DERMOSCOPY OF THE MONTH

Recurrent Vulvar Melanoma – a Case Report

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Abstract

Melanoma rarely develops in the genital area. It is responsible for 5% of all vulvar malignancies. Postmenopausal women are usually more affected and the main differential diagnosis is vulvar melanosis and vulvar nevi. There are limited numbers of studies on dermoscopic features of mucosal melanoma, particularly early-stage lesions. Dermoscopic criteria have been described for the diagnosis of vulvar melanosis, and observational studies have been conducted to define the dermoscopic features of nevi and melanoma on the vulva. We are presenting the case of a 69-year old female with suspected recurrence of vulvar melanoma who previously had surgical removal of mucosal lentiginous melanoma on the left labia minor in June 2017. Five months after the primary melanoma surgery, the patient noticed de novo pigmentation at the left and right labia minor and urethral opening. On clinical examination, irregular light-brown pigmentation with ill-defined borders was evident on the labia minora of the vulva and around the external urethral orifice. On dermoscopy, irregular pigmented network, with white scar-like and structureless pinkish areas was evident. Incisional biopsy of the vulvar mucosa revealed melanoma in situ, confirming the local recurrence. CT scans of the head, thorax, abdomen and pelvis and gynaecological examination revealed no secondary deposits. Ultrasound of the regional inguinal lymph nodes revealed enlarged suspected pathologic involvement of the lymph nodes in both inguinal regions. Lymph node fine needle aspiration of lymph nodes in the left and right inguinal area revealed pleomorphic infiltrate of lymphoid cells with hemosiderin or melanoma pigment in the cytoplasm. Cystoscopic findings were within normal range. Interdisciplinary tumour board indicated wide excision of melanoma with margins of 1 cm and resection of the urethra, as well as biopsy of the enlarged left inguinal lymph node. Histopathological analysis of the resected mucosa revealed lentiginous spread of melanocytes showing moderate atypia, with focal pagetoid spread, without mitoses and ulceration and without invasion of lamina propria. The resection margins were tumour-free. Non-specific lymphadenitis was diagnosed on lymph node histopathological analysis. The patient was regularly monitored by a dermatologist and urologist, and had no recurrence. The accurate and prompt diagnosis is essential in the case of the vulvar melanoma which has unfavourable and unpredictable prognosis, with a tendency of local recurrences and regional and distant metastases in the case of invasive melanoma. In order not to miss early mucosal melanoma, dermatologists and gynaecologists should not avoid biopsy of lesions that demonstrate any clinical or dermoscopic feature of atypical melanocytic lesion, especially in case of the development of irregular pigmentation that expands and changes over time, the appearance of a solitary amelanotic papule or nodule requires excision or, in case of large diameter lesions, incision biopsies. Larger studies are needed to define more rigorously clinical and dermoscopic criteria that accurately distinguish early mucosal melanomas from benign skin lesions.

Key words: Vulvar Neoplasms; Melanoma; Dermoscopy; Diagnosis; Neoplasm Recurrence, Local; Case Reports

Introduction

Genital pigmented lesions are a diagnostic challenge because a differential diagnosis

includes nevus, genital melanotic macules (lentiginosis, melanosis), angiokeratoma, seborrheic keratosis, squamous cell carcinoma

Figure 1 a and b. Irregular light to dark brown pigmentation was present on the left and right labia minora, spreading to the urethral orifice

(SCC), basal cell carcinoma (BCC) and melanoma. Genital melanoma and vulvar melanoma, in particular, is a rare entity. It is responsible for 5% of all vulvar malignancies (1). Mucosal melanoma is a rare disease, accounting for approximately 1.4% of all melanomas and only 0.03% of all new cancer diagnoses (2-4). Mucosal melanomas arise from mucosal epithelium anywhere but are most commonly found in three areas; the vulvov-

gina (18% of cases), the anorectum (24% of cases) and the oral cavity, nasal cavity or sinuses (55% of cases) (5). Vulvar melanoma more frequently occurs in postmenopausal women, and long-term prognosis is poor due to the high rate of recurrence (6, 7).

