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Case Report

Challenges in Diagnosis and Surgical Management of Locally Advanced Vulvar Melanoma

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Abstract

Vulvar melanoma (VM) is an uncommon aggressive gynecological malignancy that accounts 2-10% of all vulvar tumors [1]. An early, accurate diagnosis is essential in reaching appropriate treatment decisions, although this can be difficult as their clinical presentation may be variable especially in amelanotic lesions such as in our case. Advanced stages of presentation affect long-term survival and the quality of life. Surgical resection with adequate free margins is the mainstay of treatment for localized disease, as to date there is no clear consensus regarding therapeutic treatment. Histopathological examination and further immunohistochemistry studies are essential in diagnosis and staging.

We report a case of a 48-year-old woman presenting with advanced stage primary vulvar melanoma and review the literature regarding the current management approach and updates of this rare gynecological cancer.

Keywords: *Vulvar Melanoma; Gynecological Malignancy; Malignant Melanoma; Melanoma Prognosis*

Introduction

The vulva is the preferred site of melanoma in the female genital tract, even though vulvar melanoma itself is a rare genital malignancy that carries a poor prognosis. One of the reasons for the poor prognosis is that patients often present at an advanced stage of the disease [2].

The specific factors that cause VM are unknown. The vulva is not a sun-exposed area and sunlight is not involved in disease onset. Age and the family history for melanomas even cutaneous has been associated with a higher risk of VM [3].

Clinical features of VM are not specific ranging from asymptomatic pigmented or no-pigmented macules with asymmetric borders to painful lesions that ulcerate easily.

Histopathological examination has a key role in the diagnosis of this malignancy. Pathology reports includes the gross size of the tumor, although sometimes the orientation of the specimen may be difficult, especially when evaluating peripheral margins. Also, the histologic type, Clarck level, Breslow thickness, mitotic rate, presence of ulceration, presence of lymphovascular invasion, features of regression and presence of tumor infiltrating lymphocytes are important features that play a role in evaluating severity and prognosis.

Immunohistochemistry studies with positive staining for S100, Melan A/MART-1 and HMB45 can help to differentiate melanoma from other pigmented vulvar lesions, but also to diagnose amelanotic melanoma [5,6].

Historically, radical vulvectomy and bilateral inguinal lymph node dissection were the recommended treatment for malignant vulvar melanoma, regardless of tumor size, thickness or depth of invasion [7,8]. Yet, over the last decade, there have been studies suggesting that acceptable survival has been achieved through less radical approaches performed on early stages as it would affect the quality of life [8,9].

Free lateral and deep margins is one of the most important factors that must be achieved after surgery however there's still no agreement on optional safety margins. In many studies or cases the onco-surgeons follow the same approach as in malignant melanoma of the skin: 0.5 - 1 cm for melanoma *in situ*, 1 cm for invasive melanoma with Breslow thickness lower or equal to 1 mm, 1 - 2 cm for Breslow thickness equal to 1.01 - 2 mm, and 2 cm for Breslow thickness more than 2 mm. The suggested optimal depth is at least 1 cm through the subcutaneous tissue until the underlying muscle fascia is reached. For advanced disease, especially those with distant metastases, the prognosis is poor. Since the disease is rare, there is a lack of systematic and effective guidelines. Chemotherapy and radiation used before surgery have shown effectiveness in reducing the primary mass and to control local disease for positive margins and lymph nodes.

The use of immunotherapy has increased over time and may improve survival.

The combination therapy successfully improved the patient's prognosis and prolonged the patient's overall survival.

Case Presentation

We present a case of a 48-year-old woman who presented to the clinic due to a lesion in the vulva, increasing in size for the past year. Her Pap smear history was normal and she did not have any history of malignancy among first-degree relatives. On gynaecological examination, a 25 mm raised amelanotic lesion on the labia minora was noted. Bilateral palpable inguinal lymph nodes were noted on physical examination. The external genitalia, uterus, and ovaries appeared normal. A decision to completely excise the lesion with free margins was recommended. Preoperative evaluation of the patient with computerized tomography (CT) of the chest, abdomen and pelvis showed bilateral inguinal lymphadenopathy, however no signs of distant metastases were noted.

