

Chapter 25 :: Parapsoriasis and Pityriasis Lichenoides

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PARAPSORIASIS

PARAPSORIASIS AT A GLANCE

- Also known as parapsoriasis en plaques.
- Parapsoriasis occurs worldwide and affects mainly adults.
- Large-plaque parapsoriasis (LPP) and small-plaque parapsoriasis (SPP) are recognized.
- Large and small “plaque” lesions actually present as flat patches rather than infiltrated plaques.
- Lesions are chronic and favor nonsun-exposed skin; LPP may be poikilodermatous.
- Pathology consists of superficial, mostly CD4⁺ T-cell infiltrate; dominant clonality is more common in LPP than in SPP.
- LPP appears to exist on a continuum with patch-stage mycosis fungoides (MF) and progresses to overt MF at a rate of approximately 10% per decade.
- SPP has minimal risk of progression to overt MF in the experience of most experts.
- Treatment options include topical corticosteroids; ultraviolet B (UVB) irradiation, and psoralen and ultraviolet A (UVA) irradiation; excimer laser; and topical cytotoxic drugs.

HISTORICAL ASPECTS

The term parapsoriasis was coined originally by Brocq in 1902.¹ As shown in Table 25-1, the currently accepted classification of parapsoriasis includes large- and small-plaque forms of parapsoriasis en plaques (often referred to simply as *parapsoriasis*) as well as acute and chronic forms of pityriasis lichenoides [known today as *pityriasis lichenoides et varioliformis acuta* (PLEVA) and *pityriasis lichenoides chronica* (PLC), respectively].² Pityriasis lichenoides was first described in 1894 by Neisser³ and Jadassohn.⁴ In 1899 Juliusberg delineated

the chronic form and named it PLC.⁵ Mucha re-described the acute form in 1916 and distinguished it from the chronic form.⁶ Habermann named the acute variant PLEVA in 1925.⁷ Mucha–Habermann disease is synonymous with PLEVA. Some authors regard lymphomatoid papulosis as a variant of pityriasis lichenoides, whereas others consider it to be a separate disease.^{2,8–10} Lymphomatoid papulosis is discussed in Chapter 144 as part of the spectrum of CD30⁺ cutaneous lymphoproliferative disorders.

EPIDEMIOLOGY

Large-plaque parapsoriasis (LPP) and small-plaque parapsoriasis (SPP) are, in general, diseases of middle-aged and older people, with a peak incidence in the fifth decade. Occasionally, lesions arise in childhood and may be associated with pityriasis lichenoides. SPP shows a definite male predominance of approximately 3:1. LPP is probably more common in males, but the difference is not as striking as in SPP. Both occur in all racial groups and geographic regions.

ETIOLOGY AND PATHOGENESIS

It is likely that a complete understanding of the pathogenesis of parapsoriasis will develop with our understanding of the pathogenesis of both chronic dermatitis and mycosis fungoides (MF), because parapsoriasis appears to bridge these disorders. The T cells that mediate most inflammatory skin diseases belong to the skin-associated lymphoid tissue (SALT).¹¹ These T cells express the cutaneous lymphocyte-associated antigen and traffic between the skin and the T-cell domains of peripheral lymph nodes via the lymphatics and bloodstream. MF (see Chapter 144) has been shown to be a neoplasm of SALT T cells. Sensitive polymerase chain reaction (PCR)-based tumor

TABLE 25-1

Classification of Parapsoriasis

1. Parapsoriasis en plaques
 - A. Large-plaque parapsoriasis variants: poikilodermatous, retiform
 - B. Small-plaque parapsoriasis variant: digitate dermatosis
2. Pityriasis lichenoides
 - A. Pityriasis lichenoides chronica (Juliusberg)
 - B. Pityriasis lichenoides et varioliformis acuta (Mucha–Habermann)

clonality assays have underscored the SALT nature of MF tumor clones by showing that they can continue to traffic after neoplastic transformation¹² and can even participate in delayed-type hypersensitivity reactions to contact allergens.¹³ This implies that rather than being a skin lymphoma per se, MF is actually a SALT lymphoma, i.e., a malignancy of a T-cell circuit rather than of one particular tissue. Trafficking of MF tumor cells has been detected even in patients with very early stage disease whose lesions were consistent clinicopathologically with LPP.^{12,14} Therefore, it can be said that at least in some cases LPP is a monoclonal proliferation of SALT T cells that have the capacity to traffic between the skin and extracutaneous sites.

