

DERMOSCOPY OF GENITAL DISEASES: A REVIEW

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ABSTRACT

The male and female external genital regions are anatomical areas in which various types of skin disorders may occur. Although most of these conditions can be diagnosed by means of clinical examination accurate and medical history, in most cases further investigations with time consuming and/or invasive procedures are needed in order to reach the correct diagnosis. Dermoscopy, as a modern non-invasive tool, is able to better diagnose pigmented and non-pigmented skin tumours along with various inflammatory and infectious skin and appendage disorders. The aim of this paper is to provide a review of the use of dermoscopy in genital disorders based on published data and to include personal experience gained from real life, focusing on any possible gender difference and whether disease mucosal/semimucosal dermoscopy features may differ from those observed on the skin. In conclusion, genital dermoscopy should always be considered during clinical inspection in order to enhance the diagnosis or to rule out those conditions that may look similar but that show a different dermoscopy pattern thus narrowing down the differential diagnoses and avoiding unnecessary invasive investigations.

INTRODUCTION

The male and female external genital regions (i.e. the penis, the glans and the scrotum in the male, and the vulva in the female) are anatomical areas in which various types of skin disorders may occur. Although most of these conditions can be diagnosed by clinical examination and an accurate medical history review, in most cases further time consuming and/or invasive procedures such as skin biopsy are needed in order to reach a correct diagnosis. Dermoscopy represents a modern non-invasive tool able to improve the diagnosis of pigmented and non-pigmented skin tumours along with various inflammatory and infectious skin and appendage disorders^[1-3]. It may also be useful for prognostic assessment and treatment monitoring^[4].

Although dermoscopy is currently used for a variety of genital disorders both in males and females, specific literature on this field is limited. The aim of this paper is to provide a review based on published data, also focusing on any possible gender difference and whether disease mucosal/semimucosal dermoscopy features may differ from those observed on the skin.

MATERIALS AND METHODS

All the studies evaluating dermatoscopy of genital disorders published in the English literature were analyzed. An electronic search from January 1995 to January 2020 was performed using PubMed database with the following keywords: (dermatoscopy [Mesh] OR dermoscopy [Mesh]) AND (genital [Mesh] OR genitalia [Mesh] OR penis [Mesh] OR penile [Mesh] OR glans [Mesh] OR scrotum [Mesh] OR vulva [Mesh] OR vulvar [Mesh] OR labia [Mesh]). In addition, pertinent references not identified by search engines and retrieved from articles/books were also considered. All studies identified as relevant, including controlled studies, case series, case reports, and reviews were analyzed.

RESULTS

PHYSIOLOGIC CHANGES

Pearly penile papules and vestibular papillae

Pearly penile papules and vestibular papillae represent common anatomical variants of the normal epithelium of respectively the glans and the vestibular mucosa^[5]. Although poorly reported on, dermoscopy features of both conditions are quite typical^[6-10], showing in males uniformly sized whitish-pink small projections, regular in morphology, with cobblestone or grape-like aggregation. Delicate vascular structures may be visible within the projections^[6-8] (**Figure 1**). Similarly, in females, dermoscopy reveals a regular, linear and usually symmetrical array of uniform-sized whitish-pink papillae, which have separate bases^[9-10]. Subtle linear vessels may be observed within the papillae.

Fordyce's spots

Fordyce's spots are ectopic visible sebaceous glands that may be located either on the penis or the vulva^[11]. Dermoscopy has been reported in males only, where in the penile shaft a typical vascular *garland-like* aspect is revealed, whose *bows* seem to wind around yellowish bunch-like lobules without crossing them^[8]. These yellowish lobules histopathologically correlate with the sebaceous structures located in the dermis or submucosa. In the prepuce, Fordyce's spots have been described as *swallow's nests* or *bottle-like* formations containing a milky-white ovoid material and surrounded by non-arborizing vessels^[12].

