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Clinicopathologic Overlap of Vulvar Psoriasis and Candidiasis

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Objectives: The study's aim is to assess if vulvar psoriasis and candidiasis may be distinguished by clinical presentation and histopathologic appearance.
Methods: The pathology database identified biopsies with corneal or subcorneal neutrophils, acanthosis, and dermal lymphocytic infiltrate. Exclusions were age younger than 18 years and unavailable or uninterpretable slides. Clinical data included demographics, comorbid conditions, symptoms, examination, microbiology, treatment, and response. Histopathologic review documented site, thickness, and characteristics of stratum corneum and epidermis, distribution of neutrophils, and infiltrate. Cases were stratified by microbiologic presence or absence of *Candida albicans*.
Results: Biopsies from 62 women with median age of 60 years were associated with *C. albicans* on vulvovaginal culture in 28 (45%), whereas 26 (42%) were negative, and 8 (13%) lacked microbiologic assessment. Swab-positive women were more likely to have diabetes, receive prereferral estrogen, and report vulvar pain. Specialist clinical impression was candidiasis in 33 (53%), psoriasis in 11 (18%), comorbid candidiasis and psoriasis in 7 (11%), dermatitis in 10 (16%), and unknown in 2 (3%). Visible fungal organisms occurred in 16 (26%) cases and were associated with diabetes and satellite lesions. Other than presence of organisms, there were no histopathologic differences stratified by microbiologic result.
Conclusions: The histopathologic triad of corneal/subcorneal neutrophils, acanthosis, and dermal lymphocytic infiltrate is common to vulvar psoriasis and candidiasis, and clinical features do not reliably distinguish between them. Microbiologic assessment and single-agent treatment are useful strategies to clarify the diagnosis.

Key Words: vulva, inverse psoriasis, mycosis, *Candida albicans*, cutaneous candidiasis, intertrigo, koebnerization, Wolf isotopic response

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Psoriasis is a chronic immune-mediated multisystem disease arising from dysregulation of interleukin (IL)-23 and IL-17 signaling pathways.[1] The two categories of skin manifestations both occur on the vulva: classic plaque type seen as red to purple well-demarcated lesions with silvery scale, and flexural or inverse psoriasis seen as erythema and fissures at skin folds.[2–4] The incidence of vulvar psoriasis is unknown; up to 40% of psoriasis patients report genital involvement and 1%–7% attending specialist vulvar clinics receive a diagnosis of psoriasis.[2] Vulvar inverse psoriasis has similar symptoms and examination to erosive or hypertrophic lichen planus (LP), dermatitis, and candidiasis.[2,5] Exposure to irritants and frictional trauma exacerbates psoriasis and may provoke the Koebner phenomenon of new lesions appearing in previously unaffected skin.[2,6]

The clinical presentation of vulvovaginal candidiasis (VVC) differs depending on location and estrogen status. Reproductive-age women primarily have vaginal involvement with variable extension to vulvar skin, with chronic or recurrent VVC common in a healthy cohort.[7–9] Postmenopausal women predominantly have cutaneous or intracrural candidiasis, usually associated with obesity, diabetes mellitus (DM), systemic or local immunosuppression, antibiotic exposure, and skin occlusion.[10,11] Cutaneous candidiasis occurs across sexes, ages, and sites, accounting for 1%–7% of dermatology clinical encounters.[10] In both cohorts, symptoms include itching, burning, dyspareunia, edema, rash, fissures, adherent debris, and abnormal discharge.[7] Skin abnormalities range from subtle erythema to violaceous or macerated rash, sometimes with peripheral scale and/or satellite lesions.[1,12] False-negative culture of vaginal swab or vulvar scrapings may occur if organism numbers are low, with recent exposure to antifungal medications, or if an uninvolved site is sampled.[13]

Histopathology of psoriasis and candidiasis both demonstrate corneal or subcorneal neutrophils, acanthosis, and dermal lymphocytic infiltrate.[14,15] Budding cells and pseudohyphae of candidal organisms in the stratum corneum (SC) may be seen in candidiasis but not psoriasis.[16] Organism detection is easier on periodic acid-Schiff (PAS) than hematoxylin and eosin (H&E) stains, but they may be sparse or absent even with obvious clinical and microbiologic disease.[14]

This common clinicopathologic presentation and a growing body of literature suggest an overlap in immunologic pathogenesis. The study's aim is to explore the relationship of vulvar psoriasis and candidiasis to determine if these entities are distinguishable or intertwined.

METHODS

The NSW Health Pathology North, John Hunter Hospital database was searched for vulvar biopsies with 1) corneal and/or subcorneal neutrophils, 2) acanthosis, and 3) dermal lymphocytic infiltrate. The Hunter New England Research Ethics and Governance Unit approved this retrospective histopathologic series (2020/ETH01880), and signed written consent was obtained for use of clinical photographs. Inclusion criteria were biopsies from hair-bearing or hairless skin with all layers of epidermis and upper dermis for review. Exclusion criteria included age younger than 18 and unavailable or uninterpretable slides.

Review of H&E-stained slides yielded data on biopsy location, site, appearance of SC and granular cell layer, rete ridge regularity and morphology, and spongiosis. Hyperproliferation of the basal and suprabasal layers was deemed "basal proliferative zone" and noted as present or absent. Measurements were recorded of stratum corneum, suprapapillary, and epidermal thickness. Frequency of neutrophils in the SC was described as scattered, unifocal, or multifocal, and their presence in epidermis and papillary dermis was noted. Infiltrate was semiquantitatively characterized as scant, moderate, or marked, with cell types recorded in descending frequency and location assessed as band-like, perivascular, or diffuse. Dermal assessment included edema, fibrosis, and ectatic vessels. Review of PAS-stained slides checked for fungal organisms in or under the stratum corneum. When multiple biopsies from a single patient and site showed similar histology, data were collected from the most representative specimen.