This view is also supported by the presence of structural and numerical chromosomal abnormalities in the peripheral blood mononuclear cells of patients with LPP.¹⁵ In this context, LPP can be regarded as the clinically benign end of the MF disease spectrum, which eventuates in transformed large cell lymphoma at its malignant extreme. To say that these diseases belong to the same disease spectrum is not to say that they are biologically equivalent disorders. To lump them all together simply as “MF” would be to ignore their distinctive clinicopathologic features, which are likely due to genetic and/or epigenetic differences, such as the *p53* gene somatic mutations observed in some cases of large cell transformation of MF.^{16–18} It is likely that several such differences separate these clinicopathologically defined disorders in a stepwise fashion analogous to the sequential acquisition of somatic mutations that occurs in the colon cancer disease spectrum as colonic epithelial cells progress through normal, hyperplastic, in situ carcinoma, invasive carcinoma, and metastatic carcinoma stages.^{19,20}

A unifying feature of the parapsoriasis group of diseases is that all of them appear to be cutaneous T-cell lymphoproliferative disorders: LPP,^{12,21–28} SPP,^{23,28,29} pityriasis lichenoides,^{28,30–32} and lymphomatoid papulosis^{23,33–35} have all been shown to be monoclonal disorders in many cases.³⁶ These relationships suggest that progression from LPP through the various stages of the MF disease spectrum is accompanied by an increasing gradient of dominant T-cell clonal density resulting from mutations that confer increasing growth autonomy to the neoplastic T-cell clone.³⁷ Interestingly, analysis of peripheral blood has demonstrated that clonal T cells are often detectable in patients with LPP/early MF^{27,28} or SPP,^{28,38} which again supports the systemic SALT nature of these “primary” skin disorders.

Dominant clonality as seen in the parapsoriasis disease group, follicular mucinosis, pagetoid reticulosis, and certain other disorders does not equate to clinical malignancy. In fact, most patients with these diseases experience a benign clinical course, and in some cases the disease resolves completely. In addition, other types of chronic cutaneous T-cell infiltrates sometimes exhibit dominant clonality, including primary (idiopathic) erythroderma and nonspecific chronic spongiotic dermatitis. This has given rise to the concept of clonal dermatitis,^{14,39} originally described in the context of clonal nonspecific chronic spongiotic dermatitis but later expanded to include other nonlymphomatous

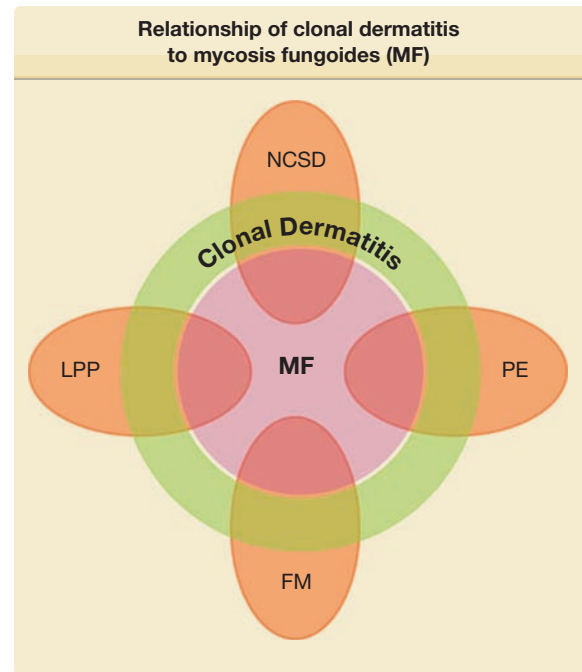


Figure 25-1 The relationship of clonal dermatitis to mycosis fungoides (MF) and various types of chronic dermatitis. The proportions of each entity that represent clonal dermatitis and mycosis fungoides vary with each disease and are not drawn to scale. FM = follicular mucinosis; LPP = large-plaque parapsoriasis; NCS = nonspecific chronic spongiotic dermatitis; PE = primary erythroderma.

cutaneous T-cell infiltrates that harbor occult monoclonal T-cell populations. Several cases of clonal dermatitis, some of which have progressed to MF, have been identified.^{14,21,39} We suspect that for each disease with a potential for progression to MF, the principal risk may reside in the subset showing clonal dermatitis, because this is the subset in which dysregulation has begun to occur.

