Clinical and Dermoscopic Features of Vulvar Melanosis Over the Last 20 Years

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Vulvar melanosis, also known as vulvar lentiginosis or vulvar melanotic macules, is a pigmentary change that accounts for most pigmented vulvar lesions in women of reproductive age.1 It presents as single or multiple asymptomatic macules or patches of varying size and color that may be asymmetric with poorly defined borders. The differential diagnosis of melanocytic lesions includes melanoma, which creates anxiety for patients and the physicians who diagnose the condition and treat the patients.

The etiopathogenesis of vulvar melanosis is poorly understood. Researchers have proposed associations between vulvar melanosis and hormonal changes, lichen sclerosus, or human papillomavirus infection.2,4-6 The diagnosis relies on clinical, dermoscopic, and histopathologic examination. Vulvar melanosis can be so black that it is almost indistinguishable from melanoma.7 It can range from “banal tan patches to wildly bizarre irregularity of pigment,”8(p455) making a clinical diagnosis potentially difficult. Researchers have identified a range of dermoscopic patterns, including ringlike, globular-like, cobblestone-like, and reticular-like, structureless, and parallel patterns.9,10

IMPORTANCE Vulvar melanosis is a common pigmentary change that accounts for most pigmented vulvar lesions. It presents as single or multiple asymptomatic macules or patches of varying size and color that may be asymmetric with poorly defined borders. The differential diagnosis of melanocytic lesions includes melanoma, which creates anxiety for patients and the physicians who diagnose the condition and treat the patients.

OBJECTIVE To evaluate the clinical and dermoscopic features of vulvar melanosis and their changes over time.

DESIGN, SETTING, AND PARTICIPANTS In this cohort study, patients with vulvar melanosis were recruited and followed up in the Department of Dermatology, University of Florence, Florence, Italy, between January 1, 1998, and June 30, 2019. Data on patient characteristics and on both the clinical and dermoscopic features of the vulvar lesions were collected. Each lesion was photographed clinically and dermoscopically at initial evaluation and at annual follow-up visits.

MAIN OUTCOMES AND MEASURES The clinical, dermoscopic, and histopathologic features of vulvar melanosis and their changes over time.

RESULTS This cohort study included 129 women (mean age at diagnosis, 46 years [range, 19-83 years]) with vulvar melanosis. A total of 87 patients (67%) with vulvar melanotic lesions were premenopausal, and 84 patients (65%) had received some type of hormone therapy. The most frequent location for vulvar melanosis was the labia minora (55 [43%]), followed by the labia majora (33 [26%]). In 39 of 129 cases (30%), the lesions increased in size and changed color after initial evaluation but ultimately stabilized. No malignant evolution was documented in any patient during a median follow-up of 13 years (range, 5-20 years).

CONCLUSIONS AND RELEVANCE This study suggests that vulvar melanosis was a benign entity, and changes in lesions over time did not signify malignant transformation. An association between hormonal status and vulvar melanosis may be hypothesized.

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Vulvar melanosis, also known as vulvar lentiginosis or vulvar melanotic macules, is a pigmentary change that accounts for most pigmented vulvar lesions in women of reproductive age.1 It presents as a single macule or patch or as multiple asymptomatic macules or patches of varying sizes and brown to black color that tend to be asymmetric and have poorly defined borders. Although the most common location of vulvar melanosis is the labia minora, nearly all vulvar sites can be affected, including the labia majora, introitus, clitoris, vestibule, and posterior fourchette.2 Vulvar melanosis is more frequently reported in perimenopausal women. Cases in young girls should prompt physicians to check for multystem genodermatoses, such as Peutz-Jeghers syndrome, Carney complex, Noonan syndrome with multiple lentigines, Bannayan-Riley-Ruvalcaba syndrome, and Dowling-Degos disease, which can be associated with genital melanoses.3

The etiopathogenesis of vulvar melanosis is poorly understood. Researchers have proposed associations between vulvar melanosis and hormonal changes, lichen sclerosus, or human papillomavirus infection.2,4-6

The diagnosis relies on clinical, dermoscopic, and histopathologic examination. Vulvar melanosis can be so black that it is almost indistinguishable from melanoma.7 It can range from “banal tan patches to wildly bizarre irregularity of pigment,”8(p455) making a clinical diagnosis potentially difficult. Researchers have identified a range of dermoscopic patterns, including ringlike, globular-like, cobblestone-like, and reticular-like, structureless, and parallel patterns.9,10
Histologically, melanosis is characterized by an increase in pigmentation confined to basal keratinocytes and melanocytes, which are arranged as single cells at the dermo-epidermal junction, without evidence of cytologic atypia. Occasionally, melanocytes show prominent dendrites. Scattered subepithelial melanophages resulting from pigmented incontinence are usually noted. Concurrent changes of lichen sclerosus characterized by a lichenoid lymphocytic infiltrate and melanophages in the setting of fibrosis may be a cause of concern because a mistaken diagnosis of regressed melanoma can be suspected and rendered. Preserved rete ridges, vacuolar basal alterations with a thickened basement membrane, and a homogenized papillary dermis are features associated with lichen sclerosis. Crowded and disordered arrays of melanocytes with nuclear hyperchromasia and atypia, thick dendrites, pagetoid spread, and a variable subepithelial inflammatory infiltrate are associated with a diagnosis of melanoma.

