Malignant Melanoma

Synonyms: Vulvar malignant melanoma is a distinct entity of mucosal melanoma.

Clinical Presentation: Vulvar malignant melanoma is mostly seen in Caucasian women. The mean age at diagnosis is 61.6 years (range 10-86). Because of its location on non-sun exposed skin with minimal exposure to ultraviolet light, vulvar melanoma is considered a distinct entity of mucosal melanoma. Melanoma is responsible for 5% of all vulvar malignancies.

The most common presenting symptoms are pain, bleeding, pruritus, and a darkly pigmented vulvar lesion or lump. At times patients may be asymptomatic. Delay in presentation is common if symptoms are few or the lesion is amelanotic (flesh colored). One quarter of vulvar melanomas are multifocal at presentation. The lesions are slightly more common on the labia majora than the labia minora.

Melanomas have 2 growth phases, radial and vertical. During the radial phase, growth is out into the epidermis. Progression to the vertical phase is characterized by malignant cells invading the dermis, and developing the ability to metastasize.

There are 3 major types of vulvar melanoma:

1. *Superficial spreading melanoma*

   These represent 47% of melanomas. They are usually flat, but can become irregular and raised, with variegated colors, peripheral notches and indentations.

2. *Nodular melanoma*
   These tumors are usually blue-black, but can lack pigmentation.

3. *Acral lentiginous melanoma*

These tumors occur more commonly in dark skinned people as flat, tan, or brown stains with irregular borders. Acral lentiginous melanomas can ulcerate in later stages.

Associations: Family history of melanoma is positive in 5% to 10% of patients with vulvar melanomas. Risk factors for malignant melanomas include: blue eyes, fair and/or red hair, pale complexion, easily freckling or sunburned skin, benign and/or dysplastic melanocytic nevi, and immunosuppressive states (transplant patients and those with hematologic malignancies). Atypical mole syndrome increases the risk of melanoma. A lower socioeconomic status is linked to more advanced disease at the time of detection.

Diagnostic Criteria: Physical examination of the vulvar area and groins should be performed. Assessment using the ABCDE rule (asymmetry, border irregularity, color, diameter, and evolving) is the same as for other cutaneous melanomas. Blue-black color, raised lesions, moles greater than 6 mm in diameter, and ragged, notched or fuzzy borders should raise suspicion. The relationship of the abnormal skin to the urethra, anus, and clitoris should be noted.

Full thickness biopsy reaching into the subcutaneous tissue should be performed. Ideally an excisional biopsy of the entire lesion should be performed, however, if not possible, the most suspicious area of the lesion should be biopsied. The specimen should be evaluated by pathologists experienced with vulvar/gynecologic pathology or who specialize in melanoma. Histochemical staining with HMB-45 and S-100 protein and Melan-A and MART-1 antibodies can confirm the diagnosis and help differentiate the lesion from other vulvar conditions.

Sentinel node biopsy is a well-established technique used in the melanoma workup. Clinical workup includes computed tomography (CT) and positron emission tomography (PET) scans of the head, abdomen, and pelvis for clinically suspected stage IIIB, IIIC or stage IV disease. CT, magnetic resonance imaging (MRI) or ultrasound of the groin and pelvis may be helpful for evaluation of local

spread. Blood for CBC, complete chemistry panel, and lactate dehydrogenase should be obtained.

No consensus exists on the most accurate staging system for vulvar malignant melanoma, although the microstaging systems of Breslow, Clark and Chung, and the macrostaging systems of AJCC and FIGO are all used.

Syndromes: Melanomas located centrally on the vulva have been correlated with reduced short-term and long-term survival, with shorter recurrence-free interval, and with a higher risk of nodal involvement in the groin.

Multifocal spread and involvement of the urethra, vagina, perineum, or anus leads to a worse prognosis. Increasing Breslow depth, ulceration, high mitotic rate, and histologic type correlate with worse prognosis. Greater tumor depth of invasion is also correlated with higher rates of nodal involvement and recurrence.

Treatment: Wide local excision with sentinel node biopsy, elective node dissection, or both is the definitive treatment for early-stage melanoma. Primary closure, skin grafting, or flaps may be needed for closure. Resection margins of 0.5 cm for in situ melanomas, 1 cm for lesions up to 2 mm thick, and 2 cm for melanomas more than 2 mm thick have been proposed. There is no survival benefit to margins greater than 2 cm, nor is there survival benefit with radical vulvectomy. Sentinel node biopsy is not indicated for melanomas less than 1 mm thick, but may be helpful for tumors between 1 and 4 mm thick. If the sentinel node is negative, no further surgical treatment is needed. If the sentinel node is positive, regional lymphadenectomy improves disease-free survival but does not prolong overall survival.

Adjuvant radiotherapy for vulvar melanoma is not routinely used, but can improve local control without benefitting overall survival. If resection margins are positive or narrow, adjuvant radiotherapy may be justified. Trials are being conducted with a combination of radiotherapy and immunotherapy with promising results.

Adjuvant chemotherapy does not show survival benefit in vulvar malignant melanoma at this time.

Nonspecific immunotherapy in the general melanoma population with cytokines and checkpoint inhibitors is being studied. Targeted therapy focuses on melanoma cells with specific gene changes on the BRAF, KIT or NRAS genes. However, in 2019 there were no studies reporting on targeted therapy for vulvar malignant melanoma.

Follow Up: Patients with vulvar malignant melanoma have a poor prognosis, with an average time to recurrence less than one year. Recurrence rates are between 42% and 70%, and the 5-year survival rates vary between 10% and 63%.

There are no guidelines regarding follow up for vulvar malignant melanoma, and schedules are based on clinical experience and custom practice rather than evidence. Recommended schedule: 6-8 weeks post op, every 3-4 months in the first two years, and twice per year in years 3 and 4.

In recurrent or metastatic vulvar malignant melanoma treatment needs to be individualized.

References:

Boer F, et al. Vulvar malignant melanoma: Pathogenesis, clinical behavior and management: Review of the literature. *Cancer Treatment Reviews* 2019; 73:91-103.

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