BENIGN LESIONS

Seborrheic keratosis

Seborrheic keratosis is unusual in the genital area, and dermoscopy has been reported both in males and females^[13-20] showing the presence of the following features that, if combined, strongly suggest such a diagnosis: fissures and ridges (which typically give a cerebriform appearance), comedo-like This article is protected by copyright. All rights reserved

openings (roundish clefts generally dark brown, gray or black), milia-like cysts (round, brilliant, whitish structures), hairpin or looped vessels, and brownish, diffuse pigmentation, with demarcated borders, sometimes with a *moth-eaten* appearance (**Figure 2**). Comedo-like openings may not be visible in the vulvar areas, due to friction^[14]. In non-pigmented lesions, dermoscopy shows elongated papillary structures containing hairpin or looped vessels, which may be similar to genital warts (see below).

Angiokeratoma

Angiokeratoma of the scrotum is quite common and its incidence increases with age. Vulvar involvement is rare and sometimes may be mistaken for other benign and malignant lesions^[21]. Dermoscopy, that has been reported in both sexes^[8,16,18,22-24], typically reveals: well-demarcated red/dark lacunae, which correspond to wide dilated vascular spaces located in the dermis and that may be partially or completely thrombosed; whitish veil, corresponding to hyperkeratosis and acanthosis; erythema and hemorrhagic crusts.

Syringoma

Syringoma is a fairly common benign adnexal neoplasm with mainly ductal differentiation that usually involves the eyelid and the upper cheek, and rarely the genitalia^[25]. Dermoscopy of genital syringoma has been described in the vulva only, showing glittering, round-shaped or oval, yellow-whitish structures over a fading pink background, that histopathologically corresponded to small colloid material-containing cystic ducts. Dotted and short linear vessels have also been detected^[26].

Melanocytic naevi

Genital melanocytic naevi are mostly diagnosed during childhood and in younger adults with a prevalence of 3.5%, and a M:F ratio of 1.3:1^[27]. Several dermoscopy studies have been reported both in males and females^[16-20,27-35], showing characteristics similar to naevi on other parts of the

body. Most naevi have a single dermatoscopic pattern (reticular, clod or structureless) or two patterns, but unusual-looking naevi may have three patterns (multicomponent)^[16,19].

INFECTIOUS DISORDERS

Genital warts

Genital warts are a highly contagious sexually transmitted disease caused by human papillomaviruses. Their dermoscopy features have been extensively described in both sexes^[7-8,36-43]. Small, papular lesions usually show a *mosaic* pattern, consisting of a whitish reticular network surrounding unaffected areas centered by dotted vessels. On the other hand, typical cauliflower-like lesions reveal multiple, irregular projections, often arising from a common base (*fingerlike* pattern), with different sizes, shapes and colors, ranging from light pink to grey-whitish to brownish (**Figure 3**). Linear, elongated vessels that may be outlined by a whitish halo are generally detected within the projections; they correspond to the proliferation of capillaries in the papillary dermis, and appear coarser in shape and size in genital warts than in pearly penile papules and vestibular papillae^[43]. Haemorrhagic splits can be observed inside the lesions^[39-40]. Other described dermoscopic patterns include *knob-like*, *brain-like* and unspecific, which in many cases can be combined^[38].

Molluscum contagiosum

Molluscum contagiosum, an infection due to a Molluscipox virus that in young adults usually affects the genital area. Dermoscopy aspect of genital lesions has been reported both in males and females^[8,37,44], showing polylobular, white-yellowish, amorphous structures and a pore/orifice that can either have a central or eccentric position. The polylobular structures histopathologically correspond to lobulated, endophytic epidermal hyperplasia with intracytoplasmic inclusion bodies, separated by fine septae of compressed dermis^[45]. Vessels are generally visible with different arrangements, namely crown, radial and/or dotted patterns. In some cases, the polylobular This article is protected by copyright. All rights reserved

structures, the orifice or the vascular component may be absent, making the diagnosis more difficult^[44].

Candidiasis

The genital region is naturally an area which is affected by *Candida spp*. infection. In a case series, dermoscopy showed two main dermoscopic features: *cottage cheese-like* structures (sparse white coating) that correspond to the presence of Candida yeast colonies growth, and blurry linear vessels, due to dilation of subpapillary vessels^[46].

