from the anterior surface of the sternocleidomastoid muscle or the ascending ramus of the left mandible*" (Figures 4 and 5).

Considering the inconclusive cytological findings, an incisional biopsy was performed. The biopsy showed "*two yellow-brown fragments, each with an ill-defined nodular contour, measuring 6 and 8 mm. The specimen consisted of mature collagenous adipose connective tissue, without evidence of parenchyma or lymphoid tissue. The nodular lesion demonstrated proliferation with apparent infiltration of the adjacent soft tissue*" (Figure 6).

The tumor exhibited a "*solid/alveolar architecture composed of small phenotype cells with round/oval nuclei. The blue cells had a high nucleus-to-cytoplasm ratio, finely dispersed chromatin (salt and pepper appearance), inconspicuous nucleoli, and scant cytoplasm. Mitotic figures and apoptotic bodies were observed*" (Figures 7 and 8).

"*Lymphatic invasion by the neoplasm*" was also identified (Figure 9). Tumor cells "*had an epithelial origin (CKAE1/3 and CAM5.2), exhibiting a characteristic perinuclear dot-like pattern. The tumor exhibited an immunophenotype characterized by CK7 negativity and CK20 positivity*" (Figures 10 and 11).

In addition, the epithelial neoplasm showed evidence of "*neuroendocrine differentiation, with positive immunoexpression of neuroendocrine markers*" (Figures 12–15).

The architectural and immunophenotypic features were consistent with those of MCC.

Full dermatological and mucosal examination revealed no skin lesions suggestive of a primary tumor.

Due to the patient's suspected allergy to contrast, she did not undergo a thorax, abdomen, and pelvis (TAP) CT scan. Instead, a fluorodeoxyglucose (FDG) positron emission

Figures 4 and 5
Axial and coronal views of a contrast-free cervical computed tomography scan showing a left cervical mass with possible extension into the sternocleidomastoid muscle and mandibular ramus