The postoperative pathology report revealed primary malignant melanoma with a maximum tumor thickness of 3 mm and ulceration. A high mitotic figure rate, and positive immunohistochemical staining for Melan A and high mitotic rate (ki67 = 60%). In addition, the tumor cells did not demonstrate BRAF mutations. The inguinal nodes removed showed metastatic disease in 6 lymph nodes.

Discussion

Vulvar and vaginal melanomas are rare entities with unknown etiology. Patients can be asymptomatic, and lesions can be amelanotic, resulting in delayed presentation. Therefore, guidelines for the management of these uncommon lesions are based on evidence and recommendations for the more common cutaneous melanomas. In addition, gynaecologic oncologists, the primary surgical specialists who manage melanomas of the female genital tract, are influenced by the management principles for squamous cell carcinoma of the vulva being the most common vulvar malignancy. Diagnosis is confirmed by a full-thickness excisional biopsy of the entire lesion. If the entire lesion cannot be removed due to surrounding vital structures, an incisional biopsy can be an alternative. Lymph node status may be used

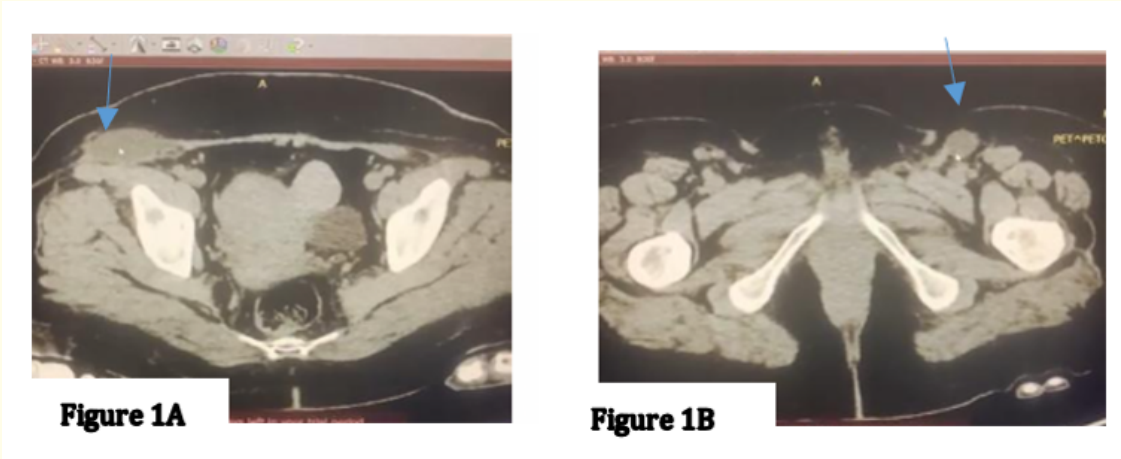

Figure 1A and 1B: *Pelvic CT-Scan. Bilateral lymphadenopathy with lymph nodes increased in size especially on the right, suggesting metastatic disease.*