Our experience suggests that vulvar melanosis has a benign clinical course. Although vulvar melanosis can change over time, it does not progress to a malignant neoplasm. This study evaluated the clinical, dermoscopic, and histologic features of a series of 129 women with vulvar melanosis, with a follow-up of approximately 20 years.

Methods

This cohort study examined the collected data of patients who received a diagnosis of vulvar melanosis based on results of both clinical and dermoscopic examinations between January 1, 1998, and June 30, 2019, at the Skin Cancer Unit of the Department of Dermatology at the University of Florence, Florence, Italy. Patients typically complete yearly follow-up visits after their initial diagnoses. The Azienda Toscana Centro institutional review board approved this retrospective study. Patients provided written consent.

The data collected in the database included the characteristics of the patients (eg, age, menopause status, and hormone use) in addition to the clinical and dermoscopic features of the vulvar lesions. Each lesion was photographed clinically and dermoscopically. The equipment used for the dermoscopic examination consisted of a handheld dermatoscope (Heine Delta 20, Heine Optotechnik). Both the clinical and dermoscopic features of all of the lesions were photographed using a high-resolution compact digital camera (Olympus Digital model No. E-520, a 7.1-megapixel digital photographic camera with a 3.8 optical zoom lens, a focal length of 28-105 mm in a 35-mm format, and a maximum lens aperture of f/2.8-f/5.6; Olympus America Inc). The dermoscopic features were photographed using Dermaphot (Heine Optotechnik), which connects the dermoscope to the camera to generate reproducible, high-quality dermoscopic images at 10-fold magnification in JPEG format. These clinical and dermoscopic images were stored on a Microsoft Windows (Microsoft Corp)-based personal computer. Biopsies were performed only for lesions suspicious for melanoma and/or for lesions that changed significantly during the follow-up period. An incisional biopsy site was chosen based on the most clinically significant areas. The clinical history of the lesions, the results of dermoscopic examinations, and the histopathologic features of the melanosis were evaluated. Three investigators (V.D.G., F. Scarfi, and A.G.) with expertise in pigmented lesions and dermoscopy and no knowledge of the clinical history of the lesions independently analyzed the archived digital dermoscopic images and completed a printed questionnaire to categorize the lesions according to typical dermoscopic pattern analysis. These dermatologists possessed identical levels of training and experience in dermatology, each with more than 5 years of practice in dermoscopy. The dermoscopic pattern and the presence or absence of dermoscopic features in a given lesion were defined by the agreement of at least 2 of the 3 dermatologists. The color of the lesion was also recorded. Histopathologic slides were reviewed by a dermatopathologist (D.M.) with expertise in melanocytic lesions to confirm the diagnosis and evaluate the dermoscopic-histopathologic associations.

Results

Of the 165 cases of vulvar melanosis that were observed between January 1, 1998, and June 30, 2019, 129 were included in this study. Thirty-six cases were excluded because of lack of data, absence of regular follow-up, or both. The mean age of patients at the time of diagnosis was 46 years (range, 19-83 years). A total of 80 patients (62%) were between 25 and 50 years of age, and only 7 (5%) were younger than 25 years. A total of 54 patients (42%) were menopausal at the time of diagnosis, and 84 patients (65%) had received hormone therapy or contraceptives or hormone replacement therapy after menopause for at least 6 months before the melanosis diagnosis. Of these 84 patients, 52 (62%) were younger than 50 years.

For the patients in this study, vulvar melanosis occurred on the labia minora (55 [43%]), on the labia majora (33 [26%]), on both the labia minora and the labia majora (19 [15%]), on the posterior fourchette (7 [5%]), on the vestibule (5 [4%]), and on the clitoris (2 [2%]). For 19 patients (15%), melanosis was multifocal (Figure 1). Regarding palpability, all of the lesions...
were flat (Figure 2). A total of 90 of the lesions (70%) were less than 10 mm in size. The median follow-up period was 13 years (range, 5-20 years). For 47 patients (36%), a histologic examination was
performed because the vulvar lesion was suspicious for melanoma and/or changed significantly during follow-up. The final histopathologic diagnosis was vulvar melanosis for all biopsied lesions. During follow-up, 4 patients received a diagnosis of lichen sclerosus, and 3 received a diagnosis of melanoma at other sites. For 37 patients (29%) who were younger than 50 years, a slow increase in size was recorded over a mean period of approximately 18 months (range, 14-23 months), followed by stabilization of the lesion. For 13 patients (10%) who were older than 70 years, a clinical regression of melanosis was observed.

