Early diagnosis of genital mucosal melanoma: how good are our dermoscopic criteria?

Tova Rogers, MFA¹, Melissa Pulitzer, MD², Maria L. Marino, MD³, Ashfaq A. Marghoob, MD⁴, Oliver Zivanovic, MD³, Michael A. Marchetti, MD¹

¹ Dermatology Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA
² Pathology Service, Memorial Sloan Kettering Cancer Center, New York, NY, USA
³ Gynecology Service, Department of Surgery, Memorial Sloan Kettering Cancer Center, New York, NY, USA

Key words: melanoma, genital, mucosal melanoma, dermoscopy

Citation: Rogers T, Pulitzer M, Marino M, Marghoob A, Zivanovic O, Marchetti M. Early diagnosis of genital mucosal melanoma: how good are our dermoscopic criteria? Dermatol Pract Concept 2016;6(4):10. doi: 10.5826/dpc.0604a10

Received: April 28, 2016; Accepted: July 25, 2016; Published: October 31, 2016

Copyright: ©2016 Rogers. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Funding: None.

Competing interests: The authors have no conflicts of interest to disclose.

All authors have contributed significantly to this publication.

Corresponding author: Michael A. Marchetti, MD, Dermatology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, 16 E 60th Street, New York 10065, USA. Tel. 646-888-6016; Fax: 646-888-6478. Email: marchetm@mskcc.org

ABSTRACT

Background: There are limited studies on the dermoscopic features of mucosal melanoma, particularly early-stage lesions. Described criteria include the presence of blue, gray, or white colors, with a reported sensitivity of 100%. It is unclear if these features will aid in the detection of early mucosal melanoma or improve diagnostic accuracy compared to naked-eye examination alone.

Case: An Asian female in her fifties was referred for evaluation of an asymptomatic, irregularly pigmented patch of the clitoral hood and labia minora of unknown duration. Her past medical history was notable for Stage IV non-small cell lung cancer. She denied a personal or family history of skin cancer. Dermoscopic evaluation of the vulvar lesion revealed heterogeneous brown and black pigmentation mostly composed of thick lines. There were no other colors or structures present. As the differential diagnosis included vulvar melanosis and mucosal melanoma, the patient was recommended to undergo biopsy, which was delayed due to complications from her underlying lung cancer. Repeat dermatoscopic imaging performed three months later revealed significant changes concerning for melanoma, including increase in size, asymmetric darkening, and the appearance of structureless areas and central blue and pink colors. Histopathological examination of a biopsy and subsequent resection confirmed the diagnosis of melanoma in situ.

Conclusion: Previously described dermatoscopic features for mucosal melanoma may not have high sensitivity for early melanomas. Additional studies are needed to define the dermatoscopic characteristics of mucosal melanomas that aid in early detection. Health care providers should have a low threshold for biopsy of mucosal lesions that show any clinical or dermatoscopic features of melanoma, especially in older women.
On examination, a 12 x 13 mm, irregular, dark brown-black patch was noted on her clitoral hood and labia minora (Figure 1). Ill-defined, patchy, light brown pigmentation on bilateral labia minora was also observed. There was no lymphadenopathy on palpation of the inguinal and femoral nodal basins. Dermoscopic evaluation of the lesion was performed using polarized contact dermoscopy with ultrasound gel and a polyvinyl chloride barrier. It revealed heterogeneous brown and black pigmentation composed of thick lines without other structures (Figure 2a). There was no evidence of blue, gray, or white colors or other dermoscopic features reported to be specific for the diagnosis of melanoma. The differential included mucosal melanosis and melanoma. Given the atypical clinical appearance of a large, asymmetric, pigmented macule with color variegation, a biopsy was recommended but was delayed due to complications from the patient's underlying malignancy. On follow-up examination three months later, repeat dermoscopic imaging with polarized contact dermoscopy using ultrasound gel and a polyvinyl chloride barrier revealed significant changes concerning for melanoma, including increase in size, asymmetric darkening, and the appearance of structureless areas and central blue and pink colors (Figure 2b). Histopathological examination of an incisional biopsy and subsequent excision revealed melanoma in situ with a characteristic proliferation of enlarged, poorly nested and confluent, severely atypical melanocytes. Other notable histopathologic findings included skipping foci of heavily pigmented dermal melanophages, variable lichenoid inflammatory infiltrate, and marked vascular ectasia and congestion (Figure 3).

**Case report**

An Asian female in her fifties was referred for evaluation of an asymptomatic, pigmented vulvar lesion of unknown duration. She denied a personal or family history of skin cancer. Her past medical history was notable for Stage IV non-small cell lung cancer diagnosed nine months prior and managed with surgery and oral erlotinib.

![Figure 1. Clinical appearance of vulvar melanoma in situ showed 12 x 13 mm asymmetric patch with color variegation on the clitoral hood and labia minora.](Copyright: ©2016 Rogers.)