Demographic data included specialist type, age, postmenopausal status, body mass index, DM, tobacco use, and immune dysfunction defined as autoimmune disease or immunosuppressive

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medications. Clinical information included symptoms and their duration, prereferral treatments, examination, comorbid vulvar dermatoses, impression, treatments, response, outcome, and duration of follow-up. Results of vulvovaginal swabs or vulvar skin scrapings performed prereferral or during specialist assessment were categorized as positive or negative for *Candida albicans* or not done. Descriptive statistics were performed and categorical data were compared with Fischer exact test.

RESULTS

There were 62 biopsies from women with a median age of 60 years (range 25–82); 5 (8%) patients were aged younger than 40. Vulvovaginal culture yielded *C. albicans* in 28 (45%), 26 (42%) were negative for *C. albicans*, and 8 (13%) lacked microbiologic assessment (Table 1). Two patients had vulvar scrapings; 1 resulted negative and 1 positive, both aligning with concurrent vaginal swab results. Two patients had *Candida glabrata* on vaginal microbiology; in both the specialist impression was psoriasis, and clinical improvement occurred without exposure to an antifungal. Specialist type, postmenopausal status, body mass index, duration of symptoms, and known extragenital psoriasis were similar across microbiologic groups. Culture-positive patients were more likely to have DM [16/28 (57%) vs 7/34 (21%); $p = .004$]. Tobacco use occurred in 1 patient with unknown status and was undocumented in 14. Four women identified as First Nations, 1 culture-positive and 3 negative. Seven had an immunosuppressive condition to include rheumatoid arthritis in 2 and 1 each with sarcoidosis, CREST, Sjogrens, multiple sclerosis, and myopathy; 4 were culture-positive, 2 negative, and 1 unknown.

Preexisting vulvovaginal conditions occurred in 14 (23%). In those with *C. albicans*, 5/28 (18%) had lichen sclerosus (LS) or LP and 1 (4%) had vulvodynia. In the culture-negative group, 3/26 (11.5%) had LS or LP and 3 (12%) had desquamative inflammatory vaginitis. Of those with no microbiologic result, 1/8 (12.5%) each had LP, desquamative inflammatory vaginitis, and high-grade squamous epithelial lesion.

Before specialist referral, 6 (21%) culture-positive women received a combination of topical corticosteroids and topical or systemic antifungals. Of these, 3 used betamethasone dipropionate and clotrimazole, 2 applied low- to medium-potency steroid with clotrimazole, 1 used betamethasone dipropionate and fluconazole, and 1 had hydrocortisone plus oral terbinafine. Among culture-negative women, 5 received combination regimens; 4 had a low- to medium-potency corticosteroid with clotrimazole, and 1 used betamethasone dipropionate and oral terbinafine. Referrers were more likely to provide topical estrogen to those who subsequently grew *C. albicans* [10/28 (36%) vs 3/34 (9%); $p = .013$].

Although rates of itch and abnormal discharge were similar across microbiologic groups, pain occurred more often in culture-positive women [17/28 (61%) vs 4/34 (12%); $p = .0001$]. Erythema was the most frequent examination finding, with variable documentation of additional descriptors like edema, erosion, fissure, and satellite lesions (Figures 1–3). Clinicians noted groin involvement in 4 each of culture-positive and negative groups.

After history, examination, and investigations, clinical impression of cutaneous candidiasis was more likely with *C. albicans* identified [24/28 (86%) vs 9/34 (26%), $p = .0001$], whereas diagnoses of psoriasis [1/28 (4%) vs 10/34 (29%); $p = .009$] or dermatitis [0% vs 10/34 (29%) $p = .0013$] were more common in culture-negative women. There were 7 diagnoses of comorbid psoriasis and candidiasis (Figure 1). Among 6 with history of psoriasis, 1 (17%) had organisms on histology and 1 was culture-positive for *C. albicans.*

Specialist provision of systemic antifungals was more likely in *Candida*-positive women [21/28 (75%) vs 11/33 (33%); $p = .001$]; prescription of topical antifungals occurred less than half as often as oral therapy but was likewise more frequent in the culture-positive group [10/28 (36%) vs 3/34 (9%); $p = .013$]. Common fluconazole regimens were 50–100 mg daily for 2–6 weeks. Specialists provided antifungals to all but 1 in the *C. albicans* group, of whom 11 also received a topical corticosteroid and 5 had ongoing potent steroid treatment of lichenoid dermatosis. Combination regimens were more common in the culture-positive group [11/28 (39%) vs 5/34 (15%); $p = .04$] and included a potent steroid with fluconazole in 5/11 (24%), a low- to medium-potency steroid with fluconazole in 4 (36%), and 1 each (9%) received clotrimazole with a medium- or high-potency steroid. In the culture-negative and unknown groups, 2 had fluconazole plus ongoing potent steroid treatment of lichenoid dermatosis and 5 had combination regimens comprised of fluconazole paired with potent steroid in 3 or medium potency in 2. Additional treatments in 3 *Candida*-positive patients were intramuscular medroxyprogesterone, tricyclic antidepressant, and antiviral. Adjunctive management in culture-negative and unknown groups included menopause replacement therapy in 2; topical clindamycin in 2; and 1 each of antiviral, antihistamine, methotrexate for LP, tricyclic antidepressant, pelvic floor physiotherapy, and laser for high-grade squamous epithelial lesion. Women were equally likely to use maintenance therapy as to cease treatment, regardless of culture result.

