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Vulvar Malignant Melanoma: A Case of Rapid Progression despite Multimodal Treatment

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Abstract

Vulvar melanoma (VM) remains a condition with an unclear etiology, making its management complex. Typically, treatment protocols for VM mirror those of cutaneous melanoma, primarily emphasizing surgical excision. This case study examines the metastatic progression in an 85-year-old woman, who experienced a concerning advancement of the disease despite receiving the standard treatment. Through an in-depth evaluation, the case illustrates the rapid progression of VM, which poses significant therapeutic challenges. The findings underscore the critical importance of early detection and aggressive treatment strategies to improve outcomes. Additionally, this case highlights the necessity for vigilant follow-up care to monitor potential metastasis and manage the disease effectively. The presentation of this case serves as a call to action for healthcare providers to be proactive in recognizing and addressing vulvar melanoma, particularly in older patients, to enhance their chances of successful intervention and management.

Keywords: Vulvar melanoma; Case study; Therapeutic challenges; Malignant

Background

Malignant melanoma is an aggressive neoplasm arising from melanocytes, the pigment-producing cells of the skin and mucosal surfaces [1]. Melanoma most commonly arises in cutaneous tissue but can also develop in extracutaneous sites, including the mucosal epithelium of the vulva, gastrointestinal tract, and uveal tract [2]. Vulvar melanoma (VM) is a rare gynecological condition comprising approximately 1% of all melanomas in women and it accounts for around 5% of all vulvar malignancies [3]. Unlike cutaneous melanoma, which is strongly associated with ultraviolet (UV) exposure, the etiology of VM remains unclear, though genetic predisposition, hormonal influences, and chronic inflammation have been suggested as potential contributing factors [4].

Given the limited treatment guidelines due to its rarity, the management of VM is often extrapolated from cutaneous melanoma protocols [5]. Surgical excision with appropriate margins remains the primary treatment, while sentinel lymph node biopsy (SLNB) and adjuvant immunotherapy or targeted therapy may be considered for high-risk or metastatic cases [6].

Despite losing its central role in medical literature during the 20th century, case reports continue to maintain significant popularity. They serve as a valuable component of various research methods, complementing more traditional approaches. Furthermore, case reports extend their usefulness

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beyond research by functioning as effective educational tools in the medical field [7]. Following that school of thought, we present this case report to highlight a case of malignant VM, which progressed to metastatic disease despite the patient undergoing multiple surgical excisions and radiation therapy.

Case Report

In January 2020, an 85-year-old woman, para 2 (spontaneous vaginal delivery) presented with a new onset post-menopausal vaginal bleed. Her relevant history revealed a past medical history of hypertrophic cardiomyopathy, hypertension, and hypothyroidism on replacement therapy, osteoporosis, colonic diverticulosis, and an abdominal wall hernia. She had two surgeries: a right knee arthroscopy and a tonsillectomy. Family history was notable for her mother being diagnosed with multiple myeloma at 92 years of age. The patient had no history of smoking and reported minimal alcohol consumption.

A pelvic ultrasound was completed to investigate the bleed, which revealed a mildly thickened endometrium with multiple cysts. She was referred to a gynecologist following the ultrasound. Her hysteroscopy and dilation and curettage (D&C) procedure uncovered a vaginal polyp towards the anterior wall close to the ureter leading to a vaginal polypectomy. The polyp specimen was sent for a pathological investigation. The pathology report showed an irregular grey-tan mucosal tissue with a black base measuring at 0.8 x 0.8 x 0.5 cm. The sample was described as fragments of squamous mucosa with ulceration and infiltration by sheets of pleomorphic malignant cells with hyperchromatic nuclei and frequent mitosis. Tumor cells were diffusely positive for vimentin, S-100 MART-1 HMB-45 and MITS. No immunoreactivity was detected for Pan-Keratin, EMA, HMWK or LCA. This immune profile was consistent with malignant melanoma. A CT-scan following the diagnosis confirmed that there was no metastasis.

A radiation oncologist followed up the patient approximately six weeks after the procedure. The clinical exam revealed no peripheral lymphadenopathy or any evidence of residual lesion in the pelvic region. Despite no apparent symptoms or visible physical changes, external beam radiotherapy was recommended and performed due to the disease's high recurring nature. The radiation therapy was completed using an anterior and posterior parallel opposed beam arrangement to cover the vulva and distal vaginal region with a dose of 5000 cGy in 20 fractions daily over 4 weeks. Beam energy was a mixed photon plan with 6 MV / 15 MV energy to allow the required target/depth dose coverage.

