Merkel cell carcinoma of the vulva

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Merkel cell carcinoma (MCC) is a rare primary neuroendocrine tumor of the skin. This tumor usually arises in elderly patients, and the head and neck area are the most common sites followed by the extremities and the trunk.[1] This uncommon tumor is a highly aggressive malignancy, which is characterized by high incidence of local recurrence, lymph node metastasis, and distant metastasis.[1] Merkel cell carcinoma of the vulva is an unusual occurrence. On literature review, we found 11 cases reported in the English literature so far.[2,3] We report a patient with huge vulvar Merkel cell tumor treated at our institution. The largest reported vulvar MCC was 8 centimeters in diameter.[4]

A 50-year-old woman, para 6, 2 years postmenopausal presented with a 3-month history of a palpable mass in the left labia majora. She was being treated for hypertension and diabetes mellitus for the last 3 years. The vulvar lump of approximately 3-4 centimeters on the left labia major had been excised in a regional hospital 2 months before admission with rapid re-growth of the mass in the same location. The specimen of the first outpatient surgery was not sent for the pathologic evaluation. Upon examination of the vulva, there was a purple (violaceous) exophytic tumor of 10x12 centimeters in left labia major with wide implantation and some ulcerated and necrotic areas on its surface. The ulcerations bled spontaneously or with minimal touch. She refused photography of the lesion. Physical examination revealed no positive finding. Examination of the inguinal region was normal, and no other lymph nodes were palpable. The preoperative chest x-ray, pelvic and abdominal CT-scan, and liver function tests were normal. Due to multiple bleeding episodes of the tumoral surface, her hemoglobin level decreased to 7 mg/dl and she received packed cell transfusions before operation. The operation was postponed for 3 weeks due to uncontrolled hypertension and difficulty in control of diabetes mellitus. In this period, the tumor enlarged rapidly to approximately 15 centimeters in diameter. Therefore, the tumor was irradiated with 2000 cGy in 10 daily fractions. She underwent radical vulvectomy. To decrease the operative time and risks, inguinal lymph node dissection was not carried out due to intraoperative hypertension and her diabetes. Histopathological examination revealed sections of the tumor composed of tumoral cells of a high-grade malignancy in deep subcutaneous tissue far from the epidermis. There was small to medium sized cells with irregular nuclei and coarse chromatin clamping and scant clear cytoplasm. All resection margins were free of tumor. The immunohistochemical staining of the tumor was negative for pancytokeratin, HMB 45, EMA, LCA, desmin, and S-100. However, stains for chromogranin, vimentin, and neurofilament were immunoreactive (**Figure 1**). The light microscopic features and immunostaining result were consistent with neuroendocrine carcinoma. Four weeks after operation due to partial wound dehiscence, split thickness skin graft was carried out for cutaneous defect. Radiotherapy was postponed for 7 weeks after initial operation because of this wound dehiscence. She received 4500 cGy pelvic and inguinal region irradiation in 22 fractions, but she refused chemotherapy. Nine months after initial operation she developed left hip pain radiating to the thigh. On pelvic examination, there was a palpable hard mass of around 3-4 centimeters in the pelvis, adjacent to the posterior aspect of the pubic bone. Tumoral recurrence was confirmed by CT-guided fine needle biopsy. She went to her home city, and we were informed that she received a few courses of combination chemotherapy. On follow up at 11 months, she had expired with a clinical diagnosis of pulmonary embolism secondary to deep vein thrombosis of the left lower extremity. The last chest x-ray one month before death was normal without any evidence of metastasis. Her family refused an autopsy.

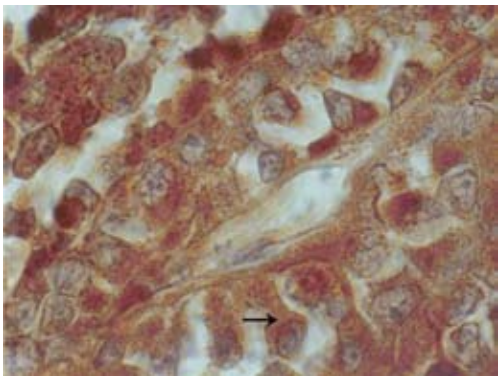

Figure 1 - Immunohistochemical staining for cytoplasmic neurofilaments shows positive reaction (arrow).