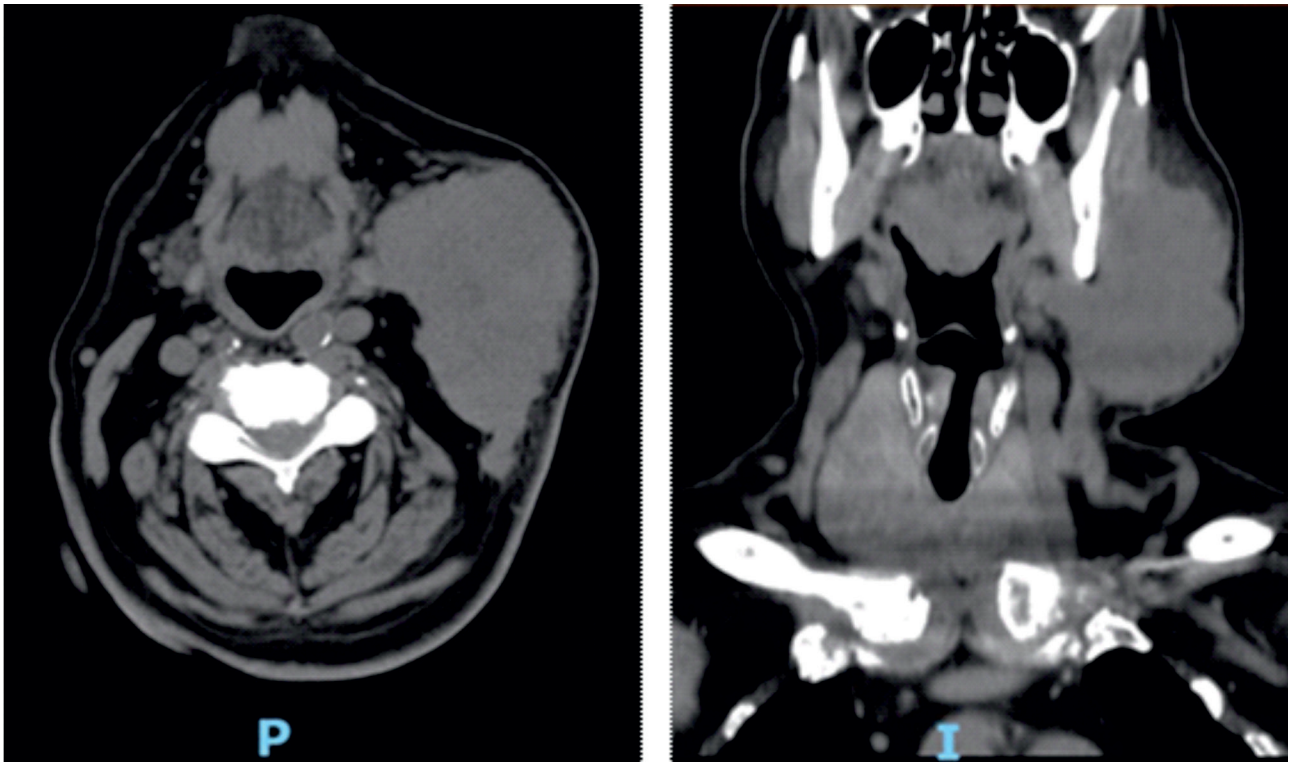


Figure 6
Hematoxylin and eosin staining, 10x5

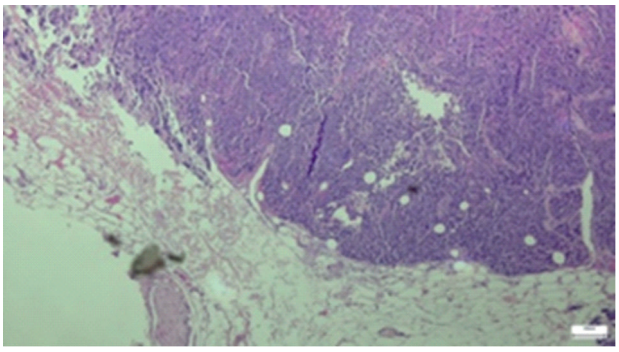


Figure 7
H&E 10x10

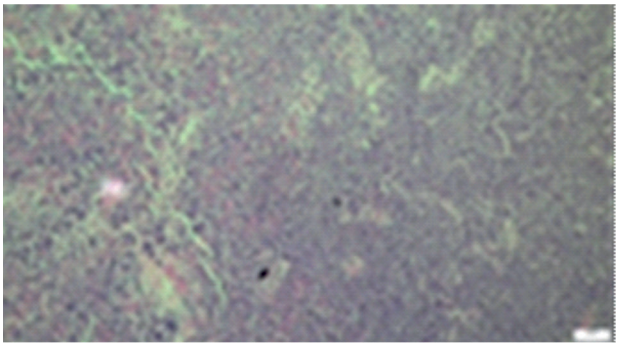


Figure 8
H&E 10x40