Dermoscopy is a non-invasive tool that helps physicians to distinguish melanomas from other pigmented and non-pigmented skin lesions. Dermoscopic criteria have been described for the

Figure 2 a and b. Melanocytic lesion: irregular pigmented network, with white scar-like and structureless pinkish areas was evident

diagnosis of vulvar melanosis, and observational studies have been conducted to define the dermoscopic features of nevi and vulvar melanoma, but clinical and dermoscopic differentiation between melanoma and melanosis is difficult (8-11).

In this article, we present a case of recurrent vulvar melanoma in a 69-year old Caucasian female.

Case Report

A 69-year old female, without a family history of skin cancer, was admitted to our Clinic to be examined for suspected recurrence of vulvar melanoma. In June 2017, mucosal lentiginous melanoma was excised on the left labia minor, and histopathology revealed melanoma in situ. On immunohistochemistry, SOX-10, Melan-A, HMB-45 were continuously expressed along the basal layer, focally in nests and in a suprabasal layer, with one HMB 45+ cell in superficial dermis, suggesting invasion. Abdominal and pelvic magnetic resonance imaging (MRI) in October 2017, showed postoperative sequelae with no signs of recurrent disease. In November 2017, light-brown irregular pigmentation appeared again, biopsy was done and on histopathology lentiginous melanocytic hyperplasia with mild and moderate atypia was described.

In the further months, pigmentation spread to the left and right labia minor area, involving external urethral orifice. A gynecologist referred the patient to the dermatologist for clinical examination and dermoscopy. On admission the patient complained of difficulty in urinating.

On clinical examination, irregular light to dark brown pigmentation was present on the left and right labia minora, spreading to the urethral orifice (**Figure 1a and 1b**). On dermoscopy, irregular pigmented network, with white scar-like and structureless pinkish areas was evident (**Figure 2a and 2b**).

Regular laboratory analyses including complete blood count, biochemistry, liver function tests, complete urinalysis, LDH, and protein S100, were all within normal range. Regional inguinal lymph node ultrasound examination revealed enlarged suspected pathologic involvement of the lymph nodes in both inguinal regions. Lymph node fine needle aspiration of lymph nodes in the left and right inguinal area revealed pleomorphic infiltrate of lymphoid cells with hemosiderin or melanoma pigment in the cytoplasm, so the lymph node biopsy with histopathological analysis was recommended. Multi-slice computer tomography (MSCT) examination of the head, chest, abdomen and pelvis revealed the absence of distant metastases. Cytoscopy revealed edema and partial pigmentation of the urethra adjacent to the external meatus, with no other pathologic findings.

Multidisciplinary tumor board consisting of urologist, consultant gynaecologist, dermatologist, plastic and reconstructive surgeon and pathologist indicated wide excision of melanoma with 1 cm margins, resection of the urethra and reconstruction, as well as left inguinal lymph node biopsy. Surgery was performed by urologist specialized in gender

Figure 3 a and b. Histopathological analysis revealed lentiginous spread of melanocytes showing moderate atypia, with focal pagetoid spread, no mitoses and ulceration, without invasion of lamina propria, and intensive inflammatory infiltrate present in lamina propria

Figure 4. Local finding two months after surgery, during follow-up

transformation and plastic and reconstructive surgeon.

Histopathological analysis revealed lentiginous spread of melanocytes showing moderate atypia, with focal pagetoid spread, no mitoses and ulceration, without invasion of lamina propria, and intensive inflammatory infiltrate present in lamina propria (**Figure 3a and 3b**). Resection margins were tumour-free, and histopathological analysis of lymph node biopsy revealed reactive lymphadenitis without pathological infiltration (0/4). Postoperative recovery was favourable, without intraoperative or postoperative complications. Multidisciplinary tumor board indicated regular follow-up. During the follow-up no signs of recurrence were noted (**Figure 4**). The last follow-up was in April 2019, without signs of local recurrence. The patient complained of urinary incontinence, and was treated by urologist with solifenacin 5 mg/day.