The postulated relationships among MF, clonal dermatitis, and selected types of chronic dermatitis are depicted in Fig. 25-1. Each of the entities shown is postulated to be at risk for MF through a clonal dermatitis intermediate. In this model, MF becomes the final common pathway for the clonal evolution of neoplastic T cells emerging from the polyclonal SALT T-cell populations present in each of the various precursor diseases.

Various viruses have been proposed to play a role in the pathogenesis of MF. None has been substantiated thus far. The most recent virus implicated in both LPP and MF is HHV-8; however, conflicting reports await resolution.^{40–42}

CLINICAL FINDINGS

CUTANEOUS LESIONS. LPP lesions are either oval or irregularly shaped patches or very thin plaques that are asymptomatic or mildly pruritic. They are usually well marginated but may also blend imperceptibly into the surrounding skin. The size is variable, but



Figure 25-2 Large-plaque parapsoriasis. Irregularly shaped patches of variable size on the arm of a 16-year-old girl.

BOX 25-1 DIFFERENTIAL DIAGNOSIS OF POIKILODERMA

- Large-plaque parapsoriasis
- Dermatomyositis
- Lupus erythematosus
- Chronic radiation dermatitis
- Bloom syndrome
- Rothmund–Thomson syndrome
- Dyskeratosis congenita
- Xeroderma pigmentosum

typically most lesions are larger than 5 cm, often measuring more than 10 cm in diameter. Lesions are stable in size and may increase in number gradually. They are found mainly on the “bathing trunk” and flexural areas (Fig. 25-2). Extremities and the upper trunk, especially the breasts in women, also may be involved. They are light red–brown or salmon pink, and their surface is covered with small and scanty scales. Lesions may appear finely wrinkled—“cigarette paper” wrinkling. Such lesions exhibit varying degrees of epidermal atrophy. Telangiectasia and mottled pigmentation also are observed when the atrophy becomes prominent (Fig. 25-3). This triad of atrophy, mottled pigmentation, and telangiectasia defines the term *poikiloderma* or *poikiloderma atrophicans vasculare*, which also may be seen in other conditions (Box 25-1).

Retiform parapsoriasis refers to a rare variant of LPP that presents as an extensive eruption of scaly macules and papules in a net-like or zebra-stripe pattern that eventually becomes poikilodermatous (Fig. 25-4).

SPP characteristically occurs as round or oval discrete patches or very thin plaques, mainly on the trunk (Fig. 25-5). The lesions measure less than 5 cm in diameter; they are asymptomatic and covered with fine, moderately adherent scales. The general health of the patient is unaffected. A distinctive variant with lesions of a finger shape, known as *digitate dermatosis*,⁴³ has yellowish or fawn-colored lesions (Fig. 25-6). It follows lines of cleavage of the skin and gives the appearance of a hug that left fingerprints on the trunk. The long axis of these lesions often measures greater than 5 cm. Chronic superficial dermatitis is a synonym for SPP.⁴⁴



Figure 25-3 Large-plaque parapsoriasis. Poikilodermatous variant.



Figure 25-4 Large-plaque parapsoriasis. Retiform variant.



Figure 25-5 Small-plaque parapsoriasis. Small, discrete patches less than 5 cm in diameter.

Digitate lesions with a yellow hue were referred to in the past as *xanthoerythrodermia perstans*.²

LABORATORY TESTS

HISTOPATHOLOGY. In early LPP lesions, the epidermis is mildly acanthotic and slightly hyperkeratotic



Figure 25-6 Small-plaque parapsoriasis. Digitate dermatosis variant. Typical "fingerprint" patches on the flank. Note that their length often exceeds 5 cm.

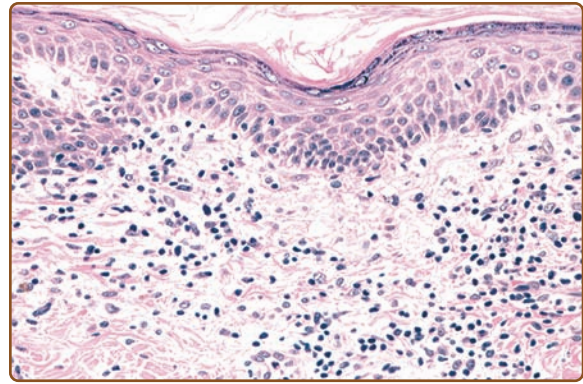


Figure 25-7 Large-plaque parapsoriasis. Mildly hyperkeratotic and focally parakeratotic epidermis with moderately dense superficial perivascular infiltrate. Lymphoid cells are mostly small, cytologically normal lymphocytes, and there is focal single-cell epidermotropism. (Used with permission from Helmut Kerl, MD.)