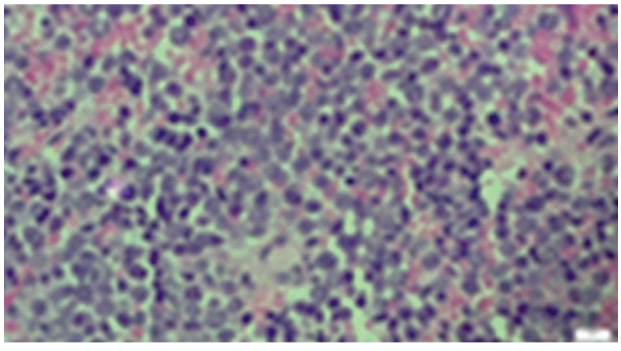


Figure 9
Lymphatic invasion

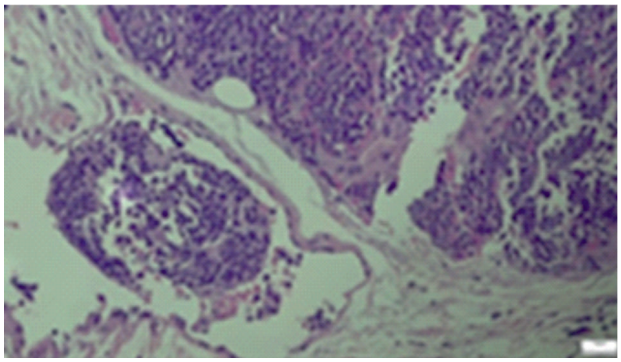


Figure 10
CK7 negative

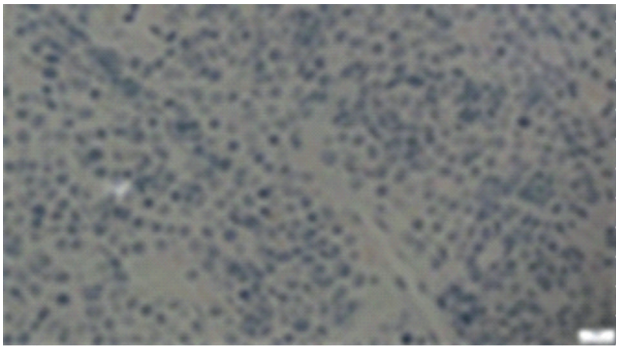
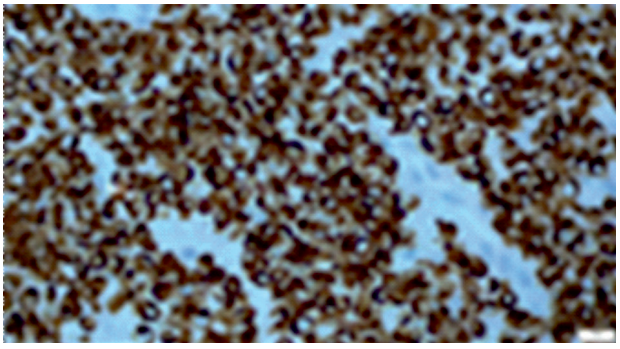


