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Vulvar pigmented lesions: a retrospective study and a review of literature

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Summary

Aims: The authors aimed to accumulate knowledge and experience on clinical and dermoscopic findings of female genital pigmented lesions. *Materials and Methods:* The study was performed on a retrospective basis by reviewing the patient files with a diagnosis of genital hyperpigmentation. Dermoscopic findings, clinical diagnosis, and histopathologic diagnosis, if any, were documented. *Results:* A total of 40 patients with 70 pigmented lesions were reported. A great majority (75%) of these 40 patients were referred by a gynecologist. The most common diagnosis was genital melanosis (68.5%). Dermoscopically, parallel and ring patterns were present in the great majority of genital melanosis (72.9%). In melanocytic nevi (MN), dermoscopy revealed reticular, globular, homogenous, and cobblestone patterns. *Conclusion:* Knowing the frequently encountered pigmented lesions of female genitalia and its dermoscopic features is helpful in the differential diagnosis of benign and malignant tumors. Pigmented lesions on the genital area are unnoticed by the patients, and their referral by a gynecologist is the commonest way to screen.

Key words: Dermoscopy; Pigmentation; Female genitalia.

Introduction

Pigmented lesions of the female genital area are seen in approximately 10% of women throughout life [1]. Though there are a number of pigmented benign lesions, the malignant potential of melanocytic lesions of the vulva are well described [2]. Furthermore, late diagnosis and poor prognosis of female genital tract (FGT) melanoma is still a major concern for clinicians. Melanocytic nevus, pigmented seborrheic keratosis, genital melanosis, and lentiginosis are benign pigmented disorders, without known transition to malignant melanoma. However, they constitute a diagnostic and therapeutic problem due to the still limited knowledge on the subject. The present is a retrospective study on clinical and dermoscopic findings of 40 patients with multiple pigmented lesions of FGT, seen at the dermatology outpatient clinic.

Material and Methods

The study was performed on a retrospective basis in 40 Turkish women, by reviewing the patient files with a diagnosis of genital hyperpigmentation who had dermoscopic imaging. Patients with a diagnosis of anogenital warts were excluded. All the patients were seen by a single dermatologist at the Department of Dermatology, between 2012 - 2013. The data regarding the patients' age, duration of the lesions, their anatomical location, number, and diameter were recorded. Dermoscopic findings with reference to the patterns defined so far, clinical diagnosis, and histopathologic diagnosis, if any, were also documented according to the patients' files. Digital dermoscopic images of all the lesions were photographed with a dermoscope which was covered by a standard stretch film to prevent contamination of the medical equipment. Tenets of the current version of the Declaration of Helsinki were followed and institutional ethical committee approval was granted.

Results

In this study, a total of 40 patients with 70 pigmented lesions were reviewed. The average age of the study group was 41.2 (range: 17−73). A great majority of 40 patients (75%) were referred by a gynecology department, where the lesions were first noticed in 24 of them (60%). The dermatologic lesions were composed of 56 solitary, seven diffuse patches, and seven multiple pigmentations. The examined 70 lesions were diagnosed under seven titles: genital melanosis in 48 of 70 (68.5%), melanocytic nevi (MN) in 16 of 70 (22.8%), blue nevus and seborrheic keratosis each in two of 70 (2.8%), post-inflammatory hyperpigmentation, Becker nevus, and melanosis in association with lichen scleroatrophicus (LSA), each in one of 70 (1.4%). In addition, physiologic pigmentation was present in six of 40 patients (15%), and cherry angiomas accompanying the lesions were found in two of 40 (5%). Every lesion was counted in terms of anatomical area and calculations were done accordingly. The most frequently involved genital area was labium minus (26.3%). The other areas, in decreasing order of frequency, were labium majus (23.6%), perianal area (23.6%), perineum - the area be-