with spotty parakeratosis. The dermal lymphocytic infiltrate tends to be perivascular and scattered (Fig. 25-7). In the more advanced lesions one observes an interface infiltrate with definite epidermotropism. These invading lymphocytes may be scattered singly or in groups, sometimes associated with mild spongiosis. In addition, the poikilodermatous lesions show atrophic epidermis, dilated blood vessels, and melanophages (Fig. 25-8). Immunohistologic studies have revealed similar features in LPP and early MF, including a predominance of CD4⁺ T-cell subsets, frequent CD7 antigen deficiency, and widespread epidermal expression of class II HLA (HLA-DR).^{22-24,45-48}

SPP exhibits mild spongiotic dermatitis with focal areas of hyperkeratosis, parakeratosis, scale crust, and exocytosis. In the dermis, there is a mild superficial perivascular lymphohistiocytic infiltrate and dermal edema (Fig. 25-9). There is no progression of the histologic features with time. Immunohistologic studies reveal a predominantly CD4⁺ T-cell infiltrate with nonspecific features resembling those seen in various types of dermatitides.⁴⁷

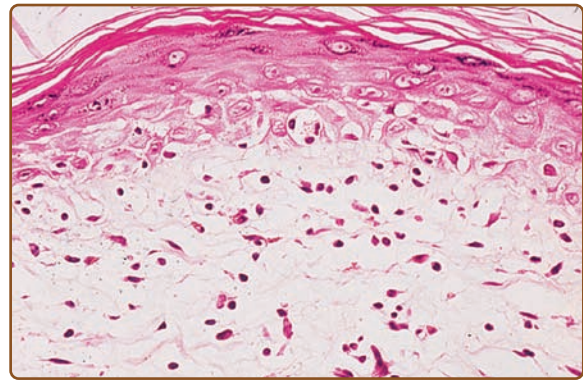


Figure 25-8 Large-plaque parapsoriasis. Atrophic variant. Sparse superficial lymphoid infiltrate with mild epidermotropism and epidermal atrophy.

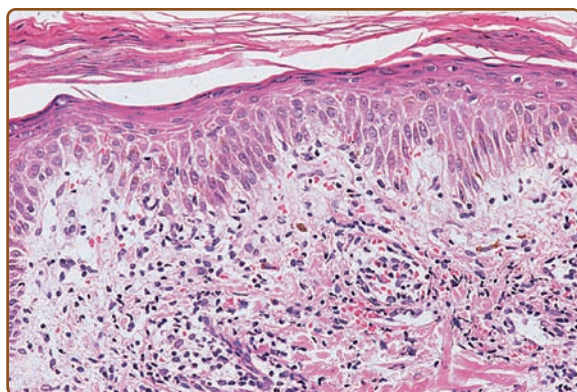


Figure 25-9 Small-plaque parapsoriasis. Superficial perivascular lymphoid infiltrate, mild spongiosis, parakeratosis, and focal scale crust.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

LPP is distinguished from SPP by the larger size, asymmetric distribution, and irregular shape of its lesions, which are less discrete and often poikilodermatous. LPP may be clinically and histopathologically indistinguishable from the patch stage of MF. Both LPP and SPP are readily distinguished from more advanced infiltrated plaques of MF because parapsoriasis lesions are, by definition, not thicker than patches or at most very thin plaques. This is so because the English equivalent of the French term *plaques* is *patches*, i.e., lesions that are essentially flat and devoid of induration or palpable infiltration.⁴⁹ Failure to appreciate this

important distinction has led to considerable confusion and misuse of the terms *large-plaque parapsoriasis* and *small-plaque parapsoriasis* by some individuals. These designations more appropriately might be thought of as *large-patch parapsoriasis* and *small-patch parapsoriasis*.