Fungal organisms were seen on H&E and PAS in 9/16 (56%) cases, PAS in 6 (11%) cases, and H&E in 1 (6%) with PAS failure (Figure 2). Diabetes [10/16 (62.5%) vs 13/46 (28%) $p = .02$] and satellite lesions [6/16 (37.5%) vs 2/46 (4%); $p = .03$] were more common in organism-positive cases. Microbiologic presence of *C. albicans* [12/16 (75%) vs 16/46 (35%); $p = .08$] and prereferral exposure to topical corticosteroids [13/16 (81%) vs 22/46 (48%); $p = .04$] were associated with organisms on histology. Clinicians more often provided systemic antifungals to those with microscopic organisms than without [13/16 (81%) vs 20/46 (43%); $p = .01$]. The remaining positive cases received clotrimazole; all responded to antifungal therapy and 7/16 (44%) continued maintenance regimens.

Histopathologic findings were similar when stratified by microbiologic result (Table 2) and presence of organisms in the stratum corneum. Most biopsies were obtained from hair-bearing skin and showed parakeratosis, hypogranulosis or agranulocytosis, elongated rete ridges with suprapapillary thinning, corneal or subcorneal neutrophils, neutrophils peppered through epidermis and dermis, and dermal lymphocytes (Figures 1–3). Erosion or ulcer was seen in 5 (8%) with 3 in the *C. albicans* and 2 in the unknown groups. Eosinophils were absent in 39 (63%), sparse in 22 (35%), and frequent in 1 (2%) case with negative PAS and positive culture; there was no difference between groups. The frequency of epidermal neutrophils, morphology of rete ridges, presence of spongiosis, location of infiltrate, and dermal plasma cells was similar across microbiologic groups. Dermal edema occurred in 15 (24%), dermal fibrosis in 18 (29%), pigment incontinence or hemosiderin in 18 (29%), and dilated capillaries in 12 (19%), with no difference between microbiologic groups.

DISCUSSION

This study confirms the histopathologic triad of corneal/subcorneal neutrophils, acanthosis, and dermal lymphocytic infiltrate is common to vulvar psoriasis and candidiasis. Clinical appearance and microbiologic results did not reliably distinguish between the two. When assessing an erythematous rash, clinicians arrived at a diagnosis of candidiasis in 65%, regardless of histologic fungal organisms. This practice pattern may reflect the poor sensitivity of single-culture vulvovaginal candidiasis, with rate

TABLE 1. Clinical Characteristics of Patients With Biopsies Showing Psoriasis or Mycosis, Stratified by Microbiology Results

	All = 62; n (%)	*C. albicans* = 28; n (%)	Negative = 26; n (%)	Not available = 8; n (%)
Specialist type				
Gynecology	47 (76)	23 (82)	20 (77)	4 (50)
Gynecologic oncology	6 (10)	3 (11)	3 (11.5)	0
Dermatology	9 (14)	2 (7)	3 (11.5)	4 (50)
Age, median y (range)	60 (25–82)	63 (31–82)	58 (25–76)	60 (47–71)
Duration of symptoms, median mo (range)	12 (0–288)	12 (3–288)	18 (0–144)	12 (12–120)
Postmenopausal status	45 (73)	22 (79)	16 (62)	7 (88)
DM*				
Yes	23 (37)	16 (57)	6 (23)	1 (12.5)
Unknown	6 (10)	1 (4)	2 (7)	3 (37.5)
Body mass index				
<30	26 (42)	12 (43)	11 (42)	3 (37.5)
30–39	8 (13)	3 (11)	3 (12)	2 (25)
≥40	14 (23)	8 (29)	6 (23)	0
Unknown	14 (23)	5 (18)	6 (23)	3 (37.5)
Extragenital psoriasis	6 (10)	1 (4)	5 (19)	0
Prereferral treatment[a]				
Topical corticosteroids	33 (53)	18 (64)	15 (58)	0
Topical antifungal	16 (26)	8 (29)	8 (31)	0
Systemic antifungal	7 (11)	3 (11)	4 (15)	0
Topical estrogen*	13 (21)	10 (36)	3 (12)	0
Antibiotic	4 (6)	2 (7)	2 (7)	0
None/unknown/other	21 (34)	6 (21)	7 (27)	8 (100)
Symptom[a]				
Itch	42 (68)	17 (61)	21 (80)	4 (50)
Pain*	21 (34)	17 (61)	3 (12)	1 (12.5)
Abnormal discharge	7 (11)	2 (7)	4 (15)	1 (12.5)
Nil/unknown	3 (5)	0	1 (4)	2 (25)
Examination - color				
Red	52 (84)	26 (93)	20 (77)	6 (75)
Gray-pink	3 (5)	0	3 (11.5)	0
Pallor	3 (5)	1 (3.5)	0	2 (25)
Normal/unknown	4 (6)	1 (3.5)	3 (11.5)	0
Examination - additional feature[a]				
Plaque	14 (23)	5 (18)	7 (27)	2 (25)
Edema	14 (23)	7 (25)	6 (23)	1 (12.5)
Erosion or fissure	11 (18)	4 (14)	5 (19)	2 (25)
Satellite lesions	6 (10)	4 (14)	2 (8)	0
None/atrophy/unknown	17 (28)	8 (29)	6 (23)	3 (37.5)
Clinical impression, n (%)				
VVC*	33 (53)	24 (86)	7 (27)	2 (25)
VVC and psoriasis	7 (11)	3 (11)	3 (12)	1 (12.5)
Psoriasis*	11 (18)	1 (4)	7 (27)	3 (37.5)
Dermatitis or lichen simplex*	10 (16)	0	7 (27)	3 (37.5)
Nil/unknown	2 (3)	0	2 (8)	0
Biopsy location				
Labium majus	28 (45)	14 (50)	11 (42)	3 (37.5)
Interlabial fold/labium minus	20 (31)	6 (21)	10 (39)	4 (50)
Perineum/perianus	8 (13)	6 (21)	2 (8)	0
Mons/groin	6 (10)	2 (7)	3 (11.5)	1 (12.5)
Treatment[a]				
Topical corticosteroids	39 (63)	19 (68)	17 (65)	3 (37.5)
Systemic antifungal*	32 (52)	21 (75)	10 (38)	1 (12.5)
Topical antifungal*	13 (21)	10 (36)	2 (8)	1 (12.5)