Scabies

The genital area is frequently involved during scabies infestation, and dermoscopy is a common diagnostic practice in many dermatologic centers. Compared to standardized skin scraping, dermoscopy is more sensitive, fast and well accepted by patients^[47]. Only one study specifically reported on dermoscopy of genital scabies (the gender was not specified)^[48], but dermoscopy features are typical. At low magnification (X10), it shows a small dark brown triangular structure located at the end of a subtle linear segment, resembling a delta wing jet with contrail; these structures correspond to the pigmented anterior part of the mite and the burrow, respectively^[47]. Higher magnifications (>X100) allow a clear visualization of the oval, translucent body of the mite and its legs, rostrum, eggs and feces^[47,49-50].

INFLAMMATORY DISEASES

Lichen sclerosus

Genital lichen sclerosus is a chronic inflammatory, immune-mediated disease which is a recognized precursor of genital cancer^[51-53]. Dermoscopy has been reported extensively in both sexes^[22,54-60]. Whitish background and patchy structureless areas, varying in colour from white-yellowish to milky-pinkish, are the most prevalent dermoscopic features (**Figure 4**). They correspond to dermal This article is protected by copyright. All rights reserved

sclerosis and hyalinization, which represent the main histopathological changes. A marked decrease in vessel concentration, configuring a sort of *vascular desertification*, has also been described. The remaining vessels are polymorphic.

Other possible dermoscopic features include red to purpuric, structureless, well circumscribed dots, globules or blotches corresponding to blood spots and mainly due to scratching, and grey-blue dots corresponding to post-inflammatory accumulation of melanophages in the dermis. They are unspecific, being also observed in other chronic genital inflammatory diseases, such as lichen planus^[61]. Finally, yellow comedo-like openings, which histologically correspond to dilated infundibula with follicular cornified plugging, that are a constant finding in extragenital sites^[62], can be observed on the involved vulvar skin^[54].

Lichen planus

Genital lichen planus is a chronic muco-cutaneous inflammatory disease quite common in males and females^[63] whose dermoscopy has been reported in females only^[61] with quite typical, linear pearly-whitish structures (Wickham striae) arranged in a reticular, annular, dotted/*starry sky* or rounded/globular configuration (**Fig. 5**). Wickham striae, that histopathologically correspond to hypergranulosis^[64], may occur in some cases as blue-white or grey-white areas, similar to a veil^[61]. Thick, linear irregular vessels and an intense reddish background are generally observed. Finally, grey-blue dots with a characteristic peppered arrangement may be observed in vulvar lichen planus due to the underlying inflammatory process.

Psoriasis

Genital psoriasis affects 30–60% of patients with an exclusive involvement in 2–5%^[65]. Dermoscopy has been reported in several cases both in males and females^[46,57,66-67], showing at low magnification (X10) a constant aspect consisting of dotted vessels and at high magnification (>X100) of dilated, tortuous, "bushy" capillaries, regularly distributed over a pale red background

(**Fig. 6**). This vascular pattern histologically corresponds to dilated, elongated, and tortuous capillary loops in the papillary dermis^[68-70]. Genital psoriasis is easily recognizable because of the lack of white scales typically observed in cutaneous plaque psoriasis that may hamper a correct visualization.

Zoon's plasma cell mucositis

Zoon's plasma cell mucositis is a benign inflammatory process that may involve external genitalia with a chronic-relapsing course. Moreover, a clinical and histopathological "zoonoid inflammation" is frequently encountered in genital dermatology as a corollary/consequence of other disorders such as lichen sclerosus, lichen planus, genital penile intraepithelial neoplasia and squamous cell carcinoma^[71]. Zoon's plasma cell mucositis and zoonoid inflammation share the same dermoscopic features, i.e. the presence of a focal/diffuse orange-yellowish structureless area, related to the hemosiderin deposition, and fairly focused curved vessels^[57,66,72-75] (**Fig. 7**). These vessels may show a serpentine, spermatozoa-like, convoluted, and chalice-shaped configuration. The easy detection of the vascular pattern is probably related to the epidermal thinning which makes dermal vessels closer to the surface.