The degree to which LPP is differentiated from early MF depends primarily on the histopathologic criteria used to diagnose the latter disorder. Unfortunately, there are no universally accepted minimal criteria for the diagnosis of MF; however, one set proposed by the International Society for Cutaneous Lymphoma is presented in Table 25-2.⁵⁰ This algorithm is based on a holistic integration of clinical, histopathologic, immunopathologic, and clonality data. It differs significantly from many prior approaches because it does not rely solely on histopathologic features.⁵¹ Assuming that histopathologic examination does not disclose features diagnostic of some other dermatosis, these criteria allow lesions to be classified as either patch-stage MF or not. For the practical purposes of clinical management, patients presenting clinically with patch lesions whose features result in a score of four points or more are considered to have unequivocal MF. Obviously, the more liberal the criteria, the more cases could be considered to be MF. However, there will always be some cases that fail to meet any specific set of criteria, and the designation *LPP* is a useful term to apply to them because it guides treatment and follow-up and conveys an understanding that the risk of dying from lymphoma is small.

The clinical and/or histopathologic differential diagnosis of LPP also includes those collagen vascular diseases and genodermatoses exhibiting poikilodermatous features, lichenoid drug eruptions, secondary syphilis, chronic radiodermatitis, and occasionally

TABLE 25-2

Algorithm for the Diagnosis of Patch-Stage Mycosis Fungoides (Four Points are Required)

Parameter	2 Points	1 Point
Clinical: Persistent, progressive patches and plaques ± Nonsun-exposed distribution Variation in size and shape Poikiloderma	Any two	Any one
Histopathologic: Superficial dermal T-cell infiltrate ± Epidermotropism Nuclear atypia	Both	Either
Immunopathologic: CD2, CD3, or CD5 <50% CD7 <10% Epidermal–dermal discordance	Not applicable	Any one
Molecular biologic: Dominant T-cell clonality	Not applicable	Present

Note: Epidermotropism implies the lack of significant spongiosis (intraepidermal lymphoid cells associated with spongiosis is termed *exocytosis* rather than *epidermotropism*). Discordance refers to differential antigen expression between the epidermis and dermis, as opposed to the biopsy specimen as a whole.

From Pimpinelli N et al: Defining early mycosis fungoides. *J Am Acad Dermatol* 53:1053, 2005, with permission.

BOX 25-2 DIFFERENTIAL DIAGNOSIS OF LARGE-PLAQUE PARAPSORIASIS (LPP) AND SMALL-PLAQUE PARAPSORIASIS (SPP)

Most Likely

- LPP
 - Tinea corporis
 - Plaque-type psoriasis
 - Contact dermatitis
 - Subacute cutaneous lupus erythematosus
- SPP
 - Nummular dermatitis
 - Pityriasis rosea
 - Plaque and guttate psoriasis
 - Pigmented purpuric dermatoses
 - Pityriasis lichenoides chronica

Consider

- LPP
 - Xerotic dermatitis
 - Atopic dermatitis
 - Dermatomyositis
 - Drug eruption
 - Erythema dyschromicum perstans
 - Pigmented purpuric dermatoses
 - Early inflammatory morphea
 - Atrophoderma of Pasini–Pierini
 - Erythema annulare centrifugum
 - Pityriasis rubra pilaris
 - Genodermatoses with poikiloderma
 - Chronic radiodermatitis
- SPP
 - Tinea versicolor
 - Seborrheic dermatitis
 - Drug eruption

Always Rule Out

- LPP
 - Mycosis fungoides
- SPP
 - Mycosis fungoides
 - Secondary syphilis

several other diseases tabulated in [Box 25-2](#). These generally can be distinguished by their associated clinical findings. Histopathologic differentiation among these diseases is covered largely in the discussion of pseudo-MF in Chapter 145.

SPP, when it presents with its distinctive digitate dermatosis lesions parallel to skin lines in a truncal distribution, stands out from other types of parapsoriasis. Individual SPP lesions may show some superficial resemblance to PLC. SPP is distinguished from psoriasis by the absence of the Auspitz sign (see Chapter 17), micaceous scale, nail pits, and typical psoriatic

lesions involving the scalp, elbows, and knees. Histologically, its mild spongiotic dermatitis and absence of other characteristic features distinguish it from PLC, psoriasis, and several of the other entities listed in [Box 25-2](#). Clinical features are also important, such as the herald patch of pityriasis rosea and the papulovesicular coin-shaped patches favoring the lower extremities in nummular dermatitis.

