Inflammatory Dermatoses of the Vulva for the General/Gyn Pathologist with emphasis in the lichenoid pattern

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Lichen Planus

• Inflammatory mucocutaneous dermatosis
  • Estimated prevalence of ~1%

• Prototypical example of lichenoid dermatitis

• Most frequently affected sites
  • Flexor surfaces of forearms
  • Dorsal aspect of hands, anterior legs, neck, presacral areas

• Oral involvement very common
Intensely pruritic violaceous papules

Wickham’s Striae
Vulvar Lichen Planus (LP)

- Isolated vulvar lesions or in a/w either oral lichen planus or generalized eruption
- Middle-aged women of all races, 4th to 7th decades
- Extremely rare in pediatric population
- ~50% of women with cutaneous LP will have genital involvement
- Wide array of clinical types may be seen
• Classical type
  • Flat top papules in the labia majora, often pruritic but can be asymptomatic
• Hypertrophic LP
  • Raised hyperkeratotic papules and plaques
• Lichen Planopilaris variant
  • Hair-bearing areas, scarring alopecia
• Erosive LP
  • Severe pain, soreness, involvement of vaginal mucosa
Vulvovaginal Gingival Syndrome

- Severe variant of erosive LP
- Vulvar, vaginal and gingival mucosal erosions
- Predilection for scarring and stricture formation
- Early diagnosis and management crucial to avoid severe consequences

<table>
<thead>
<tr>
<th>Clinical Criteria</th>
<th>Histopathologic Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of well demarcated erosions or glazed erythema at the vaginal introitus</td>
<td>Presence of a well-defined inflammatory band in the superficial connective tissue that involves the dermo-epidermo junction</td>
</tr>
<tr>
<td>Presence of a hyperkeratotic white border to erythematous areas/erosions +/− Wickham’s striae in surrounding skin</td>
<td>Signs of basal cell layer degeneration, e.g., Civatte bodies, abnormal keratinocytes or basal apoptosis</td>
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<tr>
<td>Symptoms of pain/burning</td>
<td>Presence of an inflammatory band that consists predominantly of lymphocytes</td>
</tr>
<tr>
<td>Scarring/loss of normal architecture</td>
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<tr>
<td>Presence of vaginal inflammation</td>
<td></td>
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<tr>
<td>Involvement of other mucosal sites</td>
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Diagnosis of erosive lichen planus affecting the vulva requires 3 of the 9 criteria listed in this table.
Prognosis/Course

• Classical LP
  • Self-limited disease, most often remits spontaneously

• Erosive LP
  • Can be persistent, some patients poor response

• Risk of SCC site depended
  • Exrogenital skin: virtually no cancer risk
  • Oral & esophageal mucosa: 5%
  • Vulva: risk unknown
Differential Diagnosis

- Challenging in evolving or partially treated lesions
- Lichenoid drug eruptions

<table>
<thead>
<tr>
<th>Lichenoid Drug Eruption</th>
<th>Lichen Planus</th>
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<tr>
<td>Presence of parakeratosis</td>
<td>Absence of parakeratosis</td>
</tr>
<tr>
<td>Disruption of granular cell layer</td>
<td>Hypergranulosis in “V” shape</td>
</tr>
<tr>
<td>Cytoid bodies in cornified or granular cell layer</td>
<td>Cytoid bodies mainly in the basal layer</td>
</tr>
<tr>
<td>Marked numbers of eosinophils or plasma cells</td>
<td>Few eosinophils</td>
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</table>
Differential Diagnosis

- **Discoid lupus erythematosus**
  - Thickened basement membrane
  - Deep perivascular/periadnexal infiltrate
  - Increased dermal mucin

- **Squamous cell carcinoma**
  - Care not to confuse pseudoepitheliomatous hyperplasia

- **Lichen Simplex Chronicus**
  - Lack marked lichenoid inflammation
  - Lack saw tooth rete ridges
Differential Diagnosis

- Early lichen sclerosus

<table>
<thead>
<tr>
<th>Clues to Early Lichen Sclerosus</th>
<th>Clues to Lichen Planus</th>
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<tr>
<td>Thickened basement membrane</td>
<td>Saw tooth rete ridges</td>
</tr>
<tr>
<td>Psoriasiform hyperplasia with</td>
<td>Wedge-shaped hypergranulosis</td>
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<tr>
<td>peppering of lymphocytes</td>
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<tr>
<td>Epidermotropism of lymphocytes,</td>
<td>Marked number of civatte</td>
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<td>especially at the basal layer</td>
<td>bodies</td>
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<tr>
<td>Lymphocyte entrapment by wiry</td>
<td>Significant vacuolar</td>
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<td>dermal fibrosis</td>
<td>alteration of the basal</td>
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<td>layer</td>
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<td>Dyskeratotic keratinocytes with</td>
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<td>overlying columns of parakerato-</td>
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<td>sis</td>
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<tr>
<td>Wide telangiectasia</td>
<td></td>
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<tr>
<td>Loss of papillary dermal elastin</td>
<td></td>
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</table>
Differential Diagnosis for erosive LP

