Neuroendocrine tumor of vulva: A case report and review of literature

ABSTRACT

Neuroendocrine tumor (Merkel cell carcinoma-MCC) of the vulva is a very rare entity with less than 15 cases reported in the English literature. It is known for its aggressive behaviour and propensity for early dissemination. The actual cell of origin and etiology of this disease is controversial. In absence of any definite guidelines for management (due to its rarity), extrapolation of data from extra-vulvar MCC seems logical. We present a case of vulvar neuroendocrine tumor who presented at a locally advanced stage.

KEY WORDS: Merkel cell carcinoma, neuroendocrine tumor of vulva, vulvar carcinoma

INTRODUCTION

Neuroendocrine tumor (Merkel Cell Carcinoma-MCC) of the skin is a rare pathological entity and is extremely rare in vulva, with less than 15 cases reported to date in the English literature.[1] It behaves extremely aggressively, producing early local recurrences and lymphatic and distant metastases. Treatment should be aggressive because of this spread pattern, even though the outcome is not satisfactory in most cases. We present an additional case of MCC of the vulva.

CASE REPORT

A 63-year-old woman evaluated for post-menopausal bleeding was found to have an ulcerated vulval mass. Examination revealed a 5×7 cm ulcerated, mobile mass involving the posterior two-thirds of the right labium majus and distal vagina. Multiple firm inguinal nodes were palpable bilaterally. Biopsy demonstrated poorly differentiated carcinoma. Metastatic work-up, which included USG of abdomen and chest X-ray, was negative. Wide local excision of the vulvar lesion and bilateral groin dissection was performed. The iliac nodes were spared as deep inguinal nodes were reported to be negative on frozen section. Histopathological examination revealed infiltrating neoplastic cells arranged in sheets and islands with overlying stratified squamous epithelium showing focal ulcerations, extensive areas of necrosis and hemorrhage. Cells were round to polygonal with vesicular to stippled chromatin, prominent nucleoli and moderate amount of eosinophilic cytoplasm [Figure 1a]. Brisk mitosis and moderate degree of pleomorphism was seen. Multiple nodes in either groin revealed metastasis with perinodal spread. No immunoreactivity for HMB45, S100 and desmin was seen, whereas cytokeratin showed paranuclear dot positivity [Figure 1b] and synaptophysin showed cytoplasmic positivity [Figure 1c]. Ki-67 staining was 50-60% [Figure 1d]. All margins were free of tumor. The microscopic morphology and the immunostaining pattern were consistent with neuroendocrine carcinoma. Post-operatively, the patient had wound breakdown. Unfortunately, the patient developed local and distant recurrence within 8 weeks of surgery and died of progressive disease before any adjuvant therapy could be delivered.

DISCUSSION

MCC is a rare form of neuroendocrine carcinoma first described in the skin by Toker[2] as trabecular carcinoma. Initially a sudoriferous (sweat gland) origin was considered but later a neuroendocrine phenotype was favored on the basis of ultrastructural features in electron microscopy and immunohistochemical-staining pattern.[3] The neoplastic cells were initially thought to arise from the Merkel cells; however, origin from a stem cell, able to differentiate along different cell lines, is favored.[4] Moreover the tumor has been recognized in many extracutaneous sites like esophagus and salivary glands.[5] Incidence peaks in 7th to 9th decades of life; however, younger age group is not exempted. Most (>85%) of these tumors arise in head and neck region and extremities with other regions of the body contributing about 15%.[1] Over the last 6 decades a wide spectrum of neuroendocrine tumors and tumors with neuroendocrine elements has been identified...
Vulval primary MCC is extremely rare, with less than 15 cases reported worldwide, and possibly this is the first case reported in India.

Old age, immunosuppression and European ancestry are high-risk factors, whereas UV radiation also contributes to the etiology of this malignancy. DNA of MCC polyoma virus (MCPyV) has been detected in tissue samples of 43-85% of MCC cases, suggesting its possible oncogenic role. A large number of genetic abnormalities have been detected in MCC cell lines and less genomic aberration is associated with improved survival. Although originating in dermis, it can involve deeper structures as well as the epidermis. The intermediate-cell type accounts for the majority of MCC tumors, although large and small-cell type variants are also known. The tumor cells share ultrastructural and antigenic features of both epithelial and neuroendocrine cells. These unique properties are exploited to distinguish MCC from morphologically similar malignancies, like lymphomas, Ewing’s sarcoma and small-cell lung cancer (SCLC). Positive staining for CK20 and absence of reactivity to thyroid transcription factor, help in distinguishing MCC from SCLC. Reactivity to CK20, chromogranin, synaptophysin, neuron-specific enolase and neural cell-adhesion molecule help in confirming the diagnosis. The case being presented here stained positive for cytokeratin, synaptophysin and vimentin.

The vulvar MCC is reported to be more aggressive than at other sites, with 100% metastatic rate at presentation. Our patient presented with a fungating primary lesion and regional nodal metastases and no evidence of distant disease. Currently there is no consensus on the optimal therapeutic approach. Extrapolating from the aggressive behavior observed in MCC at other sites, adjuvant radiation and/or chemotherapy is a reasonable consideration. Surgery forms the mainstay and involves excision with wide margins. Inguinal dissection is needed for enlarged nodes; however, sentinel node biopsy may be reserved for clinically normal groin. The disease often recurs but is highly sensitive to radiation. Adjuvant radiotherapy is generally recommended. Chemotherapy often is used for palliation and provides overall response rates of approximately 70%; however, the disease often recurs within a few months. The 3-year survival in such patients is 17%. Our patient underwent wide local excision of the primary lesion with bilateral groin dissection. Inspite of extensive surgery, the patient developed recurrence and succumbed to her disease, thus proving its aggressive behavior.

To conclude there is no conclusive evidence as to the best treatment approach for the patients of vulvar MCC. But extrapolating the data from extra-vulvar MCC sites seems logical keeping in view its rare occurrence in vulva. Further the cases presenting with locally advanced disease (as in our case) are unlikely to achieve cure. Hence, treating these patients with neo-adjuvant chemotherapy in an attempt to downstage the disease and eliminate distant micrometastasis may be a rational approach. We could not initiate systemic therapy in our patient because of delay caused by wound breakdown.

REFERENCES


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