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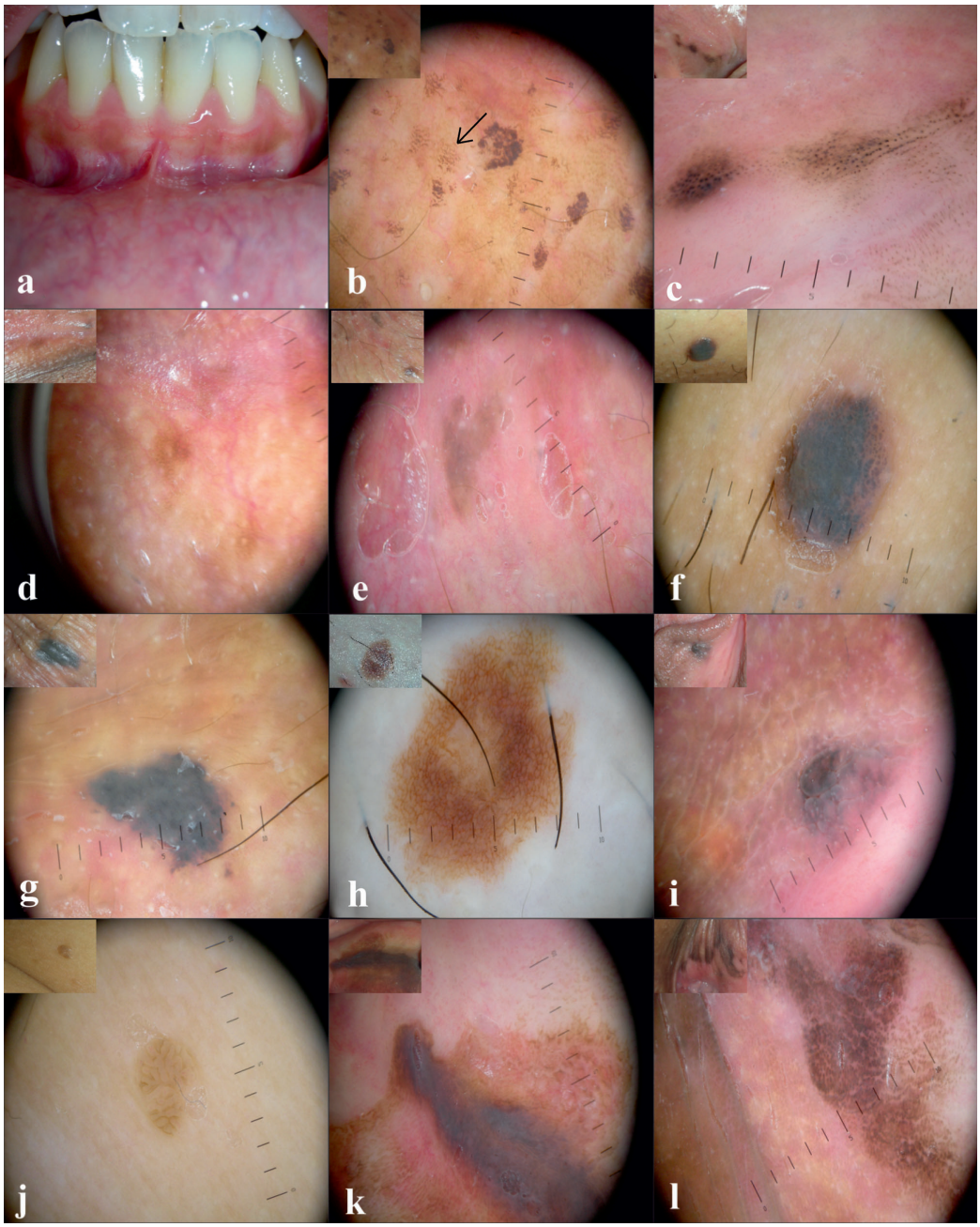

Figure 1. — Dermoscopic pattens of pigmented lesions of vulva and gingiva. a) Mandibular gingival pigmentation. b) Lentiginosis with parallel pattern. c) Lentiginosis with parallel pattern. d) Lentigo / melanosis with ring pattern. e) Melanosis with homogenous pattern. f) Melanocytic nevus with globular pattern. g) Blue nevus with blue globules. h) Melanocytic nevi with reticular pattern. i) Melanocytic nevus with cobblestone pattern. j) Seborrheic keratosis with cerebriform pattern. k) Parallel - ring and blue homogenous patterns. Histopathologic result is melanosis. l) Globular and parallel pattern. Histopathologic result is melanosis. Original magnification × 10.

tween posterior part of external genitalia and anus - (12.5%), forchette (9.7%), mons (2.7%), and clitoris (1.3%). Only four (10%) of the patients reported a surgical intervention (laser, cauterization) on the genital area. Oral mucosal involvement was found in 12 (30%), who had gingival pigmentation (Figure 1a), and four had additional buccal pigmentation. Axillary pigmentation and melanonychia was observed in two (5%) patients.