- Autoimmune blistering disorder (eg BP)
  - DIF: Linear IgG and C3 in BP
  - Bright globular cytoid bodies + for broad array of immunoreactants
- Differentiated VIN
  - Circumferential/symmetric flat erosions - LP
  - Unilateral erythematous plaque - dVIN
  - P53 staining limited utility in distinguishing erosive LP
Lichen Sclerosus (LS)

• One of the most **common** causes of symptomatic vulvar disease
• Anogenital area- 85-98%
• Extragenital area- 15-20%
• Bimodal peak: prepubertal and postmenopausal
• Maybe asymptomatic but commonly pruritus and soreness frequent complains
Well-developed LS
Prognosis/Course

- Early/mild cases spontaneous remission may occur
- In general it runs a chronic clinical course with episodes or relapse and remission
- Topical steroids suppress symptoms
- Scarring in a subset of patients, irreversible
- Low risk of progression to SCC (1-5%)
Differential Diagnosis

• Chronic radiation dermatitis
  • Clinical history
  • Presence of large, atypical pleomorphic fibroblasts

• Lichen Planus
  • Basement membrane thickening, psoriasiform hyperplasia, lymphocytic epidermotropism, wiry fibrosis with lymphocytes favor LS

• dVIN
  • Challenging as 80% of dVIN may have adjacent LS
dVIN vs LS

• Presence of premature keratinization in dVIN
  • Hypereosinophilic appearance

• Confluent basal layer keratinocytic atypia with frequent mitoses

• P53 marker maybe limited in differentiating LS vs dVIN
Lichenoid Drug Eruption

• Similar clinical and histologic features to lichen planus

Gold
Antimalarials
Beta-blockers
Lithium
Thiazide diuretics

Furosemide
Spironolactone
Ethambutol
TNF-alpha
Inhibitors
• Prolonged latent period from the introduction of the drug to the cutaneous eruption
• Clinical lesions maybe identical to lichen planus
  • More generalized distribution with sparing of classic sites of involvement of lichen planus
  • Lack of Wickham’s striae
  • Sparing of mucous membranes
  • Frequent photodistribution
**Lichenoid Drug Eruption**

- Presence of parakeratosis
- Disruption of granular cell layer
- Cytoid bodies in cornified or granular cell layer
- Marked numbers of eosinophils or plasma cells

**Lichen Planus**

- Absence of parakeratosis
- Hypergranulosis in “V” shape
- Cytoid bodies mainly in the basal layer
- Few eosinophils
Fixed Drug Eruption

• Readmission of the offending drug leads to lesions recurring at the exact site as previous eruption

• Drugs frequently implicated
  • Anti-inflammatory (e.g. ibuprofen), salicylates, oral contraceptives and others

• Days to weeks after first exposure

• Subsequent exposures within 24h
Differential Diagnosis

• Erythema multiforme
  • Clinical history essential to reach a diagnosis
  • More diffuse distribution of lesions with classic targetoid appearance
• Resolving or partially treated lichenoid processes
  • Clinical history of recurrence in the same anatomic location essential
Discoid Lupus Erythematosus

- Chronic form of lupus erythematosus, one of the most common presentations of lupus affecting the vulva
- Vulvar lesions rare
- 17-67 year-old, usually with known history of discoid or systemic lupus
- May progress to scarring if left untreated
- Overall prognosis depends on extend of lesions and presence/absence of systemic lupus
Differential Diagnosis

• Must be differentiated from most common lichenoid dermatoses such as lichen planus and lichen sclerosus
  • Deep dermal perivascular infiltrate with associated increased dermal mucin
  • Presence of prominent eosinophils, unlikely lupus
  • Direct immunofluorescence also useful
    • Often positive lupus band
Lichenoid Contact Dermatitis

- Inflammatory response of the skin to an external irritant or allergen
- Relatively common and may be superimposed on other vulvar conditions
- Commonly erythematous patches and plaques with various degrees of vesiculation and scale
- Patch testing maybe of value for diagnosis and identifying causative agent
Plasma Cell Vulvitis

• One or multiple shiny, glazed erythematous patches, and plaques with an orange hue
• Often bilateral, symmetrical, sharply demarcated 1 to 3 cm patches
• Most patients post-menopausal women
• Inner face of labia minora and periurethral mucosa most frequently affected
• Frequent pruritus, burning pain and dyspareunia
Prognosis/Course