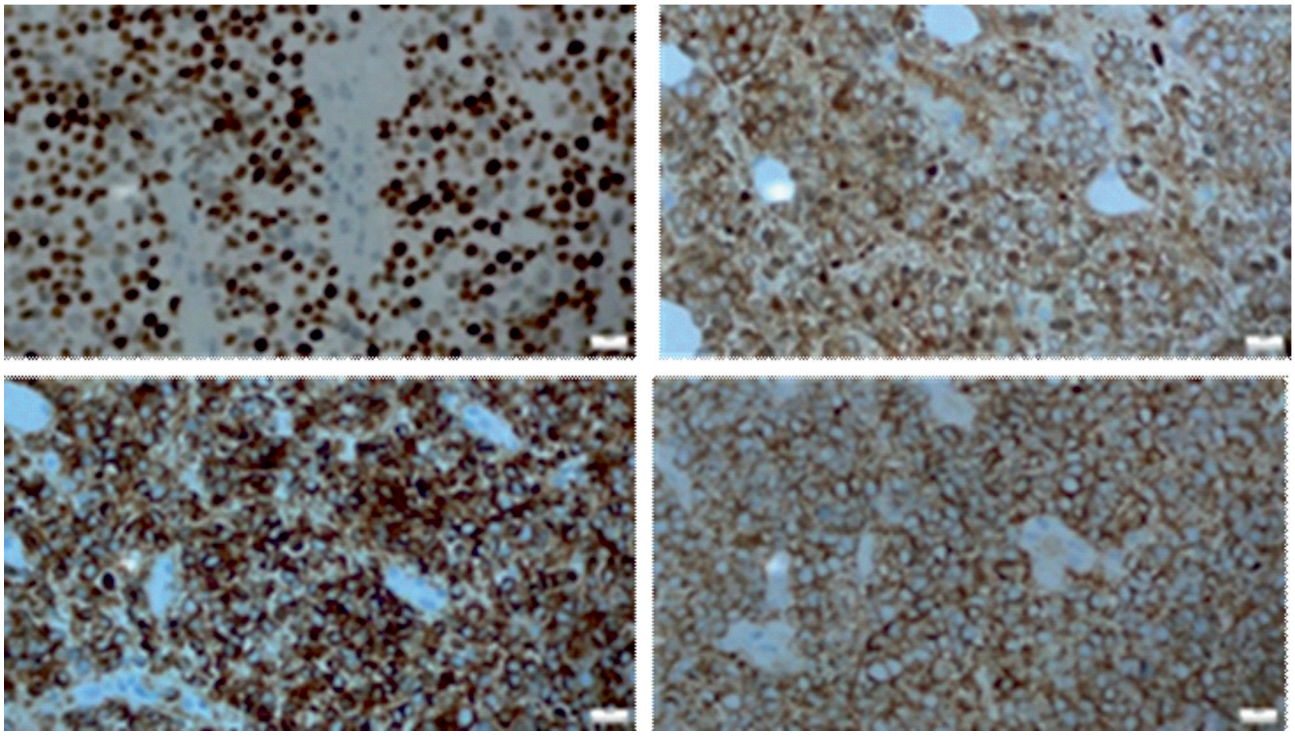
Figure 11
CK20 positive



tomography (PET) scan was performed for staging. The scan identified a "*large hypermetabolic mass in the left cervical region (maximum standardized uptake value [SUV] = 13.8) with central hypometabolic areas suggestive of necrosis, consistent with malignancy. Possible extension to the left mandibular ramus could not be excluded. Additional hypermetabolic foci were identified in the left lower paratracheal (maximum SUV = 6.4), subcarinal (maximum SUV = 7.9), and left bronchial-hilar (maximum SUV = 4.1) lymph nodes, which are equally suspicious of a malignant etiology in this context*" (Figures 16–18).

The case was reviewed in a multidisciplinary tumor board meeting. Given the unresectable nature of the mass, immunotherapy with avelumab was recommended. The cervical mass was considered the primary tumor. Thus, the disease was staged as $cT_4N_0M_{1a}$ (stage IV), according to the eighth edition of the *American Joint Committee on Cancer*,

Figures 12, 13, 14 and 15
Immunoexpression of neuroendocrine markers: Insulinoma-associated protein 1, neuron-specific enolase, chromogranin A, and synaptophysin, respectively



based on the absence of regional lymph node involvement (cT4) and presence of distant lymph node metastases (cM1a).

After the first session of immunotherapy with avelumab, the mass exhibited progressive growth, culminating in skin fistulization and associated hemorrhage (Figure 19).

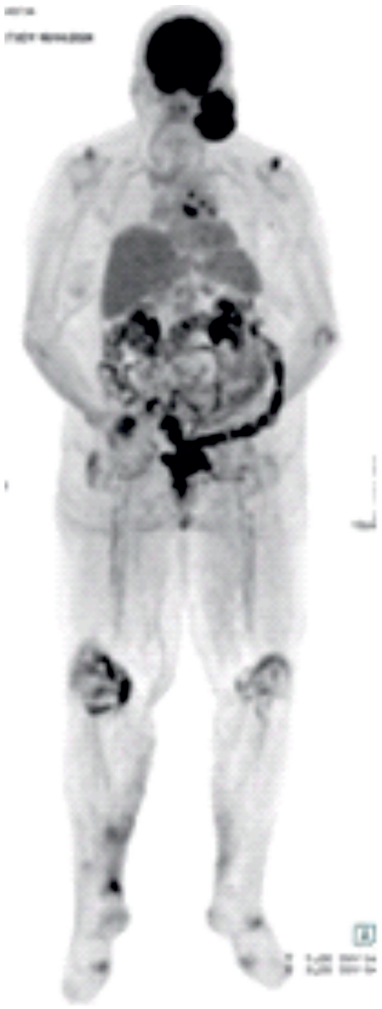
Once we confirmed that the patient did not have a contrast allergy, a repeat contrast-enhanced cervical CT scan was performed for better characterization of the lesion and evaluation for embolization. The scan revealed "*an extensive, infiltrative, and expansile lesion with left upper cervical facial involvement, extending into the masticatory and the parapharyngeal spaces and involving the left side of the mandible. The lesion measured 107 mm in maximum diameter and presented hypervascular areas, multiple flow voids, and a feeding pedicle on its medial surface*" (Figures 20 and 21).