A total of eight predominant patterns were identified by dermoscopic analysis in the present study. The parallel pattern was defined as linear and curved streaks made of lines or globules parallel to the skin surface [3] and was observed in 37.3% of the lesions (Figures 1b, 1c). The ring-like pattern that was characterized by multiple round to ovoid structures with a hyperpigmented rim was found in 20% of the lesions (Figure 1d) [3]. The homogenous or structureless pattern, which shows a diffuse homogenous pigmentation [3], was present in 17.3% of them (Figure 1e). The globular pattern composed of aggregated round to ovoid brown to blue pigmentations was seen in 13.3% (Figure 1f, 1g). The reticular-like pattern displaying an ovoid or round honeycomb appearance was observed in 6.6% (Figure 1h) [3]. The

cobblestone pattern composed of aggregated and angulated globules in a raised lesion and cerebriform pattern resembling the sulci and gyri of the brain surface were noticed in 2.6% of the lesions (Figure 1i, 1j). There was more than one pattern in some of the mentioned lesions above (Figure 1k, 1l). There was no prominent dermoscopic vascular pattern or polycircular pattern to report among these lesions. Histopathology was made only in three patients, with the results reported as 'lentigo', 'lentiginosis', and 'seborrheic keratosis'.

Discussion

Pigmented lesions of female genital tract, which are present in 10-12% of the general population, are a major concern for both clinicians and patients, and account for 20% of vulvar disease lesions [4].

The pigmented lesions, classified as melanocytic hyperplasia (nevus, melanoma), epidermal hyperpigmentation without prominent epidermal hyperplasia (lentigo, melanosis, post-inflammatory hyperpigmentation), and non-melanocytic lesions (seborrheic keratosis and pigmented intraepithelial neoplasia) are mostly benign with atypical clinical findings causing diagnostic difficulties.

In the present retrospective study group, the women were commonly middle aged; the average age was 41.2 years. The diagnoses were made after clinical and dermatoscopic examinations, except for three patients. Genital melanosis was the most frequent diagnosis (68.5%) and the labia minora were the most often involved site (26.3%), as in the other studies [5]. Based on clinical inspection, there are several entities comprising genital melanosis. Lentigo is a small, < four-mm, hyperpigmented, brownish macule that may be found anywhere on the vulvar skin or mucosa [6]. Lentiginosis is characterized by multiple asymptomatic, asymmetric tan to black colored small macules with irregular borders [6, 7]. Venkatesan *et al.* reported lentigines in 68% of pigmented vulvar lesions in reproductive age women [7]. Larger brown-to-black macules ≤ ten cm in diameter, often showing irregular margins and asymmetry, multifocality, and pigment variegation have been defined as melanosis [6, 8]. Though these lesions are not similar clinically, they show a similar histopathology of increased pigmentation of basal keratinocytes with slightly increased or normal number of melanocytes. It occurs most often in premenopausal women and involves mucous membranes [5]. As is known, despite the atypical clinical appearance, progression to melanoma is not known. Not to cause any ambiguity on this subject, melanotic macule/melanosis has been used for all these three benign pigmented lesions of mucosa-lentigo, lentiginosis, and melanosis.

Dermoscopy is a non-invasive diagnostic tool for pigmented skin lesions, though we have less experience on this anatomical area. In 2004 Francesca *et al.* identified three major dermoscopic patterns in benign mucosal melanotic macules/melanosis, known as parallel pattern, structureless pattern, and reticular-like pattern [9]. In their cases of 11 vulvar melanosis, they reported one (10%) parallel pattern and ten (90%) structureless pattern. They concluded that the presence of structureless and parallel patterns may exclude diagnosis of malignancy [9]. Afterwards in 2008, Angela *et al.* reported a ring-like pattern in a larger series of 87 lesions of vulvar melanoses [10]. In another study of 24 mucosal melanotic macules on the FGT, six different dermoscopic patterns were observed including dotted-globular pattern, homogeneous pattern, ring-like pattern, fingerprint-like pattern, and two new dermoscopic patterns, namely the fish scale-like pattern and hyphal pattern which were then considered to be variants of ring-like pattern and found to be distinctive for melanosis [1]. In Lin *et al.* study [1] benign lesions showed dotted globular (25%), homogenous (25%), scale-like/hyphal, and ring (50%) patterns. Finally in 2014, the parallel-like pattern and ring-like pattern detected in flat, brown macules of the mucosal areas were accepted as strongly predictive of benign vulvar mucosal melanosis [11]. As a sum, dermoscopy may show structureless, reticular, parallel or ring-like patterns in melanosis [7]. Ferrari *et al.* proposed to use these patterns with confidence in the non-invasive diagnosis of melanosis [4]. However, their inference is open to discussion, because structureless pattern and reticular pattern have been detected in melanoma, too [1, 4]. In patients with genital melanosis, the present authors detected structureless pattern in 18% of the lesions, which were multiple, small, one- to three-mm in diameter and light brown in color and not suspicious for melanoma. Instead, parallel and ring patterns were present in the great majority (73%) of the lesions. In our study, population fish scale-like pattern and hyphal patterns were also frequently encountered and grouped under the ring pattern. Lastly, globular pattern was only seen in 8.1% of the genital melanosis lesions. The clinical-dermoscopic correlation was found to be relevant according to the features reported so far.

