

Pigmented Vulvar Lesions—A Pathology Review of Lesions That Are Not Melanoma

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■ **Abstract:** Clinicians caring for women are encouraged to be liberal in biopsying pigmented lesions of the vulva because of the importance of early detection of melanoma for better prognosis. This article reviews the histological diagnosis of nonmelanoma pigmented lesions. ■

Key Words: vulva, vulvar neoplasms, vulvar diseases

Clinicians caring for women are encouraged to be liberal in biopsying pigmented lesions of the vulva because of the importance of early detection of melanoma for better prognosis and because, on genital skin, significant and less significant lesions can appear grossly similar and less characteristic than on extragenital skin [1, 2]. Histologically, most of these pigmented lesions are unrelated; however in clinical practice, the differential diagnosis often included melanoma. Pigmented lesions are not rare in the vulva, affecting up to 10% of women at some point [2]. This is not unexpected because there is a greater density of melanocytes in genital skin [2]. When biopsies from these lesions arrive at the pathology laboratory, they may be seen by pathologists who do not subspecialize in gynecologic or dermatologic pathology. This article reviews the histological diagnosis of nonmelanoma pigmented lesions (see Table 1). Although dermatopathologists are familiar with most of these entities, general and gynecologic pathologists may be less so. As with all specimens,

pathological diagnosis is much improved if a clinical history (why the biopsy specimen was taken, and from where, at the least) is provided. Good reviews of the clinical appearance of these lesions are available [1, 2]. It should be mentioned that as measurement of depth is critical for melanomas, that if concern is high, a knife excision rather than a distorting punch biopsy should be considered.

NORMAL VULVAR PIGMENTATION

In normal vulvar pigmentation, melanin granules are contained within the cytoplasm of the squamous cells of the basilar layer (see Figure 1). The basal layer also contains scattered melanocytes, which produce the melanin, packaging it into melanosomes, which are then transferred to the keratinocytes. More darkly pigmented skin and mucosa shows greater amounts of melanin-containing keratinocytes; however, the number of melanocytes is the same in all skin tones.

DEFINITIONS

It is important for clinicians to be able to comprehend their reports. Some brief definitions of *dermspeak* as they pertain to pigmented lesions are as follows:

Melanocyte—cells that produce the pigment melanin.

Melanosome—membrane-bound packages of melanin that are produced by melanocytes and transferred to keratinocytes.

Melanophages—macrophages that have ingested melanin.

Acanthosis—thickening, blunting, and fusion of the rete pegs of the squamous epithelium.

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Table 1. Nonmelanoma Pigmented Lesions of the Vulva

Melanin-related vulvar lesions that may appear pigmented
Melanos/lentigo
Postinflammatory hyperpigmentation
Lichen simplex chronicus
Seborrheic keratosis
Condyloma acuminatum
VIN
Nevi/dysplastic nevi
Basal cell carcinoma
Dermatofibroma
Nonmelanocytic vulvar lesions that may appear pigmented
Acanthosis nigricans
Angiokeratoma
Purpura
Kaposi sarcoma

VIN, vulvar intraepithelial neoplasia.

Hyperkeratosis—an increase in the anucleated keratin layer.

Parakeratosis—nucleated keratinized squamous cells on the epithelial surface.

Papillomatosis—the formation of papillary projections of squamous epithelium, giving an irregular surface, as in condyloma acuminatum.

Pigment incontinence—spillage of melanin into the dermis. It may remain loose in the dermis or be ingested by melanophages (see previous mention).

MELANOSIS/LENTIGO

Lentigines are smaller areas of pigmentation (freckles), and melanos is more widespread. Melanos can be extensive on the vulva, where it affects the non-keratinized portions of the labia and introitus [1] and, hence, raises concern for melanoma by the extent and