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TABLE 1. *(Continued)*

	All = 62; n (%)	*C. albicans* = 28; n (%)	Negative = 26; n (%)	Not available = 8; n (%)
Barrier ointment	17 (27)	4 (14)	7 (27)	1 (12.5)
Topical estrogen	4 (6)	1 (4)	2 (8)	1 (12.5)
None/unknown/other	12 (19)	3 (11)	9 (35)	5 (62.5)
Treatment with combination of steroid and antifungal*	23 (37)	16 (57)	6 (23)	1 (12.5)
Outcome				
Improved, treatment ceased	25 (40)	12 (43)	8 (31)	5 (62.5)
Improved, maintenance therapy	25 (40)	11 (39)	14 (54)	0
Not improved	3 (5)	2 (3)	1 (4)	0
Unknown or no follow-up	9 (15)	3 (5)	3 (12)	3 (37.5)
Follow-up, median mo (range)	6 (0–82)	7 (0–82)	6 (0–36)	12 (2–24)

*$p < .05$.

[a]Cases may have more than 1 symptom, examination feature, or treatment.

VVC indicates vulvovaginal candidiasis.

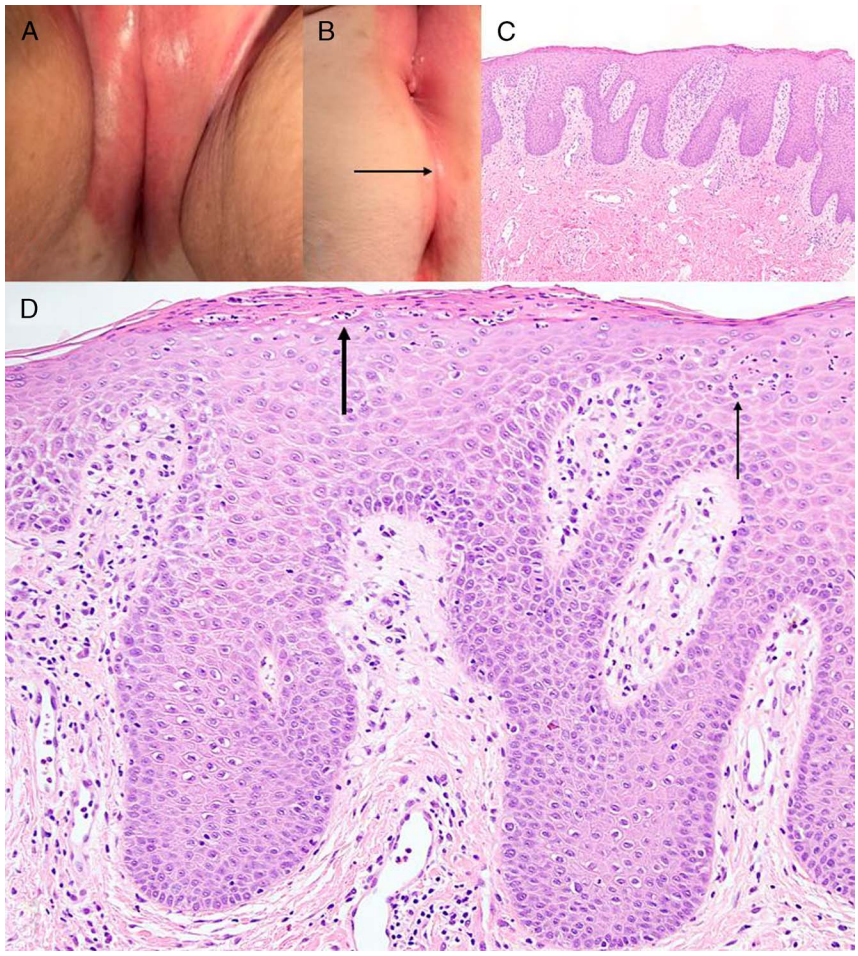

FIGURE 1. A 69-year-old with obesity and scalp psoriasis presented with 2 years of vulvar itch and pain; vulvovaginal culture was negative, clinical impression was comorbid psoriasis and candidiasis that improved with fluconazole and methylprednisolone aceponate ointment treatment then maintenance. A, vulvar erythema and edema extending to groins. B, moderately demarcated symmetric erythema over perianal skin and natal cleft (arrow). C, biopsy of labium majus shows hair-bearing skin with thin confluent parakeratosis (PK), hypogranulosis, acanthosis with elongated rete ridges, and papillary perivascular lymphocytic infiltrate; hematoxylin and eosin (H&E) ×40. D, subcorneal neutrophils (thick arrow), spongiosis, and epidermal neutrophils (thin arrow), periodic acid-Schiff (PAS) negative for organisms; H&E ×100.