The most common dermoscopic parameter was a homogenous or nonhomogeneous diffuse pigmentation (97 of 129 [75%]) that was characterized by light brown, dark brown, and/or black color without other distinguishing aspects (Figure 1B). A parallel pattern was detected in only 15% of the analyzed lesions (19 of 129). A total of 10% of cases (13 of 129) presented a nonspecific pattern owing to the absence of well-defined or recognizable dermoscopic features. A ringlike pattern (Figure 2B) was found in 19 cases (15%). In general, globular or reticular patterns were not present.

The lesions showed no pigmented network. Furthermore, the vascular pattern was difficult to characterize and could not be assessed because of the specific anatomy of the site, which highlighted a large number of vascular structures on the entire vulvar mucosa (Table 1). The colors that were detected by dermoscopic examination were shades of light to dark brown in all cases and black in 77 cases (60%). These colors were mixed to varying degrees within the same lesions. Blue and gray colors were recorded in only 9 cases (7%) (Table 2).

**Discussion**

The clinical features of vulvar melanoses can overlap with those of melanoma. They can be asymmetric and unilateral with an intense and even nonhomogeneous pigmentation that is either focal or diffuse. Because of its inconspicuous location, patients may not be aware of the presence of vulvar melanosis, and an adequate medical history is very difficult to achieve for physicians. Moreover, the traditional rule of asymmetry, border irregularity, color variation, diameter greater than 6 mm,
and evolving in a new or changing lesion (the ABCDEs) is not useful in the clinical diagnosis of pigmented lesions of the vulva, in which the history of the lesion is often not known.\(^2\) Therefore, it is important for all physicians (both gynecologists and dermatologists) who treat patients with these lesions to be aware of their characteristics to arrive at a correct diagnosis without subjecting the patient to unpleasant and often unnecessary biopsies or excisions at this particular site.

In this study, the epidemiologic, clinical, and dermoscopic characteristics of a large series of cases of vulvar melanosis were followed over time. The mean age of diagnosis was 46 years (range, 19-83 years), and 67% of lesions appeared in patients younger than 50 years, which suggests that hormonal status may have a role to play in the etiopathogenesis of vulvar melanosis. Although the small number of patients in our series does not allow us to draw definitive conclusions, this association is further supported by the absence of reports of vulvar melanosis before menarche, both in the present study and in the literature. Furthermore, 65% of patients had received hormone therapy. In about 30% of patients, vulvar melanosis increased in size and changed in pigmentation for a mean of 18 months (range, 14-23 months) from the time of diagnosis. All patients who showed this evolution were premenopausal women, which is another piece of possible evidence of an association between hormonal status and melanosis. Furthermore, in the literature\(^20\) and in our experience, melanoses of the male genital mucosa occur less frequently than those of the female genital mucosa. As estrogens stimulate skin pigmentation by increasing melanin synthesis,\(^21\) sex-related differences in both serum estrogen levels and estrogen receptor expression may validate our findings. In particular, serum estrogen levels are higher in premenopausal women compared with both men and postmenopausal women,\(^22\) and cutaneous estrogen receptor expression is lower in men compared with women and decreases among women after menopause.\(^23\) Regarding the dermoscopic diagnosis, the present study indicates that the classic cutaneous dermoscopic parameters were not easily detectable at the level of the genital mucosa or were not particularly reproducible among observers. Even new features that have been described by various dermatologic schools, such as the ringlike pattern that was found in only 15% of the patients in the present study, are not a reliable and accurate diagnostic dermoscopic clue. Instead, a dermoscopic color assessment of the lesion was a useful and significant tool for diagnosing vulvar melanosis. The colors that were present in the vulvar melanoses of the patients were various shades of brown (100%) and black (60%) (Figure 3C and D). Dermoscopically, these colors correspond to superficial structures, which correspond to the histopathologic condition of melanosis that is characterized by hyperpigmentation of basal keratinocytes. Conversely, a vulvar atypical melanocytic lesion, such as melanoma, shows, in addition to black and/or brown colors, a combination of gray, blue, or white colors, which are almost never observed in benign vulvar melanosis (Figure 3A and B).\(^20\) The presence of these colors is due to deeper lesions infiltrating the dermis, such as melanoma. In vulvar melanoma, even when the Breslow depth is less than 1 mm, we frequently observe a blue-white veil, white structures, and an atypical vascular pattern (such as milky red areas and atypical vessels), which are lacking in vulvar melanosis. These structures and patterns represent dermoscopic features of thick cutaneous melanomas (such as a Breslow depth \(\geq 1\) mm).\(^16\) Therefore, in a pigmented vulvar lesion, the presence of black and/or brown colors with a homogenous or nonhomogeneous arrangement and without red, gray, or blue colors and/or without typical dermoscopic parameters for melanocytic lesions allows for a diagnosis of vulvar melanosis with good diagnostic accuracy (Table 2). In this series, no lesion underwent a malignant evolution, and no patient developed vulvar melanoma of either a melanotic macule or normal genital skin during the follow-up period. These data suggest that vulvar melanosis is a benign entity that is unlikely to be associated with the risk of developing vulvar melanoma. With respect to comorbidities and associations with other pathologic conditions, no significant findings emerged from the present study, although we noted 4 cases of lichen sclerosus. These cases appeared after the diagnosis of vulvar melanosis among patients older than 65 years and are compatible with advanced age.

