Clitoral metastasis of vulvar melanoma treated with talimogene laherparepvec

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INTRODUCTION

Vulvar melanoma (VM) comprises approximately 0.8% of melanomas in women.[1] Unfortunately, VMs have a markedly worse prognosis than other cutaneous melanomas, with a 5-year survival rate of 47% versus 92%, respectively.[2] To our knowledge, no guidelines currently exist for the treatment of VM specifically. Generally, the treatment of localized tumors involves surgical excision. Metastasis to visceral organs is common; however, clitoral metastasis is exceedingly rare, and usually results in clitorectomies—a morbid procedure.[3]

Talimogene laherparepvec (T-VEC) is a genetically modified oncolytic herpes virus) that results in direct tumor destruction and promotes host antitumor immunity via the expression of granulocyte-macrophage colony-stimulating factor.[4] T-VEC is a Food and Drug Administration–approved monotherapy for the treatment of surgically nonresectable melanoma. Overall response rates range from 30% to 60%, with the most common side effects being transient flu-like symptoms.[5,6] Patients that achieve a complete response tend to have a durable response with nearly 90% of complete responders reaching the 5-year survival benchmark in a phase III clinical trial.[6] In addition to being a treatment option that offers local disease control without removing cancerous tissue, there is evidence that it can work synergistically with systemic immunotherapy.[7] Here, we present a case of clitoral metastasis of VM treated successfully with T-VEC.

Abbreviations used:

T-VEC: Talimogene laherparepvec
VM: vulvar melanoma

CASE REPORT

A 68-year-old woman was originally diagnosed with stage pT2a, pN0 BRAF-wild type malignant melanoma of her left labia minora that was treated with radical left vulvectomy and negative sentinel lymph node biopsy. Twenty months following surgery, her disease recurred in her left inguinal lymph nodes for which she underwent left ilioinguinal lymph node dissection (1 of 8 positive nodes) and began adjuvant nivolumab monotherapy shortly thereafter.

Six months into the treatment with nivolumab, she presented with a bleeding lesion on her clitoris. On physical examination, she was found to have a moist, exophytic, pink/red papule on the glans clitoris (Fig 1), which was confirmed via a biopsy sample analysis as metastatic amelanotic melanoma (Fig 2, *A*). Positron emission tomography/computed tomography showed no evidence of distant metastasis. A clitorectomy was discussed with her surgeon;

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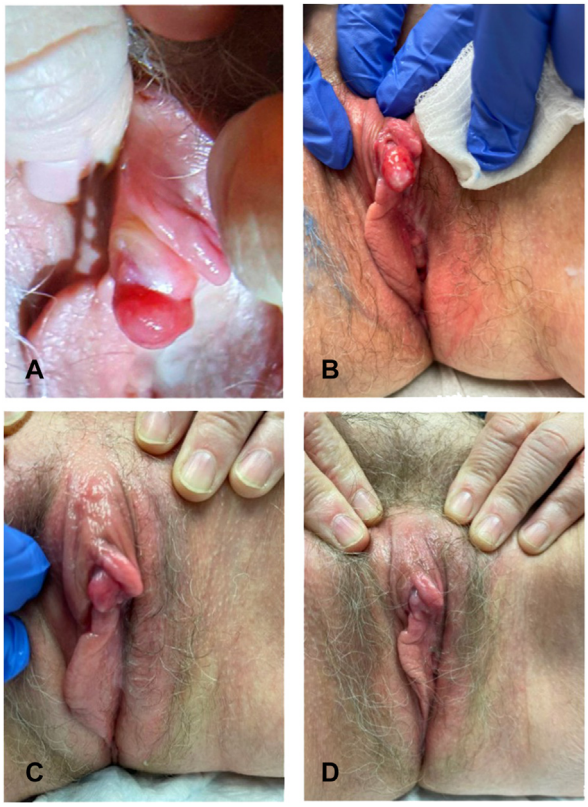

Fig 1. A, Biopsy-proven metastatic amelanotic vulvar melanoma presenting as a moist, exophytic, pink/red papule on the glans clitoris before treatment with talimogene laherparepvec. **B,** Zoomed-out version of (**A**). **C,** Clitoral metastasis before talimogene laherparepvec injections without hood retraction. **D,** Resolution of clitoral metastasis after 9 cycles of talimogene laherparepvec injections.

however, the patient deferred due to cognitive risks of another exposure to general anesthesia and assured loss of sexual function.