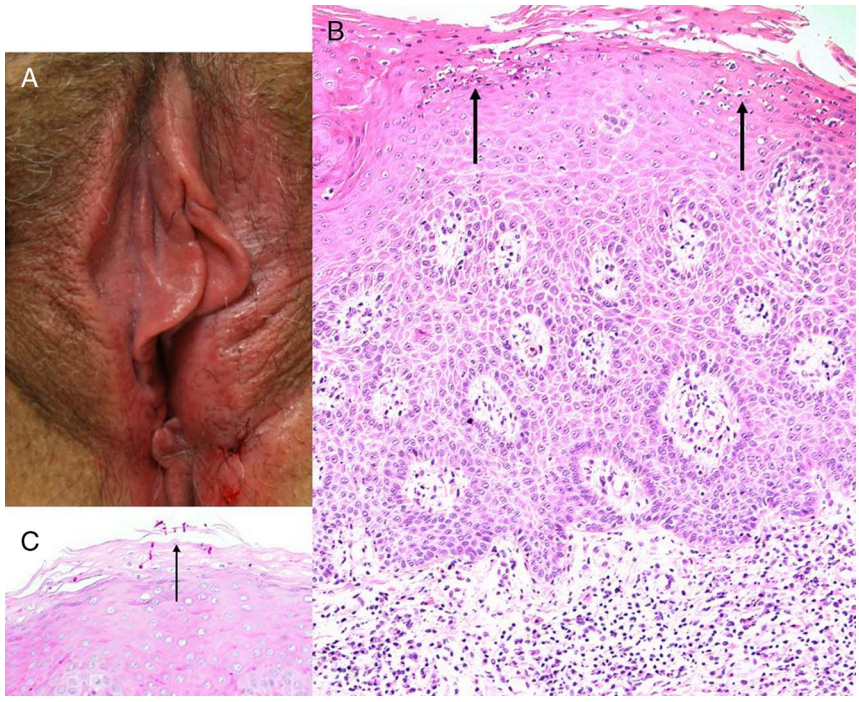

FIGURE 2. A 55-year-old postmenopausal woman with obesity and diabetes mellitus (DM) presented with 1 year of vulvar itch and pain; vulvovaginal culture grew *Candida albicans*, clinical impression was candidiasis that resolved with fluconazole and hydrocortisone ointment. A, confluent vulvar erythema and edema over hairless and hair-bearing skin extending to medial labia majora. B, biopsy of perineum diagnostic of mycosis shows hair-bearing skin, PK, subcorneal pustules (thick arrows), acanthosis, spongiosis, and dermal lymphocytic infiltrate; H&E ×100. C, PAS ×200 shows fungal elements in stratum corneum (thin arrow).

estimates of 18%–68%.[8,13] Antifungal treatment usually resulted in resolution of symptoms and signs, reinforcing the clinical diagnosis.

Cohort demographics reflect known risks for cutaneous candidiasis: postmenopausal status, DM, obesity, and immune dysfunction. In contrast, the mean age of symptom onset in vulvar psoriasis is 30 years.[6] However, psoriasis and candidiasis are not mutually exclusive. Patients with psoriasis are more likely than those unaffected to grow candida on skin and fecal culture, immunosuppressive psoriasis therapies facilitate conversion from candidal colonization to pathogenicity, and use of IL-17 inhibitors in psoriasis is associated with 3- to 25-fold risk of candidiasis.[1,17–19]

The prolonged interval from symptom onset to referral and noncollection of microbiology in 13% reinforce previous findings that clinical recognition of vulvar psoriasis and cutaneous

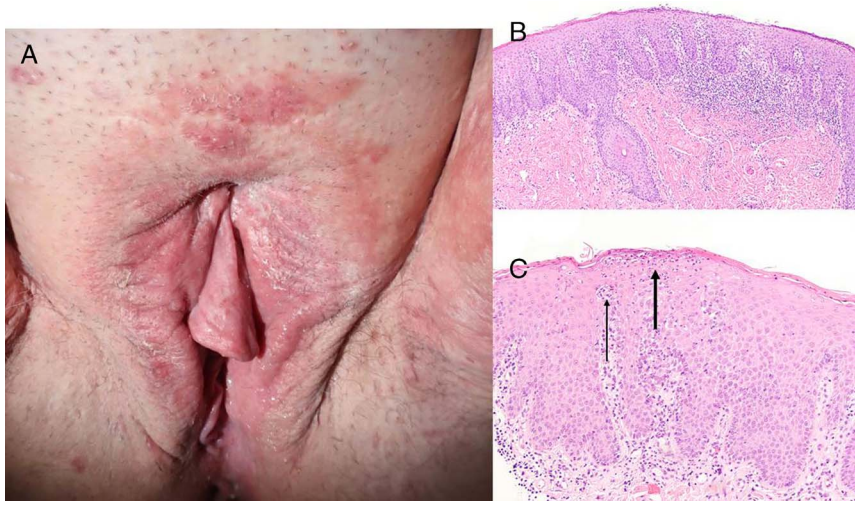

FIGURE 3. A 41-year-old premenopausal woman with obesity, autoimmune disease on a biologic, and recent antibiotic use presented with 1 year of pain and abnormal discharge; vulvovaginal culture was negative, clinical impression was candidiasis that resolved with fluconazole and betamethasone dipropionate ointment. A, extensive nonconfluent erythema, edema, scale, and satellite lesions over vulva, groins, and inner thigh. B, biopsy of interlabial fold shows hair-bearing skin, acanthosis with regular rete ridges, and perivascular lymphocytic infiltrate; H&E ×40. C, thin confluent PK, hypogranulosis, corneal pustule (thick arrow), suprapapillary neutrophils (thin arrow), PAS negative for organisms; H&E ×100.