Vulvar melanosis may be associated with lichen sclerosus which was also experienced in one case in the present small series. The present authors detected a homogenous light brown pigmentation around atrophic round macules of LSA, which they assessed as a post-inflammatory process. Since LSA may accompany melanoma [7] or a special subset of MN that tends to be unusually dark and small [5], follow up is indispensable in these patients. Some authors support removal of any pigmented lesion found within LSA [7]. However, the present authors believe that we still need to know more about malignant potential of these pigmentations to excise every one of them.

MN was the second common (22.8%) pigmented lesion found in the present study. The morphological hallmarks of a MN include young age [4], small size, even brown or tan

color, well-demarcated regular borders, and a size smaller than seven mm [5, 7]. Most of the time MN is solitary. It has been estimated that 23% of pigmented vulvar lesions are MN [7]. In the present study, 16 of 70 lesions were diagnosed with MN. They were commonly located on the labium majus, perianal area, perineum, mons pubis, and labium minus. The average age was 38.9 years in the present MN patients. The low incidence of MN in older age group was explained by involution of these lesions [4]. We have limited knowledge on the dermoscopic patterns of vulvar nevi. In the literature, the most common patterns were found to be homogenous, cobblestone, and globular [12]. Additionally parallel and non-specific patterns were also reported [4]. In the present patients dermoscopy revealed reticular, globular, homogenous, and cobblestone patterns. Parallel and ring patterns were rare.

A clinical diagnosis of blue nevus was made in 5% of the present patients, though it is recorded to be quite rare [7]. Blue nevus is usually solitary and found on the buttocks, the sacral region, and occasionally on the dorsal aspects of the hands and the feet. Clinically, they usually present as pigmented papules, plaques, or nodules with dark-bluish or blue-black coloration [13]. Two blue nevi with a diameter of 6×4 mm and 9×6 mm found in the present patients were located on labium majus. Both of them showed globular blue pattern. The present authors believe they may be frequent on vulvar region but lack of routine genital examination hides such patients. There was only one case with multiple post-inflammatory pigmentation due to electrocauterization, in whom ring pattern was identified dermoscopically.

The present authors detected oral mucosal pigmentation in 30% (12/40) of their patients. None of them was associated with a syndrome. Gingival pigmentation found in them all, was striking. Buccal pigmentation was present in only four patients: two of them coexisting with gingival pigmentation and two were isolated. Patients with gingival pigmentation had a clinical diagnosis of melanosis in eight cases, melanocytic nevus in three cases, and Becker's nevus in one case. With the exception of Becker's nevus, all the patients who had oral mucosal pigmentation showed two or more genital pigmented lesions. Oral mucosal involvement may be a frequent accompanying sign in benign lesions and the present authors believe oral mucosal examination should be done in each patient.

Physiologic pigmentation, which is common in dark complexioned, is macular, symmetric hyperpigmentation accentuated at the posterior introitus, tips of labia minora, and perianal skin [7]. Of the present 40 patients, it was found in six (15%), whose pigmentation was located symmetrically on labia minora. The degree of hyperpigmentation is known to change during increased hormone secretion of adolescence and pregnancy. None of the present patients were pregnant at the time of examination and none was known to have an adrenal endocrine disorder.