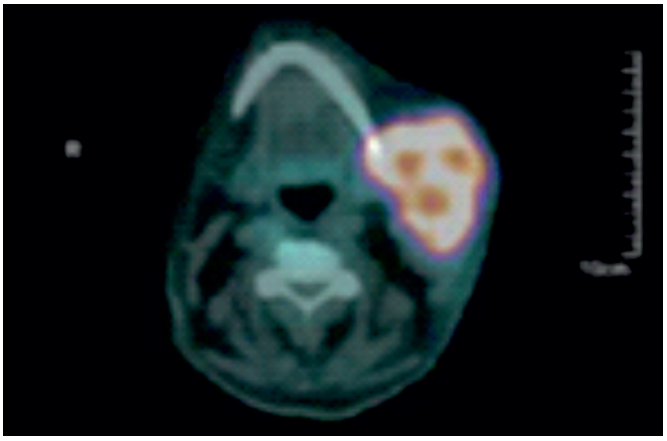
Consequently, the patient was admitted for angioembolization of the mass. The procedure involved "*selective catheterization of the left external carotid artery, the primary vascular supply to the tumor, and selective catheterization and embolization of the lingual artery and a ramus of the left internal maxillary artery using glue (Glubran diluted at 5% with Lipiodol). The procedure resulted in reduced arterial blood supply to the mass.*" Nevertheless, despite this intervention, the patient experienced persistent and recurrent episodes of active hemorrhage, requiring multiple blood transfusions.

During hospitalization, the patient's overall clinical condition deteriorated, accompanied by the onset of multiple complications. A severe acute respiratory syndrome coronavirus 2 infection required a 20-day period of isolation, which significantly delayed the treatment.

After returning to the ward, edema of the right upper limb (RUL) was observed at the site of vascular access. Doppler ultrasonography of the RUL demonstrated "*partial thrombosis of the right humeral vein, with proximal extension into the ipsilateral axillary and subclavian veins near the catheter. Additionally, a*

Figures 16, 17 and 18
Fluorodeoxyglucose-positron emission tomography showing hypermetabolic activity in the left cervical mass and left paratracheal, subcarinal, and bronchial-hilar lymph nodes