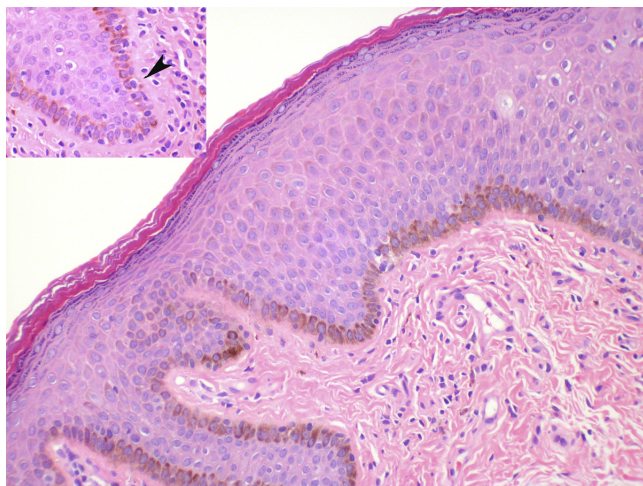


Figure 1. Normal vulvar epithelium—melanin-containing keratinocytes are seen along the basal layer. Scattered melanocytes are present (inset, arrow).

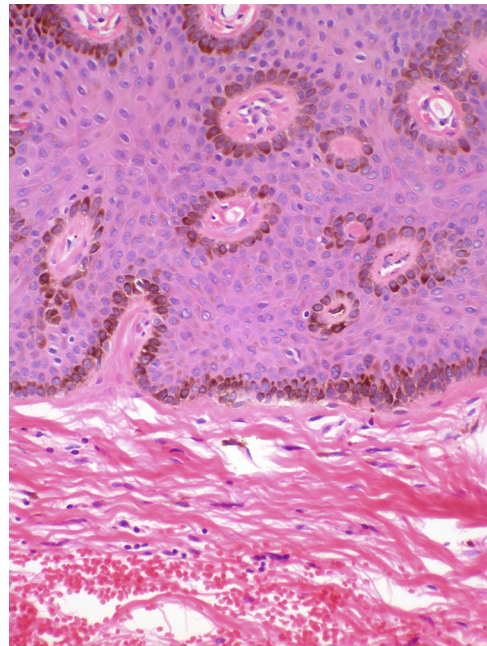


Figure 2. Lentigo/melanos. These lesions show increased pigmentation of the basal layer.

darkness of the lesion. It is asymptomatic and usually discovered incidentally. No therapy is required. Histologically, there is increased melanin in the basal layer of the squamous epithelium, and there may be an increase in melanocytes [1] (see Figure 2). Melanophages may be seen in the upper dermis [3].

POSTINFLAMMATORY HYPERPIGMENTATION

After a variety of inflammatory conditions, the vulvar skin may show hyperpigmentation, particularly in dark-skinned

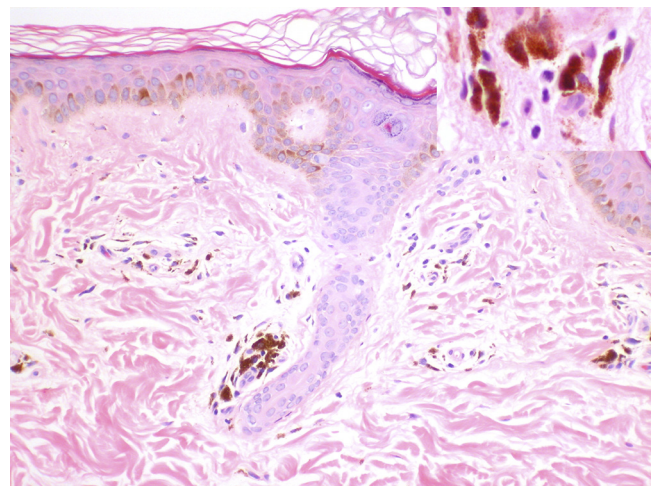


Figure 3. Postinflammatory hyperpigmentation demonstrating pigment incontinence in the dermis. Inset shows granular melanin pigment.