It is important to differentiate malignant pigmented lesions from other benign entities. Melanoma of vulva represents 5 - 10% of all vulvar malignancies and 1 - 3% of all melanomas [2, 5, 7]. Vulvar melanoma may present as macules, papules, or nodules of irregular pigmentation, asymmetric borders, and a diameter larger than seven mm [2, 5]. Primary vulvar melanoma most commonly develops on the labia majora, followed by the labia minora and clitoral hood [2, 5, 7]. Blue black or gray colors are suggestive of melanoma [5]. However, about one-fourth of all vulvar melanomas are amelanotic [5]. Vulvar melanomas show a poor prognosis with a five-year survival of about 55% [5]. Thus, it is of great importance to make an early diagnosis.

There are a few studies investigating the dermoscopic patterns in melanoma. Accordingly, the combination of blue, gray, or white color plus structureless zones was highly predictive of melanoma [2, 14]. A multicomponent pattern composed of irregular dots and globules, multiple colors, a blue-white veil, and atypical vessels were also found in melanoma patients [1, 2, 4]. Ferrari *et al.* stated the importance of reticular depigmentation found in 80% of their cases [4].

Biopsy indications have been established according to the experience gained so far. Rapidly growing pigmented lesions and lesions showing black, blue,white or gray colors [14], and those showing multicomponent pattern [4], reticular depigmentation [3], and blue white veil [4] in dermoscopy are guides for biopsy. Furthermore, a biopsy is required for solitary pigmented lesions larger than one cm. Presence of a papular component or erosions accompanied by pain or pruritus necessitates a biopsy to rule out melanoma or pigmented vulvar intraepithelial neoplasia (VIN) [7]. An exclusive case of genital melanosis induced by bladder melanoma precludes generalization [7]. The present authors performed a biopsy in 3/40 patients which yielded diagnoses of genital melanosis and seborrheic keratosis.

In this study, nearly all of the patients (75%) had been referred to dermatology by the gynecologist. Patients are not aware of their pigmented lesions on the vulva due to the anatomical structure of this region, which cannot be observed directly. Most of the time, dermatologic examinations are performed on a complaint oriented basis due to the large surface area of 1.7 m^2. Furthermore, patients reject inspection of the area without prior decision and preparation. Hence, it is a very important point for the gynecologist to observe the area for pigmented lesions and refer the patient to dermatology consultation if necessary. In this way we may be able to detect early melanomas.

Though annual control visits were planned for the present patients, only two out of 40 (5%) came for a control visit in the following year. In the following second year two more control visits occurred, that made a sum of 10%. Hence, clinical follow-up did not seem to be a reliable

method of tracking such patients. The reason may be the prior preparation needed and the inconvenience due to the anatomical area. In these patients, the present authors believe that it is very important to make a decision on the first examination, and clinically or dermoscopically atypical lesions should be excised with a low threshold for indication.

Retrospective studies have some limitations. Therefore they are not suitable for very rare diseases. Indeed, the present authors did not detect any melanomas or syndrome associated with vulvar pigmentations. It should be kept in mind that this study was comprised of 70 pigmented lesions in 40 cases. Histopathology is the gold standard for diagnosis. However, in this retrospective series, histopathology was performed in only 7.5% of the patients for clinically suspicious lesions. Accordingly we have scarce data on clinicopathological correlation. Another issue may be the patient population that is mostly referred by a gynecologist. However, this is a fact that should be considered and points to the need for collaborative work with gynecologists for early detection of risky patients rather than selection bias.

Conclusion

The present authors documented the clinical and dermoscopic features of 70 pigmented lesions on the FGT, including genital melanosis, MN, blue nevi, post-inflammatoty pigmentation, seborrheic keratosis and Becker nevus. In this study, genital melanosis with parallel and ring patterns is the most common female genital lesion, followed by MN with reticular, globular, homogenous, and cobblestone patterns. Gingival mucosal pigmentation is a frequent counterpart (30%). Pigmented lesions on the genital area are unnoticed by the patients, and referral by a gynecologist is the prominent way to screen these lesions. It is a fact that melanomas are diagnosed at late stages of the disease and have a poor prognosis. The present authors hope that this study may arouse curiosity and serve to enrich the limited knowledge on this subject. Lastly, clinical follow up is not a reliable option in this subset of patients owing to the 5% control visits in the following year. With the limited knowledge on the subject, they believe that pigmented lesions of the FGT require further investigations.

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