



## Merkel cell carcinoma of the oral cavity: A case report

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### ABSTRACT

Merkel cell carcinoma (MCC) is a rare, but highly aggressive neuroendocrine neoplasm. It usually affects the head and neck region of the skin exposed to ultraviolet radiation from the sun. Although rare, there are primary oral cavity cases reported in the literature. Herein, we present an 80-year-old male case with a mucosal MCC located in the oral cavity as evidenced by both morphological and immunohistochemical findings.

**Keywords:** Merkel cell carcinoma, neuroendocrine neoplasm, oral cavity.

Merkel cell carcinoma (MCC) is a rare, but highly aggressive neuroendocrine neoplasm. It usually affects the head and neck region of the skin exposed to ultraviolet radiation from the sun. Although rare, there are primary oral cavity cases reported in the literature. The first three cases of MCC (formerly known as a trabecular carcinoma) were described in 1972.<sup>[1,2]</sup> The first oral MCC case was reported in 1988.<sup>[3]</sup> Primary MCCs of the oral cavity are extremely rare, with only 26 cases reported in the literature to date.<sup>[4]</sup>

In this article, we present an oral MCC case and discuss its histological and immunohistochemical features in the light of literature data.

### CASE REPORTS

An 80-year-old male patient presented to our clinic with oral hemorrhage and pain for the last three months. Physical examination of the patient revealed a 3×3-cm hemorrhagic ulcerous

mass in the buccal and lingual gingiva of the left alveolar arch in the anterior of the mandible. Positron emission tomography-computed tomography (PET-CT) revealed pathological fluorodeoxyglucose (FDG) uptake (maximum standardized uptake value [SUV<sub>max</sub>]: 15.6) by the mass and a suspected bone destruction in the mandible. Pathological FDG uptake was also observed in the lymph nodes of the neck, lung, adrenal gland, and brain. An incisional biopsy was obtained. On microscopic examination, infiltration of the tumor by atypical epithelial cells with large hyperchromatic nuclei along with a salt-and-pepper appearance that formed solid islands and cords under squamous epithelium was observed. The tumor had a high mitotic activity and pleomorphism. Immunohistochemical (IHC) examination of the tumor demonstrated immunoreactivity for pancytokeratin (AE1/AE3), insulinoma-associated

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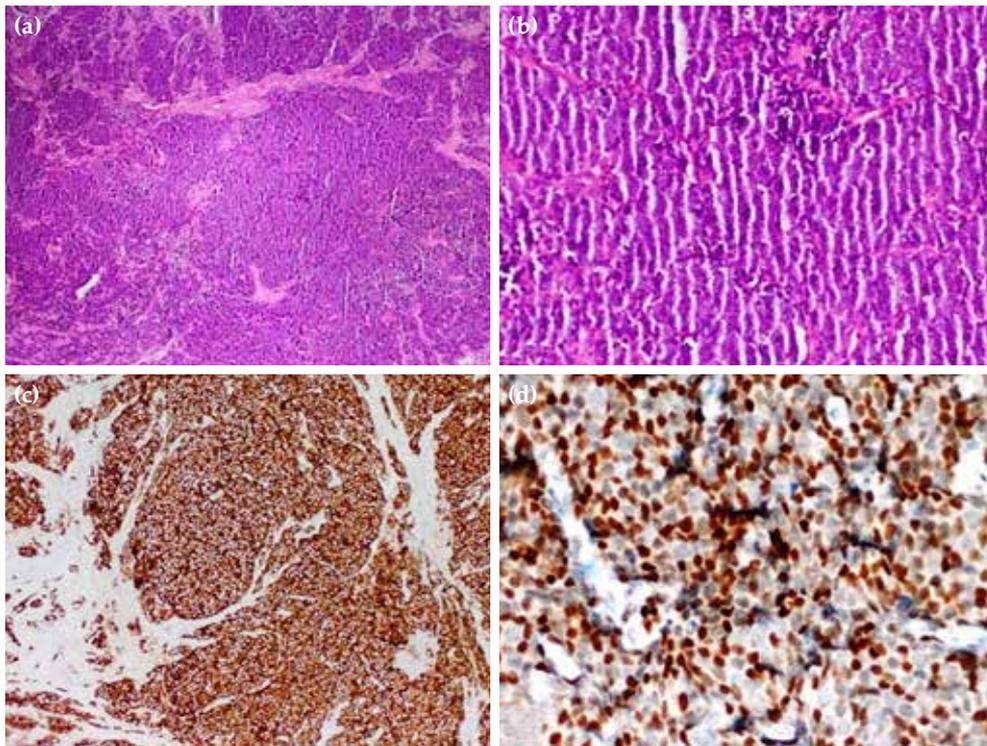
**Figure 1.** A macroscopic view showing hemorrhagic ulcerous lesions, extending from left alveolar arc in oral cavity (yellow arrows).