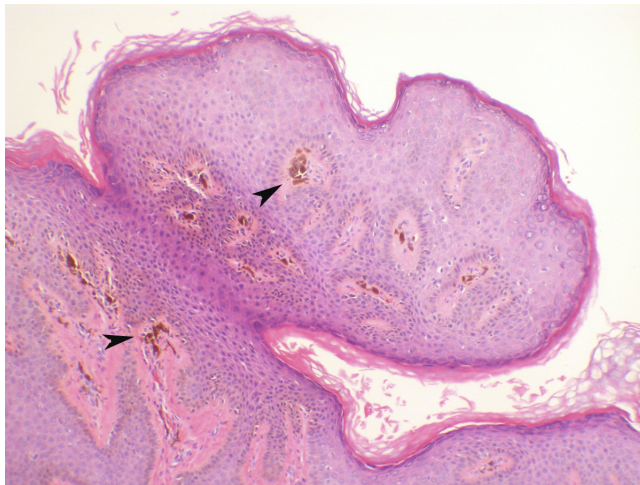


Figure 4. Skin tag with pigment incontinence (arrowheads).

individuals [1]. A known history of the underlying process is helpful in suspecting the diagnosis clinically. Histologically, there is melanin found in the dermis, either extracellularly or inside melanophages (see Figure 3), known as pigment incontinence. It is likely that this occurs secondary to disruption of the basement membrane from a wide variety of inflammatory conditions, including lichen sclerosus and lichen planus, as well as less common ones on the vulva [2].

ACANTHOSIS NIGRICANS

Acanthosis nigricans is associated with insulin resistance and obesity. Grossly, it appears as pigmented velvety skin plaques in areas such as the neck and groin. It may contain skin tags, which may appear pigmented as well.

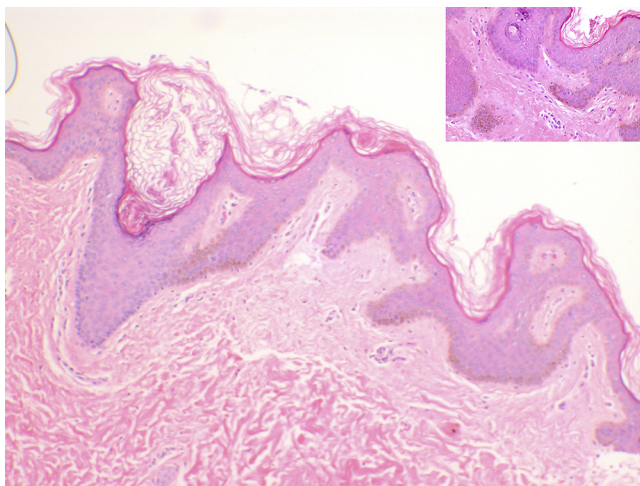


Figure 5. Acanthosis nigricans. The lesion shows hyperkeratosis and papillomatosis. Pigment is present in the basal layer but not increased (inset).

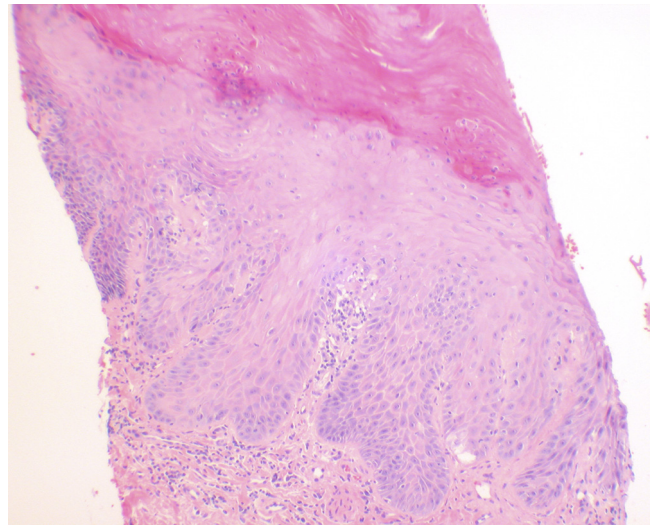


Figure 6. Lichen simplex chronicus showing marked acanthosis and hyperkeratosis. This lesion is frequently associated with pigment incontinence (not shown) and may have a clinically pigmented appearance.

The hyperkeratosis contributes to the brown appearance (see Figures 4 and 5). Therapy is not required. Histologically, acanthosis nigricans shows hyperkeratosis and papillomatosis without increased melanin or melanocytes or significant acanthosis [1, 3].