Lichen simplex chronicus

Genital lichen simplex chronicus is common in females, especially in mid-to-late adult life^[76]. Dermoscopy has been described in vulvar localization only, as a pinkish-whitish background topped with white-greyish structureless patches, varying in size, with a tendency to coalesce^[77]. These patches likely correspond to the orthokeratotic epidermal hyperplasia found on histopathology. In cases of noticeable lichenification, a surface showing a pattern of gyri and sulci can be observed. The pinkish-whitish background is characterized by a dense vascularization, mainly composed of linear, serpentine and dotted vessels, diffusely arranged within the affected surfaces.

HYPERPIGMENTATIONS

Melanosis

Genital melanosis involving the semimucosa may clinically mimic melanoma thus creating concern in both patients and physicians. Dermoscopy of genital melanosis has been extensively reported in both sexes^[17-18,20,78-86], showing a parallel (linear and curved streaks/lines/globules running parallel that may have a fingerprint-like aspect), globular (round-to-oval globules), reticular (ovoid- or round-shaped honeycomb disposition), or ring-like (multiple round-to-ovoid structures, sometimes arranged in a grape-like manner) pigmentation pattern with well-defined borders (**Fig. 8**). Homogeneous brown to gray-blue structureless areas may also be detected, especially in large lesions.

MALIGNANT NEOPLASMS

Melanoma

Vulvar melanoma is the second most common vulvar malignancy, accounting for 2.4–10% of all vulvar tumors, that in about 20% of cases may develop as a multifocal neoplasia^[86], while primary penile melanoma is very rare^[88]. A few cases of dermoscopy of male and female genital melanoma have been described^[16-18,29,35,83,89-98]. Overall, the dermoscopic patterns do not differ from melanomas at other body sites including: asymmetry of structure, multiple colours, blue-grey or white structures, structureless areas, multicomponent patterns and polymorphous vessels. Abrupt cut-offs, reticular depigmentation, atypical network or streaks, multisided black dots and ulceration represent further dermoscopic features^[18,99]. To date, the real impact of dermoscopy on early diagnosis of genital melanoma has yet to be defined^[93].

Intraepithelial neoplasia

Genital intraepithelial neoplasia is widely accepted as the precursor lesion of invasive squamous cell carcinoma in both males and females^[100-101]. The terms Bowen's disease, erythroplasia of This article is protected by copyright. All rights reserved

Queyrat and bowenoid papulosis are still used to indicate its clinical variants. Dermoscopy has been described in both sexes revealing structureless areas varying in colour from dull pink to bright red to whitish, and dotted, glomerular and/or linear vessels with variable size and irregular or patchy distributions^[16-18,29,66,102-112]. White scales, due to parakeratosis, may be observed. The pigmented variant of genital intraepithelial neoplasia generally reveals gray-brownish dots, diffusely arranged with either irregular or parallel distribution and corresponding to the presence of melanophages in the papillary dermis^[113-114].

Basal cell carcinoma

Vulvar basal cell carcinoma represents 1-5% of all vulvar cancers^[115], while penile and scrotal basal cell carcinoma is even more rare, accounting for less than 0.03% of all BCCs in men^[116-117]. Dermoscopy features have been described for vulvar basal cell carcinoma only, revealing fine, reddish, well-focused arborizing or linear vessels^[18,118-120]. The presence of blue ovoid nests is a further aid in arriving at a correct diagnosis. Homogeneous whitish shiny areas, which may correspond to peritumoral fibrosis, can provide an additional clue indicating vulvar basal cell carcinoma.

OTHER DISORDERS

Sporadic reports describe the dermoscopy features of other genital disorders in both sexes, such as clear cell acanthoma^[121], eruptive vellus hair cysts^[122], lichen aureus^[123], median raphe cyst^[124], metastasis^[29], Mondor's disease^[125], neutrophilic sebaceous adenitis^[126], Paget disease^[127], porokeratosis ptychotropica^[128], post-inflammatory pigmentation^[16-17], pseudoxanthomatous mastocytosis^[129], purpura^[16], tick bite^[130-131], and verruciform xanthoma^[132-134].