![Figure 2. Polarized contact dermoscopic images of vulvar melanoma in situ. (a) Baseline dermoscopic image showed heterogeneous and asymmetric brown and black pigmentation composed of thick lines. (b) Repeat dermoscopic imaging three months later showed increase in size, asymmetric and multifocal darkening, and the appearance of structureless areas and central blue and pink colors.](Copyright: ©2016 Rogers.)
Clinically, VM can present as flat or raised lesions with irregular borders and are often greater than 7 mm in size [7]. A majority of VM are pigmented, however, amelanotic VM accounts for 4% to 27% of cases [2,4]. Late symptoms include bleeding and pruritus, while many lesions, especially early lesions, can be asymptomatic [2]. Most VM are diagnosed at locally advanced stages. A 2015 study that included 63 cases of VM demonstrated a median Breslow thickness at presentation of 3.3 mm (range: 0-20mm) [1]. Regional nodal disease is not uncommon at presentation [4].

The most common histological subtypes of VM are superficial spreading and nodular [1,8]. Compared to cutaneous melanoma, VM show distinct genetic mutations. A 2014 study evaluating the genetic profiles of VM found KIT mutations in 18% of cases (7/39) and NRAS mutations in 12% of cases (5/42). No mutations in BRAF (0/39) or EGFR (0/30) were found [9]. The overall prognosis of VM is worse than that for cutaneous melanoma, with 61% versus 91% five-year melanoma-specific survival rates, respectively [8]. It is

**Conclusion**

Vulvar melanoma (VM) accounts for 1% to 3% of all melanomas arising in women [1]. It most frequently occurs in the fifth or sixth decade of life, suggesting that clinicians should have a heightened suspicion for melanoma when evaluating pigmented mucosal lesions in older women [2-4]. The incidence is slightly higher in Caucasians compared to Hispanics, Asians, Blacks, and American-Indians [5]. Risk factors include chronic inflammation, such as that associated with lichen sclerosis [6]. The differential diagnosis of pigmented vulvar lesions includes vulvar nevi and vulvar melanosis (also referred to as vulvar lentiginosis or vulvar melanotic macule), particularly in younger individuals. Vulvar nevi tend to present clinically as evenly pigmented papules or macules with regular borders. Their colors range from red to dark brown-black and they typically measure less than 1 cm. Vulvar melanosis is characterized by single or multiple, irregularly pigmented, tan to black macules or patches with uneven borders [6].

![Figure 3. Histopathology of vulvar melanoma in situ. (a) Photomicrograph of initial biopsy specimen showing a broad, asymmetric, junctional melanocytic proliferation with variable epidermal acanthosis and dermal clusters of heavily pigmented melanophages (hematoxylin-eosin stain, original magnification x100). (b, c, d) Images of excised specimen showing confluent, severely atypical melanocytes with pagetoid spread (b), hematoxylin-eosin stain, original magnification x400), areas with lichenoid lymphoid infiltrates and melanophages (c), hematoxylin-eosin stain, original magnification x200), and the intersection of congested and ectatic vasculature with dermal melanophages and junctional melanoma (d), hematoxylin-eosin stain, original magnification x200). [Copyright: ©2016 Rogers.]](image-url)
unclear if the poorer prognosis associated with VM is due to later detection or more aggressive biological behavior [10].

Dermoscopic features of VM have been described. Blum et al evaluated 11 cases of VM, 10 of which were invasive, and found that the presence of blue, gray, or white colors with or without structureless areas had 100% sensitivity for melanoma [11]. de Giorgio et al described a case of superficial spreading melanoma of the vulva with a Breslow depth of 0.5 mm that presented with a blue-gray area and whitish veil [12]. Lin et al evaluated the dermoscopic features of 40 pigmented mucosal lesions in Japanese patients, including 8 melanomas, 2 of which were vulvar. They found that 6 of the 8 melanomas (75%), including both vulvar lesions, had multicomponent patterns. The vulvar lesions also had multiple colors and blue-white veils [13]. These findings are in contrast to the described dermoscopic features of vulvar melanosis, which include a ring-like pattern, a homogeneous or structureless pattern, a reticular pattern, and a globular pattern [14-16]. A limitation of the studies evaluating the dermoscopic morphologies of mucosal melanoma is that the studied lesions were clinically detected and often of an advanced stage; it is therefore unknown if the application of these criteria will aid in the detection of early mucosal melanomas. Consistent with this limitation, Betti et al described a case of melanoma in situ on the glans penis with an irregular pigment network but no other worrisome features [17].

In order to not miss an opportunity for early detection of mucosal melanoma, health care providers should have a low threshold for biopsy of lesions that demonstrate any clinical or dermoscopic features concerning for melanoma. This is especially true for older patients. Larger studies are needed to more rigorously define clinical and dermoscopic criteria that accurately distinguish early mucosal melanomas from benign skin lesions.