Sometimes patients with MF may exhibit small patches of disease at presentation; however, these lesions typically have histopathologic features at least consistent with MF and generally are associated with larger, more classic lesions of MF elsewhere on the skin. They also may show poikilodermatous features not seen in SPP. Furthermore, the presence of well-developed, moderate to thick small plaques, as seen in some MF patients, is incompatible with the diagnosis of SPP because the latter disorder includes only lesions that are no more than patches or very thin plaques. It is also important to recognize that partially treated or early relapsing lesions of MF may show only nonspecific features that should not be taken as evidence of a pathogenetic link to SPP or any other dermatosis.

COMPLICATIONS

LPP can be associated with other forms of parapsoriasis and overt cutaneous lymphomas as detailed elsewhere in this chapter. Both LPP and SPP occasionally can develop areas of impetiginization secondary to excoriation.

PROGNOSIS AND CLINICAL COURSE

Both LPP and SPP may persist for years to decades with little change in appearance clinically or histopathologically. Approximately 10% to 30% of cases of LPP progress to overt MF.^{2,52–54} In this context, LPP represents the clinically benign end of the MF disease spectrum, with transformation to large cell lymphoma at the opposite extreme. The rare retiform variant is said to progress to overt MF in virtually all cases.²

In contrast to LPP with its malignant potential, SPP is a clinically benign disorder in the experience of most experts. Patients with this disease as defined in this chapter rarely develop overt MF.^{11,44,55,56} Despite this fact and what most observers consider to be its nonspecific histopathologic features, some authors favor lumping SPP within the MF disease spectrum as a very early, nonprogressive variant.^{55,57} This issue has been debated at length.^{31,57,58} A few studies report progression from SPP to MF in about 10% of cases but may have used different criteria than described in this chapter.^{53,54}

TREATMENT

Patients with SPP should be reassured and may forego treatment. The disease may be treated with emollients,

BOX 25-3 TREATMENT OF LARGE-PLAQUE PARAPSORIASIS AND SMALL-PLAQUE PARAPSORIASIS

FIRST LINE

- Emollients
- Topical corticosteroids
- Topical tar products
- Sunbathing
- Broadband UVB phototherapy
- Narrowband UVB phototherapy

SECOND LINE

(Mainly for large-plaque parapsoriasis cases considered to be early mycosis fungoides)

- Topical bexarotene
- Topical imiquimod
- Psoralen and UVA phototherapy
- Topical mechlorethamine
- Topical carmustine (BCNU)
- Excimer laser (308 nm)

topical tar preparations, topical corticosteroids, and/or broadband or narrowband UVB phototherapy (Box 25-3).⁵⁹ Response to therapy is variable. Patients should initially be examined every 3 to 6 months and subsequently every year to ensure that the character of the process is stable.

LPP requires more aggressive therapy: high-potency topical corticosteroids with phototherapy such as broadband UVB, narrowband UVB, or psoralen and UVA (PUVA). The goal of treatment is to suppress the disorder to prevent possible progression to overt MF. Other methods of treatment, such as topical nitrogen mustard, have been used, particularly for the poikilodermatous type. Localized lesions may respond to excimer laser (308 nm).^{60,61} The patient should be examined carefully every 3 months initially and every 6 months to 1 year subsequently for evidence of progression. Repeated multiple biopsies of suspicious lesions should be performed. Cases that satisfy the clinicopathologic criteria for early MF can be treated with broadband UVB, narrowband UVB, PUVA, topical nitrogen mustard, topical bexarotene gel, topical imiquimod, or topical carmustine (BCNU).⁶² Electron-beam radiation therapy generally is reserved for more advanced, infiltrated lesions of MF.

PREVENTION

Because LPP and SPP are uncommon diseases that appear to affect patients randomly, there are no known preventive measures.

PITYRIASIS LICHENOIDES

PITYRIASIS LICHENOIDES AT A GLANCE

- Pityriasis lichenoides et varioliformis acuta (PLEVA) and pityriasis lichenoides chronica (PLC) represent two ends of a disease spectrum; both entities and intermediate forms can coexist.
- All forms are characterized by spontaneously resolving, temporally overlapping crops of papules.
- PLEVA papules last for weeks and may develop crusts, vesicles, pustules, or ulcers.
- PLC papules persist for months and develop scales.
- All forms contain interface, cytolytic T-cell infiltrates with variable epidermal destruction.
- In PLEVA, CD8⁺ cells predominate.
- In PLC, CD8⁺ or CD4⁺ cells predominate.
- Dominant T-cell clonality can be detected in all forms, more often in PLEVA than in PLC.
- Treatment depends on severity and ranges from topical steroids, systemic antibiotics, UV irradiation, and psoralen and UVA to systemic immunosuppressants.