DISCUSSION

In the last years, the use of dermoscopy beyond pigmented lesions has undergone a tremendous expansion in different fields of dermatology including genital disorders^[2,77,99,135-137]. Recognition of specific dermoscopy patterns may increase diagnostic accuracy and improve differential diagnosis and patients affected by external genital disorders have a greater possibility to be diagnosed "non-invasively". Major criteria to be addressed in the dermoscopic assessment of genital conditions generally include vascular pattern evaluation (vessel morphology and arrangement) and the presence of extra-vascular components singularly or in mutual combination that can be highlighted also in case of early, minimal or non-specific clinical presentation. As regards equipment, we suggest the use of polarized, non-contact dermoscopy in order to prevent the transmission of infectious diseases. In addition, the use of a videodermatoscope that avoids close proximity between the examiner's head and the genitalia, is recommended.

In our review, we have found several genital dermatoses showing a peculiar dermoscopic pattern with no gender difference. Although dermoscopy of Fordyce's spots has been described in males only and lichen planus, lichen simplex chronicus, syringomas and basal cell carcinoma in females, the dermoscopic aspects in different gender is similar, in our opinion.

We also explored a possible difference between the dermoscopic aspects observed in the genital area compared to extragenital skin. Again, we found no major differences, except for psoriasis and lichen sclerosus of the genital semimucosa; in psoriasis there was no evidence of white scales (because of the lack of hyperkeratosis) and in lichen sclerosus there was a lack of comedo-like openings (due to the absence of hair follicles). Therefore, we believe that expertise in dermoscopy of the skin can be generalized to genital lesions. Although most dermoscopy studies do not clearly report the specific localization of the lesions within the external genital area (mucosa *vs* semimucosa *vs* skin) overall, we expect to find no substantial differences.

In conclusion, dermoscopy of the genital area should be considered during clinical inspection especially in the presence of non-diagnostic lesions. It may also help to rule out those conditions This article is protected by copyright. All rights reserved

that may appear similar but that show a different dermoscopy pattern (**Table I**) thus narrowing down the differential diagnoses and avoiding unnecessary invasive procedures.

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FIGURE LEGENDS

- **Figure 1** Pearly penile papules: multiple small papules of the corona glandis appearing at dermoscopy (x10) as small, regular, uniformly sized projections.
- **Figure 2** Seborrheic keratosis of the vulva: brown, roundish patch showing at dermoscopy (x10) a well-demarcated, brownish, diffuse pigmentation, comedo-like openings (arrow) and milia-like cysts (arrowhead)
- **Figure 3** Genital wart of the frenulum: cauliflower-like lesion showing at dermoscopy (x10) multiple, whitish-pink, irregular projections of different size, containing linear, elongated vessels
- **Figure 4** Penile lichen sclerosus: whitish patches of the glans and inner prepuce showing at dermoscopy (x10) milky-pinkish, structureless areas and polymorphic vessels.
- **Figure 5 -** Vulvar lichen planus: small whitish lesions revealing at dermoscopy (x10) linear pearly-whitish structures (Wickham striae) arranged in a reticular configuration.
- **Figure 6 -** Psoriasis of the glans penis: minimal erythematous lesions showing at dermoscopy (x10) regularly distributed dotted vessels over a pale red background.
- **Figure 7** Zoonoid inflammation: non-specific erythematous patch on the glans and inner prepuce showing at dermoscopy (x10) diffuse orange-yellowish structureless areas and fairly focused curved vessels.
- **Figure 8 -** Vulvar melanosis: clinically irregular pigmented patch showing at dermoscopy (x10) parallel pigmentation pattern with linear and curved streaks/lines/globules.