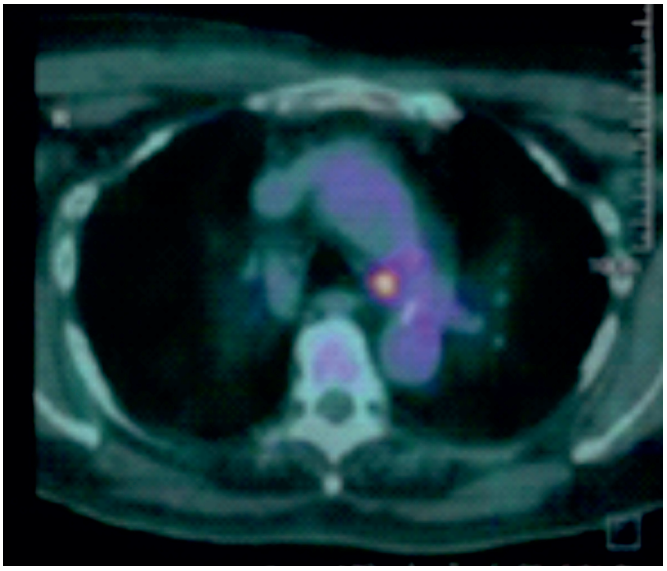
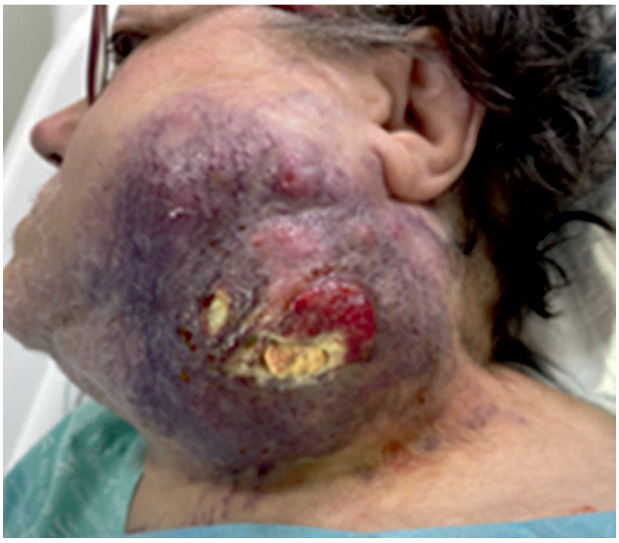


Figure 19
Cervical mass progression with growth and fistulization



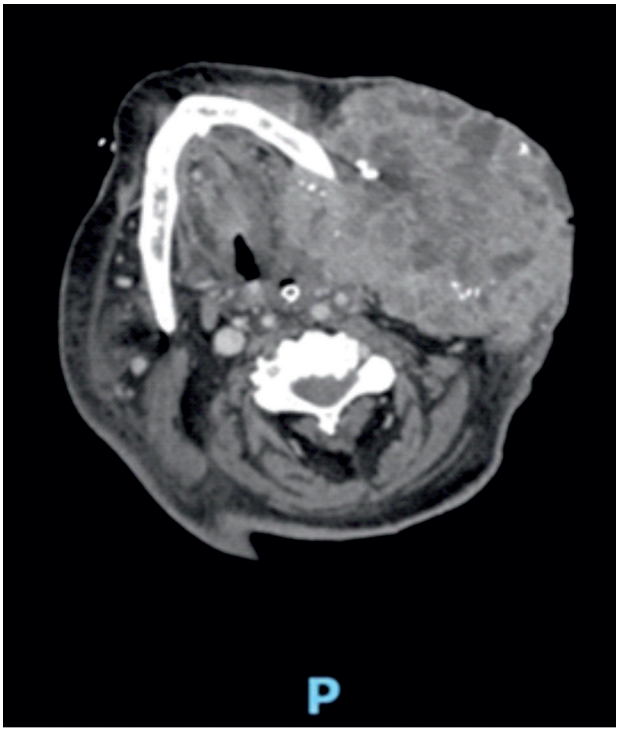
thrombus was identified in the right basilic vein, adjacent to the catheter." Due to the high risk of hemorrhage, anticoagulation therapy was withheld.