LICHEN SIMPLEX CHRONICUS

Formerly termed *squamous cell hyperplasia*, this lesion is now referred to by the dermatology terminology, *lichen simplex chronicus*, and is the manifestation of an

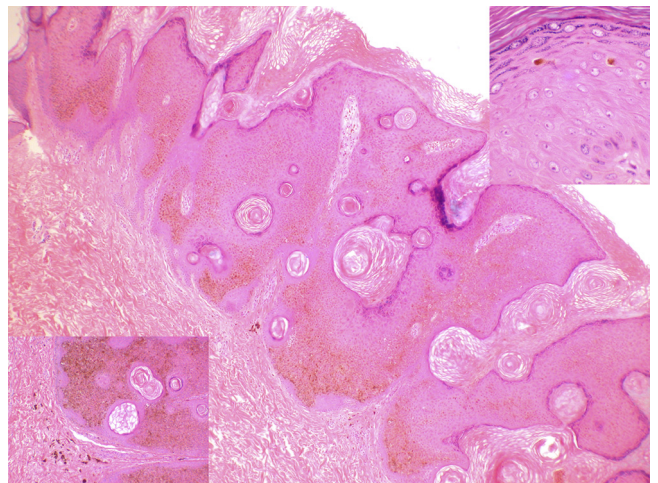


Figure 7. Pigmented seborrheic keratosis. Characteristic of seborrheic keratosis is hyperkeratosis, acanthosis, and pseudohorned cysts containing keratin (large image). There may be occasional intraepithelial dendritic melanocytes (right upper inset), and pigmentary incontinence (left lower inset).

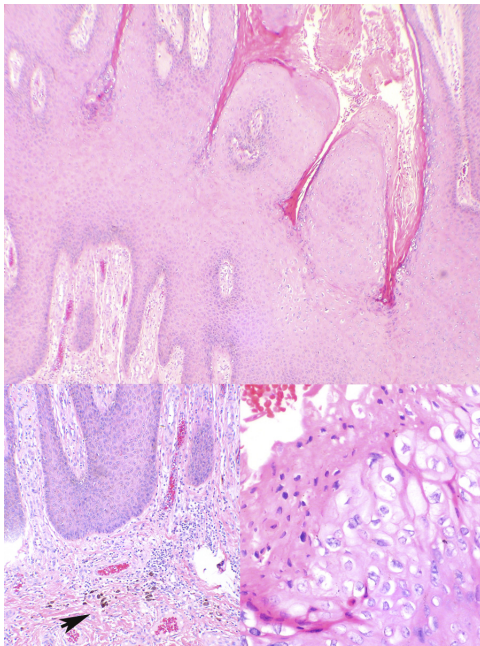


Figure 8. Condyloma acuminatum showing papillomatosis (top image), as well as pigment incontinence (left lower inset). The hallmark of HPV infection is the koilocyte, cells with wrinkled nuclei, with atypia within a perinuclear halo (right lower inset).

uninterrupted itch scratch cycle. It may appear dark or pigmented, and the skin appears thickened, with increased prominence of markings. Histologically, there is hyperkeratosis, acanthosis, and a dermal chronic inflammatory infiltrate. Pigment incontinence may be seen (see Figure 6). It is usually treated with topical steroids.

SEBORRHEIC KERATOSIS

Seborrheic keratoses are common benign lesions common on aging white skin. They are often reddish brown

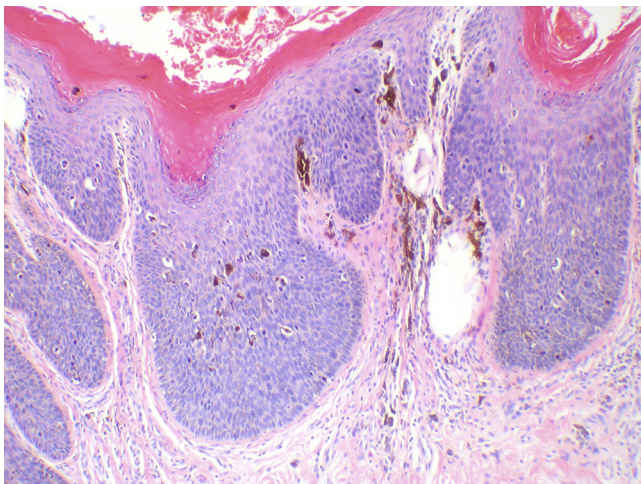


Figure 9. VIN showing melanin both in the dysplastic epithelium, as well as pigment incontinence.