Discussion

Genital pigmented lesions can be found in up to 10-12% of the general population [12]. Vulvar cancer is a rare neoplasm, accounting for less than 1% of malignant neoplasms among women. It represents 3-5% of malignant neoplasms of the female genital organs and has an estimated incidence of 1-2 cases per 100,000 women/year among women diagnosed with vulvar cancer in the United States (11). A vast majority (80%) of vulvar cancers are squamous cell carcinomas (SCC), whereas basal cell carcinomas (BCCs) and melanomas are less common, representing 8 and 6% of all vulvar cancers respectively (13). Sarco-

ma, basal cell carcinoma, and vulvar Paget's disease account for less than 2% of cases (14). The labia major is the most commonly affected site (52%) followed by the labia minor (18%), clitoris (10-15%) and Bartholin's glands (1-3%) (15). Postmenopausal women have a higher incidence of vulvar melanoma than premenopausal women, as was the case with our patient (12). Vulvar melanoma is a rare disease with different histological types. The order of incidence is as follows: mucosal lentiginous (27-57%), nodular (22-28%), unclassified (12-16%), and superficial spreading (4-56%) (16, 17). Risk factors include chronic inflammation, such as those associated with lichen sclerosis (18).

Differential diagnosis includes the following lesions: benign pigment lesions (lentigo simplex, vulvar melanosis, acanthosis nigricans, seborrheic keratosis, intradermal, junction or complex nevus), pigmented vulvar intraepithelial neoplasia, vulvar squamous cell carcinoma (SCC), basal cell carcinoma (BCC) and Paget's disease (10).

In dermoscopy, the combination of blue, grey, or white colour with structureless zones are the strongest indicators of vulvar melanoma when differentiating between benign and malignant mucosal lesions as Blum et al. described [11]. Furthermore, polymorphous vessels are also a hint for malignancy, particularly melanoma (19, 20).

Early signs of a melanoma of the mucosa can include the presence of structureless parts and grey colour. Additional late-stage signs in larger lesions can include the presence of multiple patterns and additional colours, especially blue or white. However, the results of study conducted by Blum et al. show that multiple colours are a better clue to malignant lesions than multiple patterns (11).

In early stages there are no associated symptoms, and without regular gynaecological follow-up, intramucosal melanoma can progress to invasive vulvovaginal mucosal melanoma that becomes symptomatic. Pruritus, vaginal bleeding or discharge, dyspareunia or palpable mass are often present (10). Our patient had mild occasional pruritus and subjective feeling of difficulty in urinating, due to the urinary meatus infiltration and oedema, with no other symptoms.

Complete excision of the lesion is indicated in cases with suspected diagnosis. Currently, surgery still remains the best option albeit with-

out the need for radical procedures. A number of studies have shown that radical surgery does not increase the patient's survival with initial disease compared to local excision with margins, and is associated with greater morbidity and anatomical disfiguring (1, 13). Consequently, radical vulvectomy with bilateral lymphadenectomy is becoming a questionable and obsolete treatment approach. Alternatively, wide local excision with a 1 cm surgical margin is recommended for lesions with a depth of less than 1 mm. For deeper lesions en bloc resection with a safety margin of 2-3 cm and regional lymphadenectomy (inguinal-femoral) is advised. Adjuvant treatment with immunotherapy, chemotherapy, and radiotherapy may be recommended in specific cases and for local recurrences and distal metastases (13, 19, 20); however, it was not the case with our patient.

Conclusion

The accurate and prompt diagnosis is essential in the case of vulvar melanoma. Generally, it has an unfavorable and relatively unpredictable prognosis, tending to recur and form metastases. Surgical treatment is the cornerstone of the therapeutic management. The initial surgical intervention must be optimally chosen in order to prevent the recurrence. The size of the tumor, the thickness and invasion degree, as well as ulceration and involvement of lymph nodes (LN), the patient's age at the time of diagnosis are essential factors influencing the survival. Women in postmenopausal age tend to have slightly higher incidence of vulvar melanoma than premenopausal women. Some studies have shown that the general prognosis of patients with vulvar melanoma is worse than the one in women with extra genital melanoma and squamous cell carcinoma of the vulva, showing a greater tendency for local and distal recurrence. In order not to miss an opportunity for early detection of mucosal melanoma, dermatologists and gynecologists should not avoid biopsy of lesions that demonstrate any clinical or dermoscopic features of melanoma, especially in older patients. Larger studies are needed to define more rigorously clinical and dermoscopic criteria that accurately distinguish early mucosal melanomas from benign skin lesions.