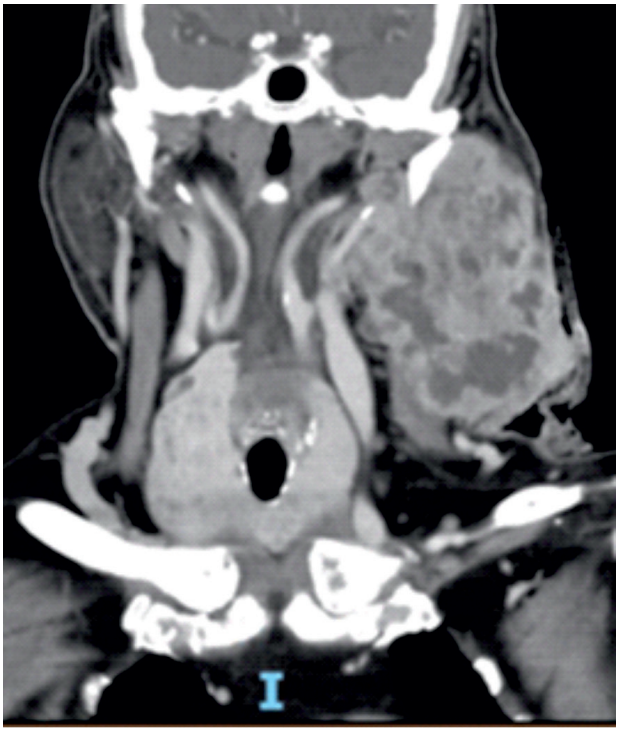
Subsequently, the patient experienced episodes of dyspnea, oxygen desaturation, productive cough, and intermittent fever. Chest radiography revealed a cotton-wool–like infiltrative pattern in the right hemithorax. Considering the thrombotic risk, CT pulmonary angiography was performed to exclude pulmonary thromboembolism. The examination found "*no evidence of pulmonary thromboembolism; pulmonary findings suggestive of inflammatory/ infectious processes, as well as progression of the underlying malignancy, indicated*

by the presence of pulmonary metastases. Prominent lymphadenopathy was noted in the right paratracheal region of the mediastinum" (Figures 22 and 23).

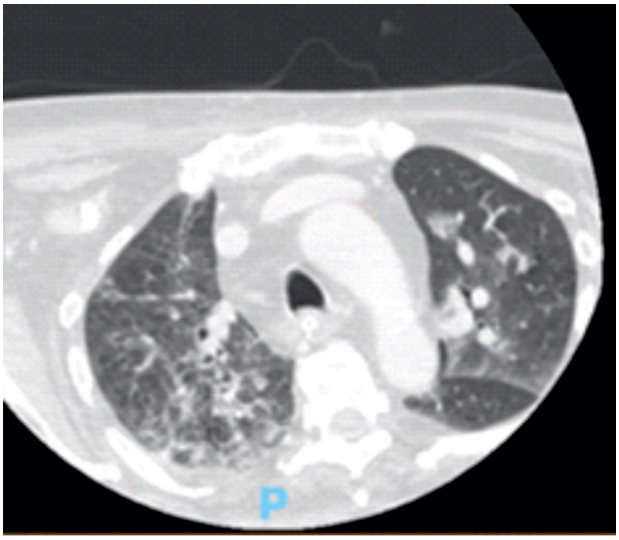
Given the multiple complications during hospitalization, clinical deterioration, and radiologically confirmed disease progression, the decision was made to discontinue immunotherapy and transition to palliative care. The patient died 6 months after the appearance of the cervical mass.

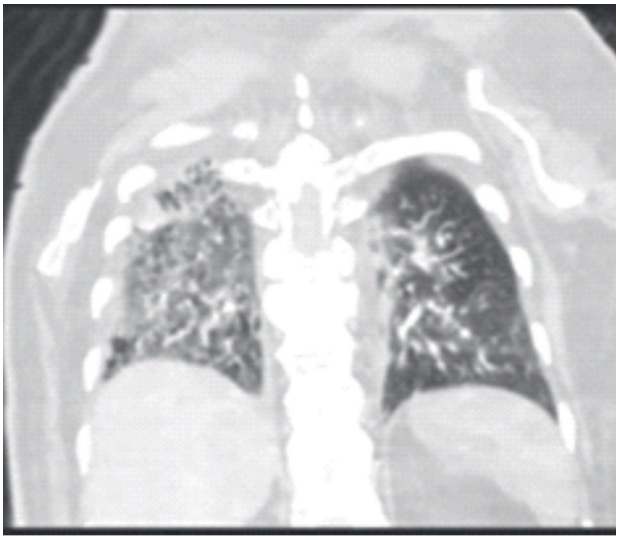
Figures 20 and 21
Contrast-enhanced cervical computed tomography scan (axial and coronal views) showing a hypervascular left cervical mass with extension to the muscle and left side of the mandible





