

Modified peripheral and central Mohs micrographic surgery for improved margin control in extramammary Paget disease



Michael S. Chang, BA,^a Patrick M. Mulvaney, MD,^a Melissa J. Danesh, MD,^a Colleen M. Feltmate, MD,^b and Chrysalyn D. Schmults, MD, MSCE^a
Boston, Massachusetts

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INTRODUCTION

Extramammary Paget disease (EMPD) is a rare intraepithelial adenocarcinoma of pluripotent keratinocyte stem cells, which typically occurs in elderly patients.¹ The current standard of care involves surgical treatment with either wide local excision (WLE) or Mohs micrographic surgery (MMS). For vulvar cases, radical resection, such as complete vulvectomy, may be performed. However, along with significant procedural morbidity, tissue margins are often positive following resection, occurring in as frequently as 97% of cases in some series.² Even with reportedly negative pathologic margins, treatment of EMPD with WLE compared to that with MMS is associated with a 2.5-fold higher risk of recurrence in patients, which is likely due to incomplete margin evaluation and tumor removal.³ Modifications to the traditional MMS technique have been described to address lesions with large surface areas in order to combine the margin control of MMS with the need for resection and reconstruction under general anesthesia.⁴ A particular challenge arises in tumors located on the genitals surrounding orifices, where inner margin control is also necessary to achieve complete tumor clearance. Here, we report a case of vulvar EMPD treated with a novel modified dual inner and outer margin technique using MMS.

Abbreviations used:

EMPD: extramammary Paget disease
 MMS: Mohs micrographic surgery
 WLE: wide local excision

CASE REPORT

A 70 year-old woman presented with recurrent vulvar EMPD and consideration for MMS to assist with tumor extirpation. In 2016, the patient underwent WLE, with multiple positive radial margins on final pathology. Dermal invasion was absent, with the exception of a minute focus on a depth of 0.01 cm. The tumor recurred locally, and multiple scouting biopsies were performed by a gynecologic oncologist, which demonstrated epidermally limited disease involving the mons along the right side of the periclitoral area down to the labia minora, as well as the left side of the clitoral hood. The patient was treated with several 3-month courses of topical imiquimod cream 5% 3 times weekly in an effort to avoid a repeat WLE. These treatments resulted in a limited response, as confirmed by persistent disease on repeat biopsies, and significant local irritation. Therefore, surgical excision was recommended.

From the Department of Dermatology,^a and Division of Gynecologic Oncology, Department of Obstetrics, Gynecology and Reproductive Biology, Brigham and Women's Hospital, Harvard Medical School, Boston.^b

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Correspondence to: Chrysalyn D. Schmults, MD, MSCE, 1153 Centre St, Suite 4J, Boston, MA 02130. E-mail: cschmults@bwh.harvard.edu.

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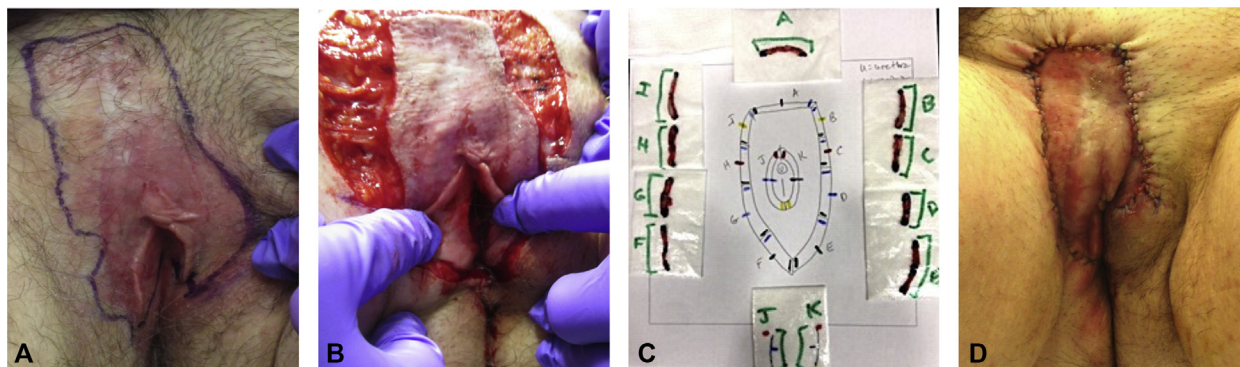


Fig 1. EMPD with dual internal and external peripheral margins via MMS. **A**, Preoperative photograph of EMPD involving the middle portion of the perineum and bilateral vulva, with clinically apparent tumor margins outlined in *blue ink*. **B**, Mohs stage-1 resection included both peripheral labial and inner mucosal margins lateral to the urethra and vulva. **C**, Mohs stage-1 map demonstrating positive peripheral margins (anterior and superior, outlined in *red*) and clear inner mucosal margins (J, K mucosal tissues, representing excised tumor margins circumferential to the urethral and vaginal orifices, are not shown, being processed). **D**, Final sutured defect for subsequent resection performed by the gynecologic oncologist. EMPD, Extramammary Paget disease; MMS, Mohs micrographic surgery.