Abbreviations

PH – B-45 - Human Melanoma Black - 45
IHH – Immunohistochemistry
LN – lymph nodes
MRI – Magnetic Resonance Imaging
LDH – Lactate Dehydrogenase
TSH – thyroid-stimulating hormone
CEA – Carcinoembryonic antigen

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Rekurentni melanom vulve – prikaz slučaja

Sažetak

Melanomi genitalnog područja, a naročito melanomi vulve su retki. Melanom vulve čini 5% svih maligniteta vulve i češće se javljaju kod žena u postmenopauzi. Glavna diferencijalna dijagnoza su vulvarna melanoza i nevusi vulve. Postoji mali broj studija o dermoskopskim karakteristikama melanoma sluzokože, a naročito lezija u ranom stadijumu. Opisani su dermoskopski kriterijumi za dijagnozu melanoze vulve, a sprovedena su i ispitivanja koja su definisala dermoskopske karakteristike nevusa i melanoma vulve.

Predstavljamo slučaj 69-godišnje žene sa sumnjom na recidiv vulvarnog melanoma koja je ranije imala operaciju mukoznog lentiginoznog melanoma na malim usnama juna 2017. godine. Pet meseci nakon resekcije primarnog melanoma, pacijentkinja je primetila novu pigmentaciju na levoj i desnoj maloj usni kao i na otvoru uretre. Na kliničkom pregledu, evidentirana je nepravilna svetlosmeđa pigmentacija nejasnih granica na malim usnama i oko spoljnog otvora uretre. Dermoskopski nalaz ukazao je na melanocitnu leziju sa nejasno ograničenom iregularnom pigmentnom mrežom, bela i ružičasta polja bez strukture. Biopsijom sluznice vulve otkriven je melanom in situ, potvrđujući lokalni recidiv. Pretragom grudnog koša, abdomena i karlicekomputerizovanom tomografijom i ginekološkim pregledom nisu otkriveni sekundarni depoziti. Ultrazvukom regionalnih ingvinalnih limfnih čvorova otkriveni su uvećani limfni čvorovi u levom ingvinumu sa sumnjom na

patološko zahvatanje. Citološka analiza levog i desnog ingvinalnog limfnog čvora i cistoskopski nalazi bili su u granicama normale. Multidisciplinarni konzilijum za melanom indikovao je široku eksciziju sa marginama od 1 cm uz resekciju uretre i biopsiju sumnjivog limfnog čvora u levom ingvinumu. Histopatološkom analizom reseciranog dela sluzokože otkriveno je lentiginozno i pedžetoidno širenje melanocita koji pokazuju umerenu atipiju, bez mitozu i ulceraciju i bez invazije lamine proprije (melanoma in situ), uz slobodne margine resekcije. Histopatološki nalaz biopsije limfnog čvora ukazao je na nespecifičnu inflamaciju, bez patoloških depozita melanoma. Tokom redovnih kontrola nije zabeležen recidiv bolesti.

Tačna i brza dijagnoza neophodna je u slučaju melanoma vulve, koji ima nepovoljnu i nepredvidivu prognozu, sa tendencijom lokalnih recidiva i regionalnih i udaljenih metastaza u slučaju invazivnog melanoma. Za sve pigmentne lezije vulve kod kojih postoji klinička i dermoskopska sumnja (razvoj iregularne pigmentacije koja se vremenom širi i menja, pojava solitarne amelanotične papule ili nodusa) neophodna je eksciziona ili u slučaju lezija velikog dijametara inciziona biopsija sa mesta sa dermoskopski iregularnim karakteristikama, naročito kod starijih pacijentkinja. Potrebne su veće studije da se jasnije definišu klinički i dermoskopski kriterijumi koji precizno razlikuju rane melanome sluznice od benignih lezija.

Ključne reči: Neoplazme vulve; Melanom; Dermoskopija; Dijagnoza; Lokalne rekurentne neoplazme; Prikazi slučajeva

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