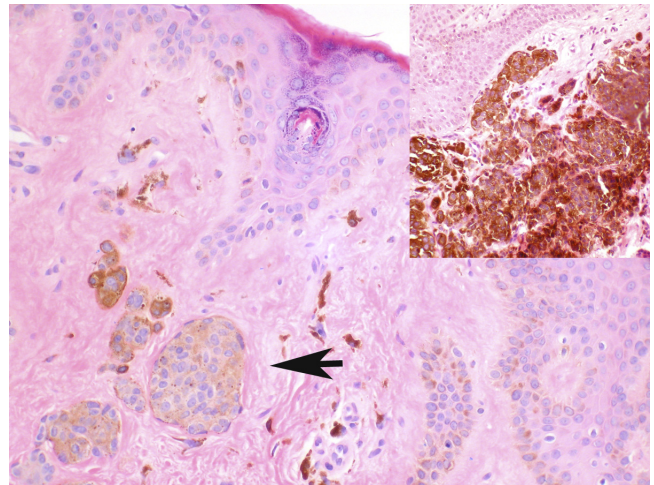


Figure 10. Intradermal nevus showing pigmented nevus cells in the dermis (arrow). In some of these lesions, the nevus cells can contain large amounts of melanin (inset).

and have a “stuck on” gross appearance. When they occur on the vulva, they may raise concern of melanoma. Histologically, seborrheic keratoses show hyperkeratosis, acanthosis, and pseudohorned cysts. Occasional dendritic melanocytes may be seen in the epidermis (see Figure 7).

PIGMENTED CONDYLOMA ACUMINATUM

Condyloma may be pigmented, particularly in darker-skinned individuals [1]. Histologically, condylomas are characterized by hyperplastic squamous epithelium, with hyperkeratosis, parakeratosis, acanthosis, and papillomatosis. The hallmark of HPV infection, the koilocyte, is a cell with an enlarged atypical raisin-shaped (wrinkled) nucleus, with a perinuclear halo. Pigmented melanocytes with prominent melanin granules may be seen in these pigmented warts [4] (see Figure 8).

PIGMENTED INTRAEPITHELIAL NEOPLASIA (VULVAR INTRAEPITHELIAL NEOPLASIA)

Grossly, vulvar intraepithelial neoplasia (VIN) may show a variety of colors, including brown, red, or white. Pigmented VIN may raise concern leading to a biopsy. In addition to the expected features of VIN, that is, maturation abnormality with disarray and atypia above the lower third of the squamous epithelium, pigmented VIN also demonstrates pigment incontinence in the papillary dermis [5] (see Figure 9).

NEVI/DYSPLASTIC NEVI

Although nevi are more common on sun-exposed skin, vulvar nevi may relate to the hormonal milieu [1].

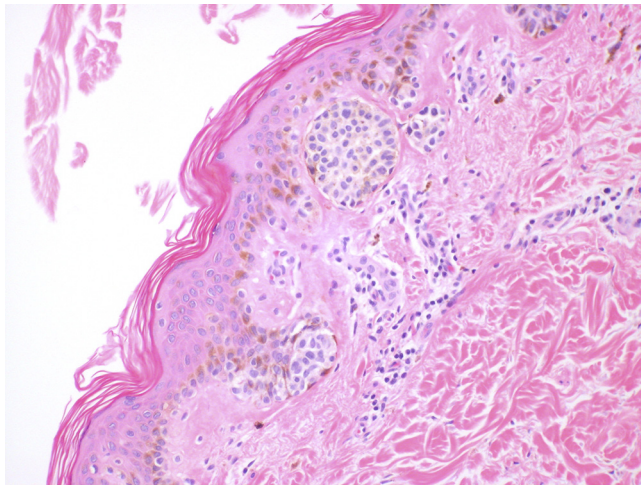


Figure 11. Dysplastic junctional nevus showing mildly atypical nests of nevus cells at the dermal-epidermal junction.