References

1. Seifried S, Haydu LE, Quinn MJ, Scolyer RA, Stretch JR, Thompson JF. Melanoma of the vulva and vagina: principles of staging and their relevance to management based on a clinicopathologic analysis of 85 cases. Ann Surg Oncol 2015;22(6):1959-66. PMID: 25384702. DOI: 10.1245/s10434-014-4215-3.

2. Dunton CJ, Berd D. Vulvar melanoma, biologically different from other cutaneous melanomas. Lancet 1999;354(9159):2013-4. PMID: 10636360. DOI: 10.1016/s0140-6736(99)00390-6.

3. Sanchez A, Rodriguez D, Allard CB, et al. Primary genitalcutaneous melanoma: Epidemiology and disease-specific survival in a large population-based cohort. Urol Oncol 2016;34(4):166.e7-14. PMID: 26739672. DOI: 10.1016/j.urolonc.2015.11.009.

4. DeMatos P, Tyler D, Seigler HF. Mucosal melanoma of the female genitalia: a clinicopathologic study of forty-three cases at Duke University Medical Center. Surgery. 1998;124(1):38-48. PMID: 9663250.

5. Hu DN, Yu GP, McCormick SA. Population-based incidence of vulvar and vaginal melanoma in various races and ethnic groups with comparisons to other site-specific melanomas. Melanoma Res 2010;20(2):153-8. PMID: 20147857. DOI: 10.1097/CMR.0b013e32833684e8.

6. Murzaku EC, Penn LA, Hale CS, Pomeranz MK, Polsky D. Vulvar nevi, melanosis, and melanoma: an epidemiologic, clinical, and histopathologic review. J Am Acad Dermatol 2014;71(6):1241-9. PMID: 25267379. DOI: 10.1016/j.jaad.2014.08.019.

7. Murzaku EC, Hayan S, Rao BK. Methods and rates of dermoscopy usage: a cross-sectional survey of US dermatologists stratified by years in practice. J Am Acad Dermatol 2014;71(2):393-5. PMID: 25037790. DOI: 10.1016/j.jaad.2014.03.048.

8. Tcheung WJ, Selim MA, Herndon JE 2nd, Abernethy AP, Nelson KC. Clinicopathologic study of 85 cases of melanoma of the female genitalia. J Am Acad Dermatol 2012;67(4):598-605. PMID: 22243767. DOI: 10.1016/j.jaad.2011.11.921.

9. Aulmann S, Sinn HP, Penzel R, et al. Comparison of molecular abnormalities in vulvar and vaginal melanomas. Mod Pathol 2014;27(10):1386-93. PMID: 24603591. DOI: 10.1038/modpathol.2013.211.

10. Ragnarsson-Olding BK. Primary malignant melanoma of the vulva—an aggressive tumor for modeling the genesis of non-UV light-associated melanomas. Acta Oncol 2004;43(5):421-35. PMID: 15360046.

11. Blum A, Simionescu O, Argenziano G, et al. Dermoscopy of pigmented lesions of the mucosa and the mucocutaneous junction: results of a multicenter study by the International Dermoscopy Society (IDS). Arch Dermatol 2011;147(10):1181-7. PMID: 21680757. DOI: 10.1001/archdermatol.2011.155.

12. de Giorgio V, Massi D, Salvini C, Mannone F, Cattaneo A, Carli P. Thin melanoma of the vulva: a clinical, dermoscopic-pathologic case study. Arch Dermatol 2005;141(8):1046-7. PMID: 16103344. DOI: 10.1001/archderm.141.8.1046.

13. Lin J, Koga H, Takata M, Saida T. Dermoscopic features of pigmented lesions on mucocutaneous junction and mucous membrane. Br J Dermatol 2009;161(6):1255-61. PMID: 19673880. DOI: 10.1111/j.1365-2133.2009.09251.x.

14. Ferrari A, Bucci P, Covello R, et al. The ringlike pattern in vulvar melanosis: a new dermoscopic clue for diagnosis. Arch Dermatol 2008;144(8):1030-4. PMID: 18711077. DOI: 10.1001/archderm.144.8.1030.

15. Mannone F, Di Giorgi V, Cattaneo A, Massi D, De Magnis A, Carli P. Dermoscopic features of mucosal melanosis. Dermatol Surg 2004;30(8):1118-23. PMID: 15274702. DOI: 10.1111/j.1524-4725.2004.30337.x.

16. Ronger-Savle S, Julien V, Duru G, Raudrant D, Dalle S, Thomas L. Features of pigmented vulval lesions on dermoscopy. Br J Dermatol 2011;164(1):54-61. PMID: 20846309. DOI: 10.1111/j.1365-2133.2010.10043.x.

17. Betti R, Menni S, Crosti C. Melanoma of the glans penis. Euro J Dermatol 2005;15(2):113-5. PMID: 15737826.