EPIDEMIOLOGY

Pityriasis lichenoides affects all racial and ethnic groups in all geographic regions.⁶³⁻⁶⁸ It is more common in children and young adults but can affect all ages with seasonal variation in onset favoring fall and winter. There is a male predominance of 1.5:1 to 3:1. PLC is three to six times more common than PLEVA.

ETIOLOGY AND PATHOGENESIS

The etiology of pityriasis lichenoides is unknown. Some cases have been associated with infectious agents such as *Toxoplasma gondii*,^{69,70} Epstein-Barr virus,^{70,71} cytomegalovirus,^{70,71} parvovirus B19,^{70,72,73} and human immunodeficiency virus.^{74,75} At least one case was linked repeatedly with estrogen–progesterone therapy, another with chemotherapy drugs, and a third with radiocontrast iodide.⁷⁶⁻⁷⁸ It is uncertain

whether these agents are actively involved in disease pathogenesis or merely coincidental bystanders; however, several cases associated with toxoplasmosis have cleared fairly quickly in response to specific therapy.⁶⁹ A tenfold higher level of maternal keratinocytes have been reported in the epidermis of children with PL compared to controls.⁷⁹

Immunohistologic studies have shown a reduction in CD1a⁺ antigen-presenting dendritic (Langerhans) cells within the central epidermis of pityriasis lichenoides lesions.⁸⁰ Keratinocytes and endothelial cells are HLA-DR⁺, which suggests activation by T-cell cytokines.⁸⁰ CD8⁺ T cells predominate in PLEVA, whereas either CD8⁺ or CD4⁺ T cells predominate in PLC.^{80–82} Many of these T cells express memory proteins (CD45RO) and cytolytic proteins (TIA-1 and granzyme B).^{72,73} Dominant T-cell clonality has been demonstrated in about half of PLEVA cases and a minority of PLC cases.^{32,83,84} In aggregate, these findings raise the possibility that pityriasis lichenoides is a variably clonal cytolytic memory T-cell lymphoproliferative response to one or more foreign antigens. Deposition of immunoglobulin M, C3, and fibrin in and around blood vessels and along the dermal–epidermal junction in early acute lesions suggests a possible concomitant humoral immune response, although this could be a secondary phenomenon.

The relationship of pityriasis lichenoides to lymphomatoid papulosis remains controversial^{10,51,80} (see also Chapters 144 and 145). Common features include dominant T-cell clonality and spontaneous resolution of papular, predominantly lymphoid lesions. Furthermore, individual lesions with the clinicopathologic characteristics of either pityriasis lichenoides or lymphomatoid papulosis can coexist in the same patient, either concurrently or serially. It remains to be determined whether this can be explained as an artifact of sampling lymphomatoid papulosis lesions at various stages of their evolution. The presence of large CD30⁺ atypical lymphoid cells is the hallmark of lymphomatoid papulosis (at least types A and C).⁸⁴ Furthermore, these cells are typically CD4⁺ and often lack one or more mature T-cell antigens such as CD2, CD3, and CD5. These features serve to distinguish lymphomatoid papulosis from pityriasis lichenoides. Although occasional CD30⁺ cells can be seen in a wide variety of dermatoses, the presence of any appreciable number should favor lymphomatoid papulosis over pityriasis lichenoides as a matter of definition. It may be that the “PLC-PLEVA” and “lymphomatoid papulosis–CD30⁺ anaplastic large cell lymphoma” disease spectra are intersecting rather than overlapping entities, i.e., although pityriasis lichenoides is a distinct cutaneous T-cell disorder, it is possible that it may sometimes serve as fertile soil for the development of the CD30⁺ T-cell clone characteristic of lymphomatoid papulosis.