- Natural history of recurrent relapses and remissions of different length
- Treatment guidelines have not been formulated
  - Topical steroids, topical calcineurin, topical imiquimod, excision
- Cases that do not respond to therapy may persist indefinitely
Differential Diagnosis

• Syphilis
  • IHC to evaluate for spirochetes
  • Minimal amount of dyskeratotic cells, presence of endarteritis and deep perivascular inflammation support syphilis

• Lichen Planus
  • In mucosal surfaces, plasma cells to a certain extend

• Other condition in the clinical differential
  • Vulvar dysplasia, SCC, Paget’s disease
Syphilis

- Sexually acquired infection caused by the spirochete *Treponema pallidum*
- The infection is chronic and passes through several stages
- **Primary syphilis**
  - Solitary, round, painless ulcer (chancre) with associated lymphadenopathy
- Subsequent hematogenous and lymphatic spread of the organisms leads to the manifestations of the **secondary stage of syphilis**
• Secondary syphilis
  • Widespread cutaneous eruption (maculopapular or papulosquamous lesions) with an associated prodrome
• Other mucocutaneous manifestations
  • red-brown oval-shaped lesions on the palms and soles and condylomata lata of the anogenital region
• Latent Stage
  • Signs and symptoms largely subclinical
• Tertiary Stage
  • Cardiovascular/neurological defects
Primary Syphilis
Secondary Syphilis
Differential Diagnosis

• Known as the great mimicker because of myriad clinical presentations

• Lichenoid presentation
  • Lichen Planus
  • Plasma cell vulvitis

• When neutrophils present at DEJ in a/w lymphoplasmacytic infiltrate ancillary staining essential

• Robust superficial and deep lymphocytic infiltrates raise DDx of lymphoma
Chronic Graft VS Host Disease

- A systemic complex immune disorder which is a complication of allogenic hematopoietic stem cell transplantation.
- May involve the female genital tract in approximately 3% of bone marrow and 15% of peripheral blood recipients.
- Dx is based primarily on the identification of typical clinical manifestations with the rapid response to super-potent topical corticosteroids.
Differential Diagnosis

- Histology maybe identical to
  - Lichen Planus
  - Lichen Sclerosus
  - Morphea
- Maybe impossible to differentiate on histologic grounds alone
- Clinical correlation and clinical Hx essential to diagnosis
Papulosquamous
Psoriasis Vulgaris

• A chronic relapsing papulosquamous dermatitis affecting approximately 2% of the population
• Genetic proclivity does exist
• Friction and occlusion caused by tight clothing may precipitate vulvar involvement by psoriasis in individuals who are already genetically predisposed
• May present as the classic form either generalized or localized to the vulva, or as inverse psoriasis that favors skin folds
Differential Diagnosis

• Recurrent vulvovaginal candidiasis
• Tinea
  • Prudent to perform PAS whenever neuts in stratum corneum and/or epidermis
• Lichen simplex chronicus
• Extramammary Paget Disease
  • Intraepidermal epithelioid neoplastic cells
  • CK7 positive
• Contact dermatitis
Vesiculobullous Disorders
Bullous Pemphigoid (BP)

- Localized vulvar involvement in the immunobullous dermatoses, though uncommon, may be misdiagnosed or go unrecognized.
- Bullous pemphigoid is the most common of the immunobullous diseases.
- 9% of adults and 40% of children have vulvar involvement.
- Several cases of BP in children show localized vulvar involvement.
Direct immunofluorescence

IgG

C3
Pemphigus Vulgaris (PV)

- Rare acquired immunobullous disorder caused by autoantibodies against desmoglein 3
- **Vulvar lesions the second most frequent site of mucosal PV**, with a frequency of approximately 22–51%
- Rarely can be the sole manifestation of the disease.
- Painful mucosal erosions and/or flaccid bullae involving the mouth or nasal mucosa, or vulvar superficial ulcers and erosions
“Tombstones!!
DIF: Intercellular IgG and C3
DDx

- Hailey-Hailey Disease
- Darier Disease
- Acantholysis of the vulvocrural area
- DIF is negative in all of the above
Cutaneous involvement by Crohn disease is a frequent extragastrointestinal tract manifestation that affects 22–44% of cases.

- Perianal fistula formation the most frequent manifestation
- Genital involvement most frequently seen in the pediatric population
  - Either by direct extension of perianal disease
  - Or metastatic Crohn disease
- Vulvar ulcers may be the initial manifestation in 25% of patients.

- Severity of skin lesions does not reflect degree of activity of bowel disease.
Differential Diagnosis

- Foreign Body Giant Cell reaction
- Hidradenitis Suppurativa
- Sarcoidosis
- Tuberculosis
- Intertrigo
- Venereal Disease
- Deep fungal infection
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