Collaborative decision-making led to a treatment plan of intratumoral injections of T-VEC started in conjunction with continued monthly nivolumab 480 mg IV with the goal of disease control.

Four weeks after initiating treatment-dose T-VEC injections (2 cycles), the clitoral tumor had a clinically-detectable reduction in size, with complete clinical and histologic resolution after 4 months (9 cycles; Figs 1, *D* and 2, *B*). Seventeen months after starting T-VEC, the patient's disease remains largely controlled. She had developed new in-transit lesions in the left inguinal region, which were also injected with a good response. She continued to receive T-VEC injections to a single mildly fluorodeoxyglucose (FDG)-avid (maximum standardized uptake value, 3.0) external iliac node present on a recent positron emission tomography scan, which was suspected to represent tumoral melanosis rather than a viable tumor. A biopsy sample analysis of this lymph node 2 months later confirmed the presence of melanosis, and no viable tumor was found. Following these biopsy results, T-VEC was suspended due to the resolution of clinically detectable tumors. However, monotherapy with nivolumab continues. The patient has not had any immune-related adverse events from concurrent administration of T-VEC and nivolumab.

Understandably, repeated T-VEC injections at a site as highly innervated as the clitoris are extraordinarily difficult to endure. Oral analgesics and topical anesthetic agents were given to improve the

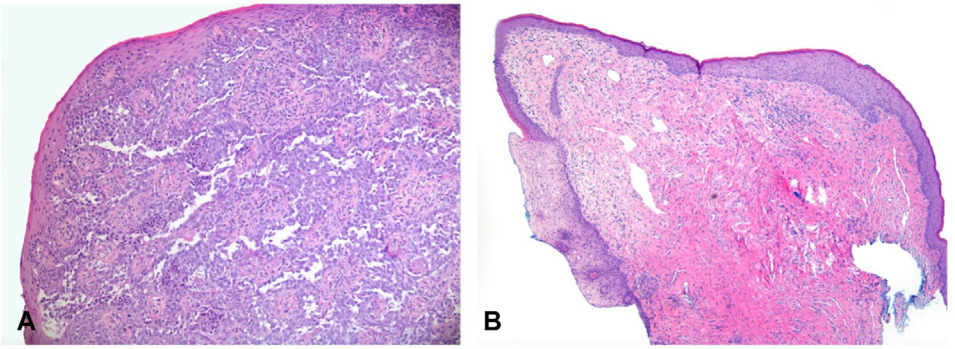

Fig 2. A, Clitoral melanoma histology before initiation of talimogene laherparepvec treatment (hematoxylin-eosin stain; original magnifications: 100). **B,** Dermal fibrosis without viable melanocytic proliferation highlighting the treatment effect after 4 months of talimogene laherparepvec injections. (**A** and **B,** Hematoxylin-eosin stain; original magnifications: **A,** ×100; **B,** ×50.)

tolerability of the procedure. Additionally, techniques from polyvagal theory were used,[8] including singing and meditation during injections to reduce pain.

DISCUSSION

Fortunately, T-VEC induced a complete response in our patient's metastatic, BRAF-wild type, anti-programmed death-1-refractory clitoral melanoma, has provided her locoregional disease control in conjunction with antiprogrammed death-1 therapy, and has allowed her to defer a morbid clitorectomy, potentially indefinitely. Her clitoral function remains unaffected by T-VEC injections. Awareness of this treatment option may be useful for other patients with locally advanced or metastatic VM, which often lacks effective medical therapy given its frequently nontargetable mutational profile and propensity for resistance to systemic immunotherapy.

Conflicts of interest

None disclosed.

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