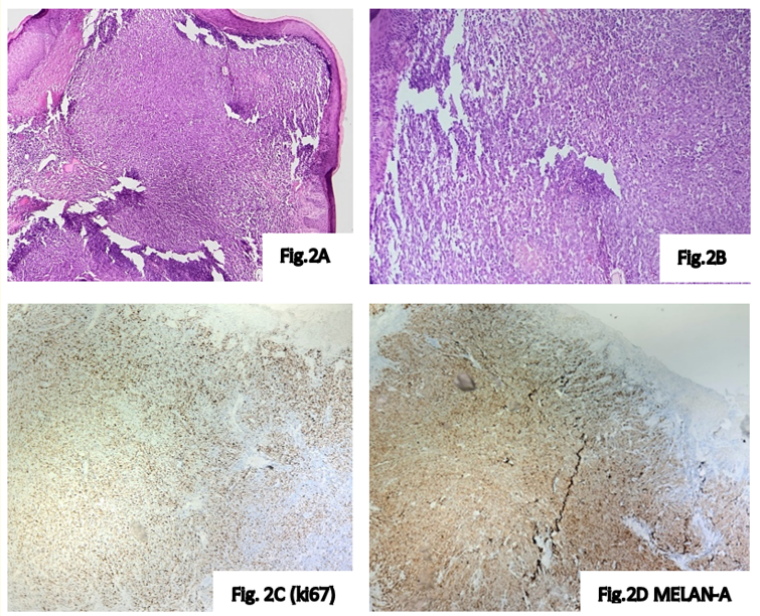

Figure 2A-2D: *H&E stained sections showed atypical melanocytes arranged as confluent nests and sheets, with prominent pagetoid spread, and absent dermal maturation.*

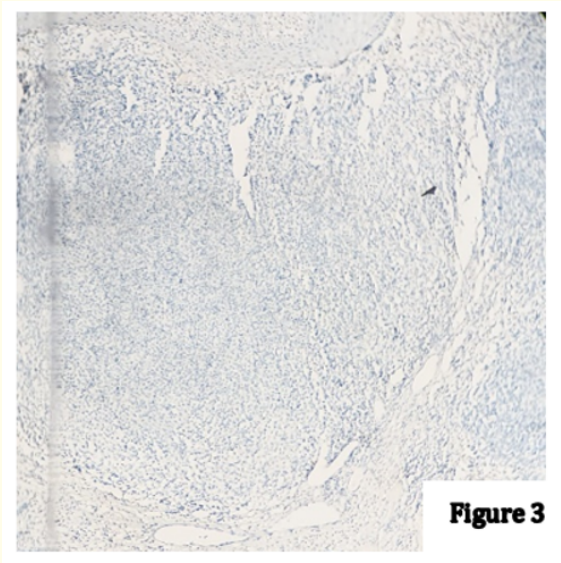

Figure 3: *BRAF negative.*

to direct adjuvant therapy. Although pathologic features such as T substage, size of the lesion, thickness, LVI, and nodal status all predict survival in vulvar melanomas, it is interesting to note that among the long-term survivors identified, T substage, reflecting both thickness and ulceration status, was quite variable. Immunohistochemical staining with HMB-45, S-100, Melan-A, and MART-1 can help to differentiate melanoma from other pigmented vulvar lesions. Therefore, it is likely that gene level alterations have a significant role in predicting tumour biology and behaviour.

The most recent AJCC staging guidelines include vulvar melanomas with cutaneous melanomas and not as vulvar cancers (squamous cell carcinoma). Surgical treatment of vulvar melanoma is WLE with negative margins. Evidence on the benefit of sentinel lymph node biopsy in vulvar melanoma is likewise scarce. The current indication for sentinel lymph node biopsy coincides with cutaneous melanoma, although the clinical benefit of completion lymphadenectomy after a positive sentinel lymph node biopsy is unknown. Delayed diagnosis contributes to poor survival and poor quality of life. Surgery is the primary treatment. Close surveillance is indicated due to the high recurrence rate of vulvar melanoma, even with early-stage disease. Since there is no research or consensus on an appropriate follow-up schedule, the regimen for vulvar invasive squamous cell carcinoma has been adopted for vulvar melanoma. Long-term follow-up recommendations are needed as recurrences after five years are unfortunately prevalent. We shared this case aiming to show that even though the presentation of this disease is rare, careful consideration must be given to its possibility as its prognosis is poor if overlooked.

Routine gynecological exams, dermatoscopic evaluation of new lesions followed by an incisional biopsy for suspicious lesions helps in the prognosis and quality of life. In the literature, it is suggested that the clinical and postoperative staging is the most significant predictor of survival [10-27].

Conclusion

Vulvar malignant melanoma is an uncommon aggressive disease with high rates of recurrence.

Early diagnosis in vulvar melanoma improves survival. Surgery seems to be the only efficient treatment approach that significantly improves prognosis of the patient. Postoperative adjuvant therapy using chemotherapy, radiation therapy, immunotherapy or targeted therapy might help prevent recurrence of the tumor however further studies are needed for a standardized therapeutic management. The survival rate is largely dependent on nodal and distant metastasis of the disease after initial tumor resection. Long-term surveillance is essential.

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