Merkel cell carcinoma is an aggressive neuroendocrine tumor of the skin that metastasizes quickly and has a 5-year mortality rate as high as 50%. The origin of this primary neuroendocrine tumor of the skin is particularly intriguing. It is thought to arise from primitive pluripotent epidermal cells called epidermal Merkel cells.[1,4] It usually arises in the head and neck and extremities of elderly people, and around 34% of the affected patients die because of the tumor. The vulvar location is unusual; moreover, 3 cases of MCC in the bartholin's gland have been reported.[3] A review of the limited case reports of vulvar MCC suggests aggressive

behavior and fatal prognosis.[2,3] Regional lymph nodes were involved early in most of the patients, and all patients followed so far developed lymph node or distant metastasis and died from their disease.[2,3] The size of the tumor in our patient increased rapidly to approximately 15 centimeters. Histologically MCC is dermal in location.[1] The MCC and small cell carcinoma are both aggressive neuroendocrine carcinomas, histologically composed of morphologically identical small cells. By light microscopy alone, it is difficult to differentiate MCC from metastatic small cell carcinoma, melanoma, and lymphoma.[3] The diagnosis is based on light microscopic appearance of small cell carcinoma and confirmed by electron microscopy detection of neurosecretory granules or immunohistochemical reactivity for neuroendocrine markers and cytokeratin.[3] Absence of other primary malignancies is also in favor of MCC and exclusion of metastatic small cell carcinoma. Recently, a new polyomavirus is discovered in MCC tissue samples. Merkel Cell Polyomavirus-DNA (MCPyV-DNA) has been reported in 43-85% of MCC cases, but it was absent in all tissue samples of morphologically similar small cell lung carcinoma. These studies suggest a possible oncogenic role of polyomavirus in the development of MCC, and MCPyV-DNA may help in the differentiation of this tumor from metastatic small cell carcinoma.[5] The MCC is an uncommon tumor and it has been difficult to establish treatment recommendations for the patients regarding the best surgical approach and usefulness of adjuvant modalities.[4] Surgery, in the form of wide local excision, remains the mainstay of MCC management.[4] Mohs surgery has recently been presented as an alternative to wide excision for tissue preservation and identification of tumors requiring very wide excision.[1] The most frequent metastatic site on MCC is the regional lymph nodes (52%). It is still unknown whether prophylactic regional lymph node dissection increases survival.[1] Studies to date have largely supported the use of the sentinel lymph node biopsy technique for predicting the likelihood of further nodal involvement, and the short-term risk of loco-regional and distant recurrence, but it is not confirmed by more recent studies.[4] There is no data on the therapeutic value of this procedure.[1] The MCC is known to be highly radiosensitive and many authors suggest routine postoperative use of radiotherapy.[1,4] Radiotherapy has been reported to be effective in treating inoperable tumors, and in prevention of loco-regional recurrence; however, it has not been demonstrated to improve survival.[1] Alternatively, prophylactic radiotherapy to the draining lymph node field can eliminate the need for additional surgery, although not without its side effects.[4] The MCC is sensitive to many chemotherapeutic agents including doxorubicin, cisplatin, cyclophosphamide, and vincristine. These agents are often used in combination, but the most effective regimen is not known. Chemotherapy has been used in metastatic MCC with a response rate of approximately 60-70%.[4] However, the result is short-term and no increase in survival has been achieved with adjuvant chemotherapy.[1] Unfortunately, the reported overall survival for such patients is only 17%, 3 years post-diagnosis.[1]

In conclusion, there is no agreement on the best therapeutic approach to MCC of the vulva, but it seems logical to carry out initial radical surgery. Adjuvant chemotherapy and radiotherapy are a reasonable consideration because of the aggressive behavior of MCC in other locations, especially the virulence of the tumor observed in all patients of vulvar MCC followed so far.

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