TABLE 2. Histopathologic Characteristics of Biopsies Showing Psoriasis or Mycosis, Stratified by Microbiology Result

	All = 62; n (%)	*C. albicans* = 28; n (%)	Negative = 26; n (%)	Not available = 8; n (%)
Site				
Hair-bearing skin	52 (84)	26 (93)	20 (77)	6 (75)
Hairless skin	10 (16)	2 (7)	6 (23)	2 (25)
SC				
PK alone	33 (53)	18 (64)	9 (35)	6 (75)
PK and HK	9 (15)	5 (18)	3 (12)	1 (12.5)
PK or HK and normal	20 (33)	5 (18)	14 (54)	1 (12.5)
Organisms in SC*	16 (26)	12 (43)	3 (12)	1 (12.5)
Granular cell layer				
Agranulocytosis	31 (50)	17 (61)	9 (35)	5 (62.5)
Hypogranulosis	27 (44)	11 (39)	14 (54)	2 (25)
Hypergranulosis	1 (2)	0	1 (4)	0
Combination	3 (5)	0	2 (8)	1 (12.5)
Epithelial thickness, mm; median (range)	0.4 (0.12–2)	0.42 (0.17–0.72)	0.4 (0.12–2)	0.43 (0.12–0.82)
Suprapapillary thickness	0.08 (0.01–0.48)	0.08 (0.02–0.4)	0.08 (0.03–0.48)	0.07 (0.01–0.14)
SC neutrophils				
Many or multifocal	35 (56)	18 (64)	13 (50)	4 (50)
Scattered foci	5 (8)	2 (7)	2 (8)	1 (12.5)
Scant	22 (35)	8 (29)	11 (42)	3 (37.5)
Epithelial neutrophils				
None or rare	13 (21)	4 (14)	6 (23)	3 (37.5)
Moderate	33 (53)	14 (50)	14 (54)	5 (62.5)
Many	16 (26)	10 (36)	6 (23)	0
Basal layer proliferative zone present	42 (68)	20 (71)	19 (73)	3 (37.5)
Rete ridges				
Regular/psoriasiform	27 (44)	13 (46)	10 (38)	4 (50)
Irregular	35 (56)	15 (54)	16 (62)	4 (50)
Spongiosis				
Present	40 (65)	16 (57)	16 (62)	8 (100)
Marked	9 (15)	5 (18)	4 (15)	0
Dermal infiltrate				
Sparse	18 (29)	7 (25)	9 (35)	2 (25)
Moderate	28 (45)	13 (46)	12 (46)	3 (37.5)
Dense	16 (26)	8 (29)	5 (19)	3 (37.5)
Infiltrate pattern				
Perivascular	45 (73)	18 (64)	21 (81)	6 (75)
Band-like	13 (21)	8 (29)	3 (12)	2 (25)
Diffuse/scattered	4 (6)	2 (7)	2 (8)	0
Neutrophils in papillary dermis				
None or rare	15 (24)	5 (18)	6 (23)	4 (50)
Moderate	41 (66)	20 (71)	17 (65)	4 (50)
Many	6 (10)	3 (11)	3 (12)	0
Dermal eosinophils	23 (37)	12 (43)	8 (31)	3 (37.5)

*$p < .05$.

HK indicates hyperkeratosis; SC, stratum corneum.

candidiasis is poor.[6,11] Association of visible fungal organisms with prereferral topical corticosteroids may signal iatrogenic exacerbation of disease. Empiric prescribing of topical estrogen, corticosteroids, antibiotics, and antimycotics to women with vulvovaginal complaints in the primary care setting is discouraged. Instead, presence of a rash should precipitate microbiologic assessment via swab, scraping, and/or polymerase chain reaction, vulvar care advice, and prompt follow-up. Lack of distinct nomenclature and clinical guidance to separate vulvar cutaneous candidiasis from VVC likely contributes to underrecognition and inadequate skin treatment.[7,11]

Use of combined antifungal and corticosteroid treatment was common in specialist-led clinics. It is unclear if the reason is uncertain clinical diagnosis, reluctance to cease topical steroids due to possible underlying dermatosis, or belief that dual therapy provides speedier symptomatic relief. The evidence for initial genital psoriasis treatment is limited and favors low- to moderate-potency topical corticosteroids, supplemented by topical coal tar preparations,

calcineurin inhibitors, or vitamin D analogs.[2,20] Several publications recommend topical antifungals over systemic agents for cutaneous candidiasis, citing efficacy, cost, ease of use, and adverse effect profile, except for severe extensive disease justifying systemic azoles for 2–6 weeks.[1,5,7,12] Scant evidence supports this approach, and use of topicals does not address vulva-specific concerns of nonvisibility and surface area of affected skin, concurrent dermatologic conditions, and propensity toward contact dermatitis.[1,2,11,21] Studies assessing combination topical antifungals with corticosteroids for cutaneous candidiasis did not demonstrate superiority of dual therapy over single-agent antimycotics.[10]