Six months following the radiotherapy, the patient underwent a follow-up evaluation, which included a pap smear test. The cytology report showed atypical squamous cells of undetermined significance and reactive cellular changes likely associated with irradiation effect. Furthermore, the vulvar examination revealed two suspicious nodules: a red non-pigmented lesion slightly left of clitoris (1.0 x 0.5 x 0.5 cm) and a firm polypoid lesion in the lower vagina involving the vaginal wall just inside the introitus (5 mm). Due to the suspicious nature of the nodule and the high average recurrence rate of vulvar melanoma, the patient and the care team decided for a radical excision of both vulvar and vaginal lesions. Both nodules were resected with a couple of centimeter margins all around. The specimens were sent to pathology, and the results confirmed the recurrence of invasive malignant melanoma. Following the excision, the patient had no evidence of recurrence or abnormalities. There was a pigmentation 2.0 x 5.0 cm streak on the left posterior labia majora, but it was determined to be benign.

Approximately a year following the surgery, the patient presented to the emergency department with a one-month history of malaise, poor appetite, abdominal discomfort, leg swelling and leg weakness. CT chest/abdomen/pelvis showed multiple new pulmonary and hepatic nodules, which were consistent with a diffuse lung and liver metastatic disease. Based on the patient's wishes, goals of care were transitioned to comfort care, and the patient passed away two weeks after. It is worth mentioning that metastasis was diagnosed only two years following the initial polypectomy, and one year following the radical excision.

Discussion

As the literature predicts VM to be a rare and aggressive malignancy, with poor prognosis (5-year overall survival rate at 47% compared with 92% for cutaneous melanoma) [8], the presented case highlights the rapid progression and therapeutic challenges associated with VM, emphasizing the need for early detection, aggressive treatment, and vigilant follow-up.

The initial diagnosis in this case was incidental, following the discovery of a vaginal polyp during a hysteroscopy and D&C for postmenopausal bleeding. The incidental nature of the case underscores the diagnostic difficulty of VM, as it may present with nonspecific symptoms such as vaginal bleeding or a mass, which can be mistaken for benign gynecological conditions. Given that VM lacks standardized screening protocols, a high index of suspicion is necessary for early diagnosis, especially in elderly postmenopausal women presenting with atypical lesions. The "ABCDE" rule (a mnemonic used to help detect early signs of melanoma, a type of skin cancer. It stands for Asymmetry, Border irregularity, Color variation, Diameter, and Evolving) [9] used in detection of cutaneous melanoma may serve a purpose in aiding patients with early detection of VM. Asymmetry refers to the idea of melanomas being often irregularly shaped. Border irregularity distinguishes melanomas from benign nevi with

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smooth, well-defined borders typically having uneven or jagged edges [10]. The color variation indicates multiple hues, such as different shades of brown, black, blue, white, or red —while benign moles are usually a uniform brown [10]. As for the diameter, melanoma is suspected if the lesions are larger than 6 mm [10]. The elevation or evolution highlights any noticeable changes in shape, size, structure, color, or symptoms signaling malignancy [10].

Despite surgical excision with clear margins being the primary treatment modality for VM [6], achieving wide margins in the vulvar region can be challenging due to anatomical constraints and the impact on function and quality of life [11]. Our patient underwent radical excision with negative margins, yet experienced recurrence within a year. This highlights the aggressive nature of VM and the potential for locoregional recurrence despite adequate surgical management. Given the high recurrence rates, SLNB is often recommended to assess for occult metastasis, but its role remains controversial due to its risk of increasing locoregional recurrence [12].

Adjuvant therapy, including radiotherapy and immunotherapy, is considered in high-risk or recurrent cases [6]. Emerging treatment options, such as immune checkpoint inhibitors, have shown promising outcomes in advanced melanoma, and their usage in VM have increased over time [13]. However, Albert and colleagues [14] showed uncertain effectiveness with no statistical difference in two-year overall survival in advanced VM patients who received immunotherapy.

Conclusion

In conclusion, this case highlights the critical need for further research into optimal treatment strategies for VM. While surgical excision currently serves as the cornerstone of treatment, it is essential to explore the potential benefits of adjunct therapies, including targeted and immunotherapies. Advancing our understanding in these areas could significantly enhance patient outcomes and inform better management practices for those affected by VM.

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