protein 1 (INSM1), and CD56. The sections were negative for p40, thyroid-transcription factor-1 (TTF-1), CK20, S-100 protein, chromogranin A,

synaptophysin, vimentin, CD34, CD99, NSE, and CD45. The Ki-67 proliferation index of the tumor was high (80 to 90%). The patient was diagnosed with a MCC. Due to the presence of distant metastases, he was considered inoperable and chemotherapy treatment planned. A written informed consent was obtained from the patient.

## DISCUSSION

Merkel cell carcinoma is a rare, but aggressive type of skin cancer originating from uncontrolled growth of Merkel cells in the skin. The etiology of MCC includes exposure to sun light, systemic immunosuppression, and a recently described human virus, Merkel cell polyomavirus (MCV).<sup>[5]</sup> The presence of MCV in the majority of MCC indicates that it may have a role in the oncogenesis. Demonstration of viral antigens helps in the differential diagnosis of MCC from other tumors. Sun exposure as a risk factor for cutaneous MCC do not apply to oral MCCs. However, immunosuppression



**Figure 2.** (a) Tumor composed of small round to ovoid cells showing trabecular and solid infiltrating patterns (H-E  $\times 200$ ). (b) Tumor composed of hyperchromatic basophilic round cells invading connective tissue stroma in the form of clusters, islands, and strands (H-E  $\times 400$ ). (c) Tumor showing diffuse positivity for CD56 ( $\times 200$ ). (d) Tumor showing diffuse positive for INSM1 ( $\times 400$ ).

and the use of tobacco and alcohol increase the risk for oral MCC, in which MCV does play a major role.<sup>[6-8]</sup> The tumor may grow rapidly, and it can manifest itself as a plaque or a nodule and can mimic other benign, malignant, or reactive lesions both clinically and histologically. Clinical differential diagnosis includes pyogenic granuloma, melanoma, squamous cell carcinoma, lymphoma, Kaposi sarcoma, small cell carcinoma, primitive neuroectodermal tumor, neuroblastoma, Ewing sarcoma, lymphoma, rhabdomyosarcoma, and primitive neuroectodermal tumor. Lesions expand rapidly, ranging from 0.5 to 5 cm, and may ulcerate in advanced stages. Due to its benign appearance MCC is diagnosed at a later stage. At time of diagnosis most lesions have metastasized to the regional lymph nodes.<sup>[4]</sup>

Histopathologically, the tumor shows small, round to ovoid primitive looking cells with a strong acidophilic staining with a salt-and-pepper-like nuclei and inconspicuous nucleoli. The IHC staining is an important ancillary test for diagnosing MCC. Due to the neuroendocrine nature of the tumor, it shows positivity for neuroendocrine markers, including but not limited to chromogranin A, synaptophysin, NSE, and CD56. A dot-like positivity for cytokeratin-20 is also very helpful for the diagnosis.<sup>[9,10]</sup> Based on morphology alone, MCC may be confused with small cell lung cancer; however, it can be distinguished by the presence of CK20 and absence of TTF-1 in IHC staining.<sup>[11]</sup>

A wide local excision is recommended in the management of the early stage disease. The presence of lymph node involvement determines survival and development of distant metastases. Postoperative radiotherapy is recommended in cases of incomplete resection or lymph node involvement. Although postoperative radiation therapy prevents recurrence, it does not increase the overall survival time.<sup>[12]</sup> Chemotherapy is used in case of a distant metastatic disease. Drug combinations, including cyclophosphamide/doxorubicin/vincristine and etoposide/cisplatin, have been shown to be effective with varying success rates. Ongoing researches with interferon, tumor necrosis factor, and imatinib may yield promising results for the future. The estimated

three-year survival of MCC has been reported as low as 50%.<sup>[4]</sup>

In conclusion, mucosal MCC is an uncommon and aggressive neuroendocrine neoplasm with a high risk for recurrence and distant metastasis. It should be considered in the differential diagnosis of head and neck mucosal lesions.

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