 Table I. Differential diagnosis of genital disorders by dermoscopy

Genital disorder with an	Main dermoscopic features	Clinically similar entities with a different dermoscopic
identified dermoscopic pattern		pattern
Pearly penile papules and vestibular	• uniformly sized whitish-pink small	Genital warts
papillae	projections/papillae	
	• linear vessels	
Fordyce's spots	• yellowish <i>bunch-like</i> lobules	Molluscum contagiosum, genital warts
	• vascular garlands-like aspect	
Seborrheic keratosis	 fissures and ridges 	Melanosis, angiokeratoma, genital warts, melanoma
	• comedo-like openings	
	milia-like cysts	
	 hairpin or looped vessels 	
	• brownish diffuse pigmentation	
Angiokeratoma	• red/dark lacunae	Seborrheic keratosis, melanoma, basal cell carcinoma,
	• whitish veil	genital warts, molluscum contagiosum, syringoma
	• hemorrhagic crusts	
Syringoma	• glittering, round-shaped or oval, yellow-	Basal cell carcinoma, genital warts, molluscum
	whitish structures	contagiosum, angiokeratoma
	 fading pink background 	
Melanocytic naevi	• similar to naevi on other parts of the body	Melanoma, melanosis, seborrheic keratosis, intraepithelial
	• reticular, clod or structureless pattern	neoplasia, angiokeratoma
Genital warts	• papular lesions: <i>mosaic</i> pattern	Pearly penile papule, vestibular papillae, molluscum
	• cauliflower-like lesions: fingerlike pattern	contagiosum, seborrheic keratosis, angiokeratoma,
	haemorrhagic splits	syringoma, basal cell carcinoma
Molluscum contagiosum	• polylobular, white-yellowish, amorphous	Fordyce's spots, genital warts, basal cell carcinoma,
	structures	syringoma, angiokeratoma
	• pore/orifice in a central or eccentric position	
	• crown, radial and/or dotted patterns	
Candidiasis	• cottage cheese-like structures (sparse white	Psoriasis, Zoon's plasma cell mucositis, intraepithelial
	coating)	neoplasia
	• blurry linear vessels	

Scabies	• low magnification (X10): <i>delta wing jet with contrail</i>	Lichen simplex chronicus
	• high magnifications (>X100): mite body, legs, rostrum, eggs and feces	
Lichen sclerosus	whitish background	Morphea
	• white-yellowish to milky-pinkish patchy	
	structureless areas	
	• vascular desertification	
	red to purpuric dots/globules	
Lichen planus	Wickham striae	Lichen simplex chronicus, psoriasis, Zoon's plasma cell
	• thick, linear irregular vessels	mucositis
	 reddish background 	
	grey-blue dots	
Psoriasis	• low magnification (X10): dotted vessels	Lichen planus, lichen simplex chronicus, candidiasis,
	• high magnification (>X100): "bushy"	Zoon's plasma cell mucositis, intraepithelial neoplasia
	capillaries	
7 1 11 11	red background	
Zoon's plasma cell mucositis	• focal/diffuse orange-yellowish structureless	Lichen planus, intraepithelial neoplasia, psoriasis, candidiasis
	areas	Candidiasis
Lichen simplex chronicus	fairly focused curved vessels	Lichen planus, psoriasis
Lichen simplex chronicus	pinkish-whitish background white gravish structuraless retakes	Lichen planus, psoriasis
	white-greyish structureless patchesdense vascularization	
Melanosis		Seborrheic keratosis, nevus, melanoma, intraepithelial
Welanosis	• parallel, globular, reticular, or ring-like pigmentation pattern	neoplasia
	• homogeneous brown to gray-blue	neoptasta
	structureless areas	
Melanoma	asymmetry of structure, multiple colours,	Naevus, melanosis, seborrheic keratosis, intraepithelial
	structureless areas, multicomponent pattern	neoplasia, angiokeratoma
	• atypical network or streaks, reticular	
	depigmentation, multisized black dots,	
	polymorphous vessels, ulceration	

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Intraepithelial neoplasia	• structureless areas from dull pink to bright	Psoriasis, Zoon's plasma cell mucositis, melanosis,
	red to whitish	melanoma
	• dotted, glomerular and/or linear vessels, with	
	irregular or patchy distributions	
	gray-brownish dots	
Basal cell carcinoma	• fine, reddish, well-focused arborizing or	Molluscum contagiosum, melanoma, angiokeratoma
	linear vessels	
	blue ovoid nests	
	whitish shiny areas	