Figures 22 and 23
Computed tomography pulmonary angiography (axial and coronal views) showing evidence of disease progression with pulmonary metastasis





Discussion

MCC may present as a benign lesion; however, biopsy is crucial in patients with risk factors or when the lesion exhibits rapid growth. A definitive diagnosis depends on histopathological and immunohistochemical examination. Once MCC is diagnosed, staging typically involves FDG-PET combined with axial imaging (CT or magnetic resonance imaging) or contrast-enhanced TAP-CT, along with cervical CT, if the tumor is in the head and neck region.[5,6]

Staging can be challenging in patients without an identifiable skin lesion suggestive of the tumor's primary origin. Approximately one-third of cases with lymph node metastasis are estimated to have a cervical mass without a recognizable skin lesion.[7,8] In such cases, the primary lesion regresses due to the intense immune response observed in these patients. The likelihood of the tumor presenting in other locations is low, as MCC cells commonly exhibit DNA mutations induced by UV radiation, suggesting a cutaneous origin. Furthermore, patients with an occult primary tumor tend to have a better prognosis, even in the presence of distant metastases, due to their heightened immunological response.[8]

In the present case, no suspicious skin lesion was identified, raising questions about the staging. Thus, the classification of regional vs. distant disease was challenging.

The absence of a TAP-CT, initially avoided due to suspected contrast allergy, also contributed to staging difficulties. However, FDG-PET enabled the identification of the cervical mass and pathologic lymph nodes in multiple chains, including the paratracheal, subcarinal, and bronchial-hilar regions, confirming distant metastases.

Thus, the cervical mass in this case may represent the primary tumor, with no regional nodal involvement but distant lymph node metastases in paratracheal, subcarinal, and bronchial-hilar regions (cM_{1a}), leading to classification as stage IV $cT_4N_0M_{1a}$. Conversely, it could also represent an occult primary tumor, with paratracheal, subcarinal, and bronchial-hilar lymph node involvement ($N_{2/3}$) and distant metastasis to the subcutaneous tissue (M_{1a}), corresponding to stage IV $cT_xN_{2/3}M_{1a}$.

The management of patients with occult primary tumors is similar to that of patients with identified primary tumors and lymph node or distant metastases (stage III/IV). First-line treatment consists of immunotherapy with avelumab or pembrolizumab. If the tumor proves refractory, chemotherapy is considered as second-line therapy.[9,10] In this case, the patient was started on avelumab monotherapy.

The prognosis of advanced MCC is poor and closely related to tumor staging. For stage IV disease, the estimated five-year overall survival rate is approximately 13.5%. Furthermore, this patient presented with some factors indicative of a poor prognosis, such as older age and cervical location.[11] Complications during hospitalization, particularly coronavirus disease, which required isolation and delayed treatment, also contributed to the unfavorable outcome. The patient died 6 months after the initial presentation.

Conclusion

MCC is a rare and aggressive malignancy with a poor prognosis. It typically presents as a skin lesion with benign appearance, but in cases with rapid growth, biopsy is crucial for histological diagnosis. In approximately one-third of cases, no primary skin lesion is identified, and the disease presents with lymph node or distant metastases.

This case illustrates the aggressive progression of MCC, resulting in pulmonary metastases and death within six months, and highlights the importance of considering it among the differential diagnoses of cervical masses, a common reason for otorhinolaryngology referral.

Otorhinolaryngologists should be aware of this entity, as most cases are in the head and neck region and early diagnosis can significantly impact prognosis.

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Data Confidentiality

The authors declare having followed the protocols used at their working center regarding patient data publication.

Protection of humans and animals

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and the 2013 Helsinki Declaration of The World Medical Association.

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Availability of scientific data

There are no datasets available, or publicity related to this work.

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