**Limitations**

Several limitations of this study need to be considered. First, our data are from a single center, potentially limiting the generalizability of our results. Moreover, although, to our knowledge, this study is the largest cohort study of vulvar melanosis to date, the number of lesions included and the

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**Table 1. Dermoscopic Features in 129 Cases of Melanosis**

<table>
<thead>
<tr>
<th>Feature</th>
<th>No. (%)</th>
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<tbody>
<tr>
<td>Diffuse pigmentation (homogeneous or dishomogeneous)</td>
<td>97 (75)</td>
</tr>
<tr>
<td>Parallel pattern</td>
<td>19 (15)</td>
</tr>
<tr>
<td>Nonspecific pattern(^a)</td>
<td>13 (10)</td>
</tr>
<tr>
<td>Ringlike pattern</td>
<td>19 (15)</td>
</tr>
<tr>
<td>Pigment network</td>
<td>0</td>
</tr>
<tr>
<td>Dots and globules</td>
<td>0</td>
</tr>
<tr>
<td>Pseudopods and streaks</td>
<td>0</td>
</tr>
<tr>
<td>Blue-white veil</td>
<td>0</td>
</tr>
<tr>
<td>Regression (gray-blue areas, white areas, or peppering)</td>
<td>0</td>
</tr>
<tr>
<td>Vascular pattern</td>
<td>NU</td>
</tr>
</tbody>
</table>

Abbreviation: NU, not useful in this anatomical location.\(^a\) Absence of well-defined or recognizable dermoscopic features.

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**Table 2. Dermoscopic Colors in 129 Cases of Melanosis**

<table>
<thead>
<tr>
<th>Color</th>
<th>No. (%)</th>
<th>Correlation with anatomical structures and histopathologic aspects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Black</td>
<td>77 (60)</td>
<td>Stratum corneum, melanin, and blood</td>
</tr>
<tr>
<td>Brown</td>
<td>129 (100)</td>
<td>Epidermis and melanin</td>
</tr>
<tr>
<td>Gray</td>
<td>9 (7)</td>
<td>Upper dermis and melanin</td>
</tr>
<tr>
<td>Blue</td>
<td>9 (7)</td>
<td>Deep dermis and melanin</td>
</tr>
<tr>
<td>Red</td>
<td>0</td>
<td>Dermis and vascularity</td>
</tr>
<tr>
<td>White</td>
<td>0</td>
<td>Depigmentation, scar, and regression</td>
</tr>
<tr>
<td>Yellow</td>
<td>0</td>
<td>Sebaceous material and hyperkeratosis</td>
</tr>
<tr>
<td>Orange</td>
<td>0</td>
<td>Erosion and ulceration</td>
</tr>
</tbody>
</table>

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Conclusions

This study presents a series of cases of vulvar melanosis with 20 years of follow-up. It suggests a role for hormonal status as a risk factor in the pathogenesis of these lesions. Approximately 30% of lesions increased in size and/or changed pigmentation and then stabilized after about 18 months without malignant evolution. Colors in the lesion are more important than the classic dermoscopic parameters in the diagnosis. Vulvar melanosis is black and/or various shades of brown, whereas the combination of red, blue, or gray colors in the lesion should be viewed with suspicion and necessitate a biopsy.

ARTICLE INFORMATION

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Author Contributions: Dr De Giorgi had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: De Giorgi, Gori, Massi.
Acquisition, analysis, or interpretation of data: De Giorgi, Salvati, Scarfi, Maida, Trane, Silvestri, Portelli, Venturi, Covarelli, Massi.
Drafting of the manuscript: De Giorgi, Gori, Salvati, Scarfi, Maida, Silvestri, Venturi, Massi.
Critical revision of the manuscript for important intellectual content: De Giorgi, Gori, Salvati, Trane, Portelli, Covarelli, Massi.

Statistical analysis: Scarfi.
Administrative, technical, or material support: Trane, Portelli.
Supervision: De Giorgi, Gori, Covarelli.

Conflict of Interest Disclosures: None reported.
REFERENCES