Histologically, a benign nevus is composed of clusters of melanocytes with no cytological atypia. Junctional nevi have these clusters located at the junction of the dermis and the epidermis. If there are cells in the dermis as well as the junction, it is termed a *compound nevus*, and an intradermal nevus has all the nevus cells in the dermis (see Figure 10). Intradermal nevi tend to be skin colored [1]. There is a tendency of atypical nevi with cytological atypia to form along the milk line. These do not signify a risk of malignant transformation [1]. Dysplastic nevi show both gross and microscopic features in between benign nevi and melanoma [1]. The histological hallmarks include cellular atypia, and

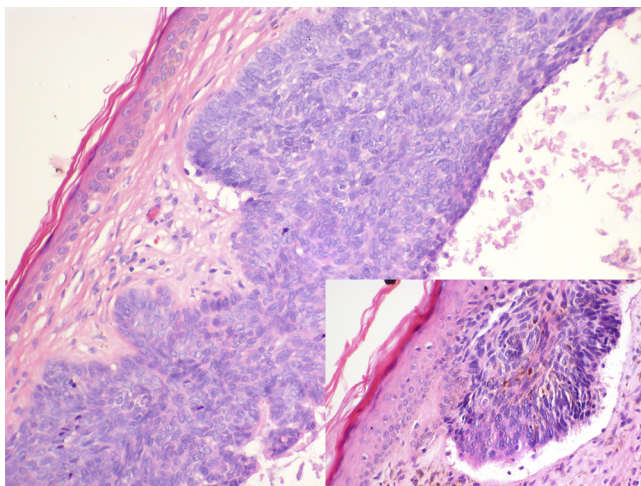


Figure 12. Basal cell carcinoma showing characteristic palisading of nuclei at the periphery of the lesion. Melanin pigment is seen in some of these lesions (inset).

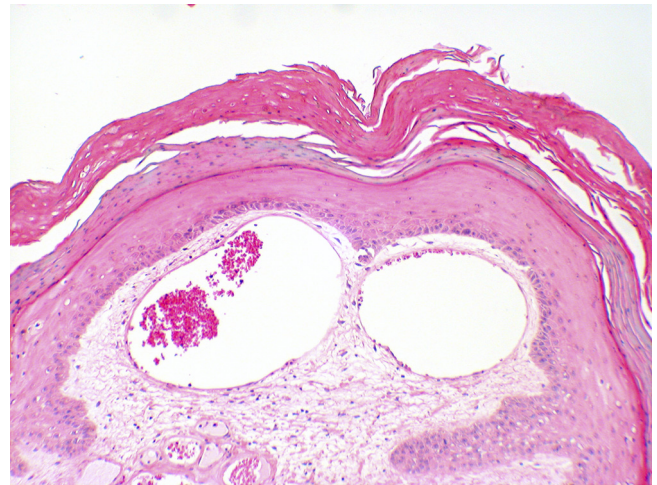


Figure 13. Angiokeratoma-dilated vascular spaces are seen beneath a hyperkeratotic overlying epithelium.

acanthosis with nests of nevus cells (see Figure 11). Fibrosis and dermal inflammation may be seen [1]. In distinction, gross irregularities of color and shape, as well as larger size suggest melanoma. Although uncommon, vulvar melanoma is the second most common vulvar malignancy after squamous cell carcinoma [6]. There is increased atypia of the cells, which tend to spread up into the epidermis. Mitotic activity may be seen.

PIGMENTED BASAL CELL CARCINOMA

Basal cell carcinomas are most often on sun-exposed skin but are known to occur on the vulva of older women. They may present with pruritis or discomfort [7]. Basal cell carcinomas show nests of proliferating basaloid cells with peripheral palisading. In addition, they may occasionally be pigmented, in which case pigment within tumor nests as well as pigmentary incontinence may be seen (see Figure 12).

ANGIOKERATOMA

Angiokeratomas are not melanocytic. They are small benign vascular lesions, similar to hemangiomas, with overlying hyperkeratosis (see Figure 13), which gives them a blue-black/purple appearance. They are often multiple.