There are several potential hypotheses for how candidiasis causes a red rash in absence of organisms on histopathology: 1) organism quantity is sufficient to drive an inflammatory response but low number and/or nonuniform distribution results in microscopic nondetection, 2) irritant dermatitis results from inflammatory mediators in vaginal discharge, or 3) candidal organisms provoke a psoriasiform inflammatory reaction.[22] The first explanation may occur sporadically or if PAS is not done but is unlikely to explain all cases.[11] If the rash relates to vaginal secretions, then abnormal discharge should be near-universal, erythema mostly central, and histopathology consistent with spongiotic tissue reaction. The concept of local psoriasiform reaction to overgrowth of *C. albicans* presents an intriguing explanation.

The Koebner phenomenon describes initiation or provocation of skin conditions in an injured area of previously healthy skin, first described in psoriasis but also documented in LS, LP, and vitiligo.[23] The vulva is exposed to numerous koebnerizing events to include minor surgery, sexual friction, hair management, and contact dermatitis.[23,24] A subtype of koebnerization is the Wolf isotopic response, defined as the appearance of a new dermatosis in the same place as an unrelated lesion, initially described as infections or immune disorders within resolving herpes zoster.[25] The tricolor vulva of psoriasis superimposed on vitiligo may represent a Wolf response.[15] Another relevant example involves a patient with intertriginous rash and positive *C. albicans* culture who improved with antifungals, then recurred with a negative culture and responded to psoriasis treatment.[24]

Interleukin-17 may be the link between psoriasis, candidiasis, and Koebner phenomena, to include Wolf isotopic response. Surface proteins of *C. albicans* behave as superantigens, activating T-lymphocytes and stimulating proinflammatory cytokine release.[5,26] Interleukin-23 promotes Th17 cells to defend against *C. albicans*; these release IL-17 to recruit neutrophils that produce antimicrobial peptides, undertake phagocytosis, and form extracellular traps.[26] This cascade resembles that seen with traumatic keratinocyte damage, in which cytokine release stimulates recruitment of Th17 cells and neutrophils, producing high concentrations of IL-17 and IL-36γ that stimulate keratinocyte proliferation, inhibit differentiation, and cause intraepidermal accumulation of neutrophils.[22] Individuals with congenital or acquired IL-17 deficiency are susceptible to fungal infections, and treatment of psoriasis with anti–IL-17 biologics increases rates of mucocutaneous and systemic candidiasis.[1] Vigorous IL-17 response to pathogenic *C. albicans* may trigger a psoriasiform rash in genetically susceptible individuals, as a Wolf isotopic response.[26] Use of systemic antifungals in psoriasis patients with candidal colonization or infection may improve psoriasis symptoms via reduction in the superantigenic cascade.[2,5] It is unclear if early detection and treatment reduces the likelihood of Wolf response, but some authors advocate for this approach.

The source of vulva-specific IL-17 cascade may be the recently described tissue-resident memory T-cells (T_{RM}). Long-lived and abundant in squamous epithelium, a subset of T_{RM} cells locally produce psoriasis-associated cytokines IL-17A, IFN-γ, and IL-22. This tissue-localized inflammatory pathway may explain recurrence of psoriasis in the same location after withdrawal of biologic therapies.[27] The clinicopathologic and immunological overlap of psoriasis and candidiasis suggests a hypothesis that candidal antigens activate T_{RM} cells, inducing the vulvar psoriasiform rash seen in candidiasis even when fungal elements are microscopically absent from affected skin.

Substantiation of these pathogenesis hypotheses is beyond the scope of this work. Study weaknesses include those inherent to the retrospective design: incomplete clinical data, interprovider practice variation, and cases of sufficient complexity to merit specialist referral and biopsy. Although 13% did not have a vulvovaginal culture, their presentation, clinical impression, histopathology, treatment, and response resembled those who had microbiologic assessment. Although the histopathological triad of corneal/subcorneal neutrophils, acanthosis, and dermal lymphocytic infiltrate captures most psoriasis and mycosis cases, some specimens lack neutrophils and would likely be assessed as nonspecific acanthotic lesions. Conversely, some examples of excoriated spongiotic dermatitis satisfy these 3 criteria and are mimics of psoriasis and mycosis. The likelihood of allergic contact dermatitis is diminished by eosinophils being absent or scant in all but 1 case. Determination of true clinical diagnoses was hampered by these issues and poor performance of microbiologic and molecular studies in distinguishing between colonization and disease.[8,11,13] Prospective studies would likewise struggle with case definition and outcome assessment given the similar presentations, comorbidities, and confounders of these 2 conditions. Local immunologic signatures of psoriasis and candidiasis have not yet been elucidated but may provide key insights.

In summary, vulvar psoriasis and candidiasis show clinicopathologic overlap. When budding cells and pseudohyphae are present in the stratus corneum, the diagnosis is mycosis. Infectious etiology is likely when vulvovaginal culture is positive for *C. albicans* but microscopy is negative for organisms; the mechanism of skin manifestations is unclear but may represent T_{RM}-driven, IL-17–mediated Wolf isotopic response seen as psoriasiform rash. Pathologist reporting of the organism-negative biopsy with corneal/subcorneal neutrophils, acanthosis, and lymphocytic infiltrate should inform the clinician that findings suggest psoriasis and/or candidiasis.