Currently, there are no standardized guidelines for the treatment of EMPD, and preferred approaches vary among gynecologic oncology, dermatology, and urology professionals.³ To optimize patient outcomes in complex cases, careful, coordinated operative management of vulvar EMPD is critical in order to maximize cure and minimize morbidity. To achieve accurate clear margins and ensure that there was no vaginal or urethral involvement, which can sometimes be unresectable, we performed a novel technique employing dual inner (mucosal) and outer (external genital skin) Mohs margins (author C.D.S.; Fig 1, A). Similar in application to the “spaghetti technique,”⁵ a thin tissue layer was excised around the clinically apparent tumor margins, both peripherally in the skin (5 mm) and circumferential to the urethral and vaginal orifices (3 mm, Fig 1, B). The inner margin was clear in the first stage. The defect was not repaired so as to allow visualization of the medial margin for subsequent excision of the central tumor-bearing island, which was planned for by the gynecologic oncologist (author C.M.F.), under general anesthesia. Four Mohs stages were required to achieve clear peripheral margins (Fig 1, C). The outer ring (ie, defect due to clearance of the peripheral margin) was temporarily repaired to ensure hemostasis and wound stability (Fig 1, D) until a planned partial superficial vulvectomy with preservation of the clitoral organ. This was performed a few days later by the gynecologic oncologist (author C.M.F.) and reconstructed using bilateral V-Y island pedicle advancement flaps by a plastic surgeon.

The vulvectomy tissue showed no dermal invasion. EMPD was confirmed by cytokeratin (CK) 7 positivity. As the patient was at an elevated risk of synchronous malignancy in the setting of EMPD, she was referred for cancer screening, including mammography, colonoscopy, pelvic ultrasound, and cystoscopy, the results of which were negative. The patient had no evidence of postoperative recurrence after 6 months, with benign findings in 2 skin biopsies of the mons and right side of the perianal/gluteal region.

DISCUSSION

EMPD is a superficial cancer usually limited to the epidermis, which can spread over a large surface area of the anogenital region. Such tumors pose a challenge in balancing the need for cure with treatment-related morbidity. Medical therapy with topical imiquimod may be used as a temporizing measure in patients who deny surgery, but it is rarely curative and is often limited by exacerbation of painful erosions and flu-like systemic symptoms. MMS offers an improved cure rate compared to WLE for EMPD, but it has not been described for internal anatomic margin control.³ In this case report, we present a novel modified MMS technique that assesses both the inner mucosal and peripheral tissue margins. Similar in approach to the “spaghetti technique,” our approach features a novel application by clearing both the inner mucosal and outer/peripheral cutaneous margins.⁵ Though multifocal EMPD has been described in the literature,⁶ this may be a rare phenomenon because MMS margins have been associated with a

low recurrence risk.³ This approach also serves as a useful adjunct to precede subsequent resection and reconstruction by other care teams by preoperatively establishing the peripheral tumor margins and determining the need for more extensive vaginal, urethral, and anal resection. These surgeries are sometimes infeasible or unacceptable to patients. Thus, knowing prior to resection the type of surgery needed to eradicate the tumor will be beneficial for patients in determining whether resection is feasible with its associated morbidity.

Apart from local involvement, EMPD is associated with secondary malignancies in 11%-54% of cases,⁷ including neoplasms of the breast, vagina, cervix, uterus, ovary, gallbladder, and liver.⁷⁻⁹ Permanent histology of the tumor is required to rule out dermally invasive EMPD or contiguous vulvar adenocarcinoma, which can be associated with a higher risk of metastasis and/or secondary malignancies. Immunohistochemical staining is unfortunately not a reliable method to distinguish primary EMPD from secondary EMPD associated with other malignancies as the positive and negative predictive values of CK-20 positivity and gross cystic disease fluid protein-15 negativity are as low as 44% and 81% and 34% and 84%, respectively.¹⁰ Therefore, all patients should be screened for secondary EMPD-associated cancers by prostate-specific antigen testing, mammography, colonoscopy, cystoscopy, and abdominal/pelvic ultrasound.⁷

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