PURPURA

Purpura grossly appears purple. It may be seen on the vulva in association with lichen sclerosus. Purpura histologically shows dilated superficial capillaries and

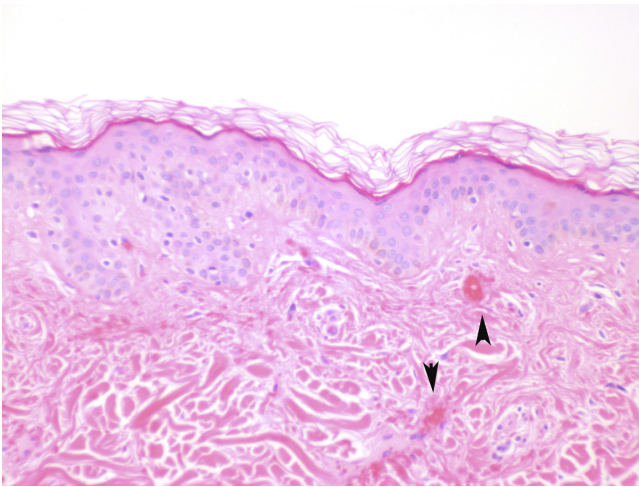


Figure 14. Purpura showing dilated a vascular space and extravasated blood adjacent (arrowheads).

extravasation of blood into the dermis. If chronic, hemosiderin may be seen (see Figure 14).

DERMATOFIBROMA

These benign lesions are often seen on the thighs and may be seen at a gynecologic examination. Grossly, they may be red-brown. Histologically, dense fibroconnective tissue is seen replacing normal dermis (see Figure 15). The basal layer of the epithelium may show increased pigmentation.

KAPOSI'S SARCOMA

Kaposi's sarcoma is rare in the vulva, but has been mistaken for a Bartholin abscess [8]. The lesions of Kaposi's sarcoma

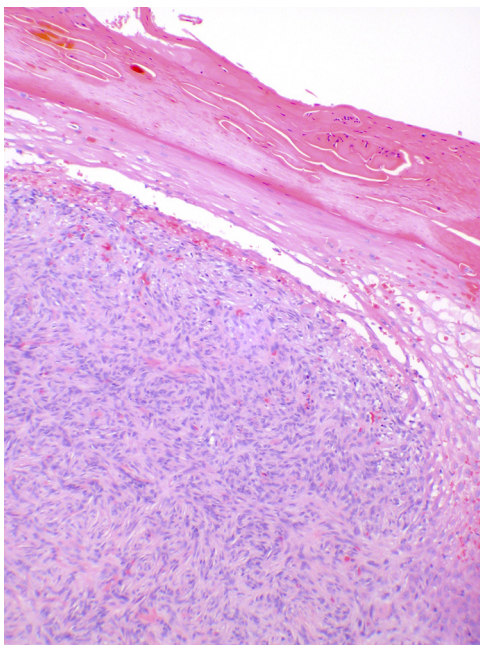


Figure 15. Dermatofibroma. A spindle cell lesion is seen in the dermis.

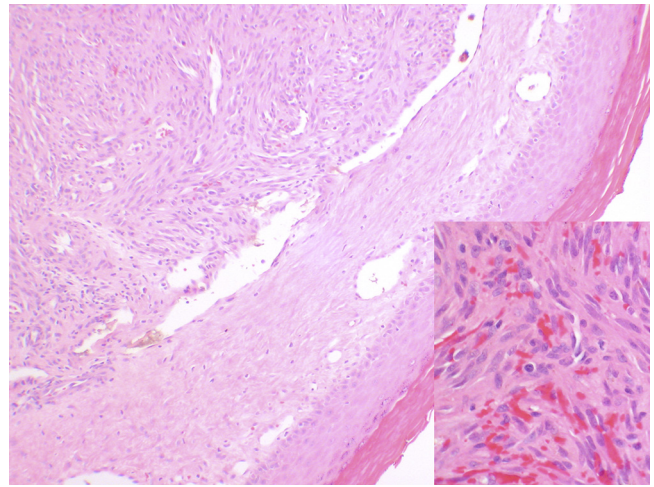


Figure 16. Kaposi sarcoma showing a spindle cell dermal lesion composed of slit-like spaces unlined by endothelium. These spaces may be filled with blood, supplying the purplish hue (inset).

are usually purple. A history of HIV, and clinical suspicion are often present. Histologically, multiple vascular spaces unlined by endothelium are seen (see Figure 16).

In summary, pigmented vulvar lesions may be received by pathology laboratories without information as to why the biopsy was performed. If a history of pigmentation is not provided, the report may not reflect that pigment is present, and the clinical question will remain unanswered.

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