REFERENCES

1. Yeung J, Bunce PE, Lynde CW, et al. Review and practical guidance on managing fungal infections in patients with psoriasis receiving anti-IL-17 therapies. *J Cutan Med Surg* 2022;26:3S–23S.
2. Meeuwis KAP, De Hullu JA, Massuger LFAG, et al. Genital psoriasis: a systematic literature review on this hidden skin disease. *Acta Derm Venereol* 2011;91:5–11.
3. Lewis FM. Chapter 49: inflammatory dermatoses of the vulva in children. In: *Ridley's The Vulva*. 4th ed. Wiley; 2022:373–84.
4. Calonje JE, Brenn T, Lazar AJ, et al. Chapter 6: spongiotic, psoriasiform and pustular dermatoses. In: *McKee's Pathology of the Skin*. 5th ed. Elsevier; 2018:180–218.
5. Armstrong AW, Bukhalo M, Blauvelt A. A clinician's guide to the diagnosis and treatment of candidiasis in patients with psoriasis. *Am J Clin Dermatol* 2016;17:329–36.
6. Kapila S, Bradford J, Fischer G. Vulvar psoriasis in adults and children: a clinical audit of 194 cases and review of the literature. *J Low Genit Tract Dis* 2012;16:364–71.
7. Mendling W, Brasch J, Cornely OA, et al. Guideline: vulvovaginal candidosis (AWMF 015/072), S2k (excluding chronic mucocutaneous candidosis). *Mycoses* 2015;58:1–15.

8. Hong E, Dixit S, Fidel PL, et al. Vulvovaginal candidiasis as a chronic disease: diagnostic criteria and definition. *J Low Genit Tract Dis* 2014;18:31–8.
9. Sobel JD. Recurrent vulvovaginal candidiasis. *Am J Obstet Gynecol* 2016; 214:15–21.
10. Taudorf EH, Jemec GBE, Hay RJ, et al. Cutaneous candidiasis—an evidence-based review of topical and systemic treatments to inform clinical practice. *J Eur Acad Dermatol Venereol* 2019;33:1863–73.
11. Day T, Borbolla Foster A, Phillips S, et al. Can routine histopathology distinguish between vulvar cutaneous candidosis and dermatophytosis? *J Low Genit Tract Dis* 2016;20:267–71.
12. Metin A, Dilek N, Bilgili SG. Recurrent candidal intertrigo: challenges and solutions. *Clin Cosmet Investig Dermatol* 2018;11:175–85.
13. Vergers-Spooren HC, van der Meijden WI, Luijendijk A, et al. Self-sampling in the diagnosis of recurrent vulvovaginal candidosis. *J Low Genit Tract Dis* 2013;17:187–92.
14. Patterson JW, Hosler GA, Prenshaw KL. Chapter 6: the psoriasiform reaction pattern and Chapter 26: mycoses and algal infections. In: *Weedon's Skin Pathology.* 5th ed. Elsevier; 2020:99–120 721–757.
15. Tin KS, Scurry J, Dyall-Smith D. Psoriasis superimposed on vitiligo: the tricolored vulva. *J Low Genit Tract Dis* 2014;18:E1–3.
16. Selim MA, Parra V, Sangueza OP. Chapter 6: infectious diseases and infestations of the vulva. In: Hoang MP, Selim MA, eds. *Vulvar Pathology.* Springer; 2015:176.
17. Taheri Sarvtin M, Shokohi T, Hajheydari Z, et al. Evaluation of candidal colonization and specific humoral responses against *Candida albicans* in patients with psoriasis. *Int J Dermatol* 2014;53:e555–60.
18. Buslau M, Menzel I, Holzmann H. Fungal flora of human faeces in psoriasis and atopic dermatitis. *Mycoses* 1990;33:90–4.
19. Waldman A, Gilhar A, Duek L, et al. Incidence of Candida in psoriasis—a study on the fungal flora of psoriatic patients. *Mycoses* 2001;44:77–81.
20. Beck KM, Yang EJ, Sanchez IM, et al. Treatment of genital psoriasis: a systematic review. *Dermatol Ther* 2018;8:509–25.
21. Nasir S, Goldsmith P. Anogenital allergic contact dermatitis caused by methylchloroisothiazolinone, methylisothiazolinone and topical clotrimazole with subsequent generalized exanthem triggered by oral fluconazole. *Contact Dermatitis* 2016;74:296–7.
22. Swidsinski A, Guschin A, Tang Q, et al. Vulvovaginal candidiasis: histologic lesions are primarily polymicrobial and invasive and do not contain biofilms. *Am J Obstet Gynecol* 2019;220:91.e1–8.
23. Zhang X, Lei L, Jiang L, et al. Characteristics and pathogenesis of Koebner phenomenon. *Exp Dermatol* 2023;32:310–23.
24. Edwards L, Lynch P. Red disorders: patches and plaques. In: *Genital Dermatology Manual*. 4th ed. Wolters Kluwer; 2022:56–87.
25. Poddar S, Das S, Sen S, et al. Could it be Wolf isotopic response?: occurrence of dermatophytoses on vitiliginous skin—case series of five cases from a tertiary care centre in India. *Indian Dermatol Online J* 2022; 13:240–3.
26. Zhou S, Yao Z. Roles of infection in psoriasis. *Int J Mol Sci* 2022;23: 6955.
27. Zhang P, Su Y, Li S, et al. The roles of T cells in psoriasis. *Front Immunol* 2023;14:1081256.