CLINICAL FINDINGS

CUTANEOUS LESIONS. PLC and PLEVA exist on a clinicopathologic continuum.^{2,51} Therefore,

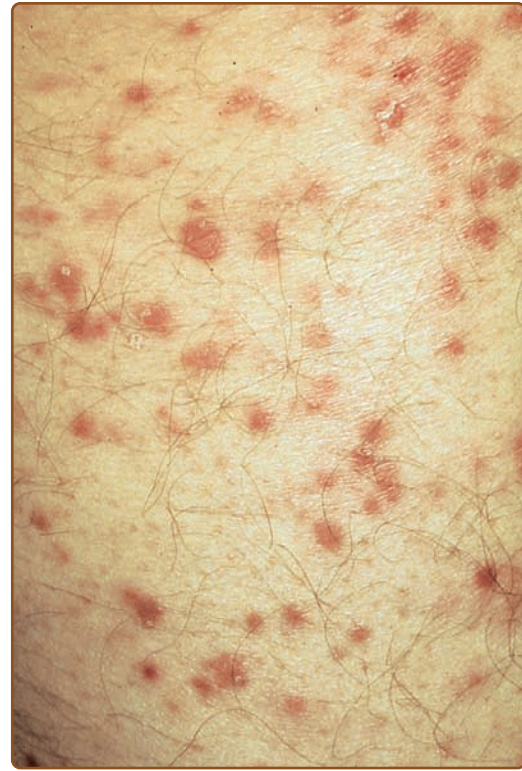


Figure 25-10 Pityriasis lichenoides chronica. Polymorphous appearance ranging from early erythematous papules to scaling brown–red lesions and tan–brown involuting, flat papules, and macules.

individual patients may exhibit a mixture of acute and chronic lesions sequentially or concurrently. In addition, lesions representing clinical or histopathologic intergrades between the extremes may also occur at any time.

Lesions are often asymptomatic but can be pruritic or burning, especially in the more acute cases. PLC typically presents as recurrent crops of erythematous scaly papules that spontaneously regress over several weeks to months (Fig. 25-10). PLEVA manifests as recurrent crops of erythematous papules that develop crusts, vesicles, pustules, or erosions before spontaneously regressing within a matter of weeks (Fig. 25-11). The more severe ulcerative variant is known as *pityriasis lichenoides with ulceronecrosis and hyperthermia* (PLUH) or *febrile ulceronecrotic Mucha–Habermann disease* (FUMHD).⁸⁵ It presents as purpuric papulonodules with central ulcers up to a few centimeters in diameter (Fig. 25-12). Some have proposed that this severe variant is actually an overt T-cell lymphoma.³¹ Pityriasis lichenoides lesions tend to concentrate on the trunk and proximal extremities, but any region of the skin and even mucous membranes can be involved. Rare regional or segmental lesion distributions have been described,^{10,86} as has rare conjunctival nodular inflammation.⁸⁷ Although there are usually numerous coexistent lesions, occasionally only a small number of lesions will be present at any one time. All forms of pityriasis lichenoides can result in



Figure 25-11 Pityriasis lichenoides et varioliformis acuta. **A.** Adolescent with multiple erythematous papules and crusted lesions in various stages of evolution. **B.** Larger papulovesicular and hemorrhagic, crusted lesions in an adult. Note varioliform scars adjacent to active lesions on posterior thigh and leg. **C.** Pustules, crusts, and necrotic-centered papules with erythematous, indurated base.

postinflammatory hypopigmentation or hyperpigmentation.⁶³ Chronic lesions can resolve with postinflammatory hypopigmentation, sometimes presenting as idiopathic guttate hypomelanosis. Chronic lesions

rarely lead to scars. In contrast, acute lesions result in deeper dermal injury and consequently often resolve leaving varioliform (smallpox-like) scars. The presence of lesions in various stages of evolution imparts a polymorphous appearance that is characteristic of pityriasis lichenoides.

LABORATORY TESTS

Miscellaneous nonspecific abnormalities in blood test results occur but are of little practical value. Leukocytosis and a decreased CD4/CD8 ratio can occur.

HISTOPATHOLOGY. As with the morphology of the clinical lesions, pityriasis lichenoides can exhibit a range of histopathologic features encompassing acute, chronic, and intermediate lesional variants (Figs. 25-13 and 25-14). All cases of pityriasis lichenoides contain an interface dermatitis that is denser and more wedge shaped in the acute lesions. The infiltrate is composed mainly of lymphocytes with a variable admixture of neutrophils and histiocytes. There is exocytosis, parakeratosis, and extravasation of erythrocytes. Epidermal damage ranges from intercellular and extracellular edema in less severe cases to extensive keratinocyte necrosis, vesicles, pustules, and ulcers. The acute variants can exhibit lymphocytic vasculitis with fibrinoid degeneration of blood vessel walls.



Figure 25-12 Pityriasis lichenoides, ulceronecrotic, hyperacute variant. Large necrotic eschar with halo erythema developing in febrile patient with antecedent pityriasis lichenoides et varioliformis acuta.

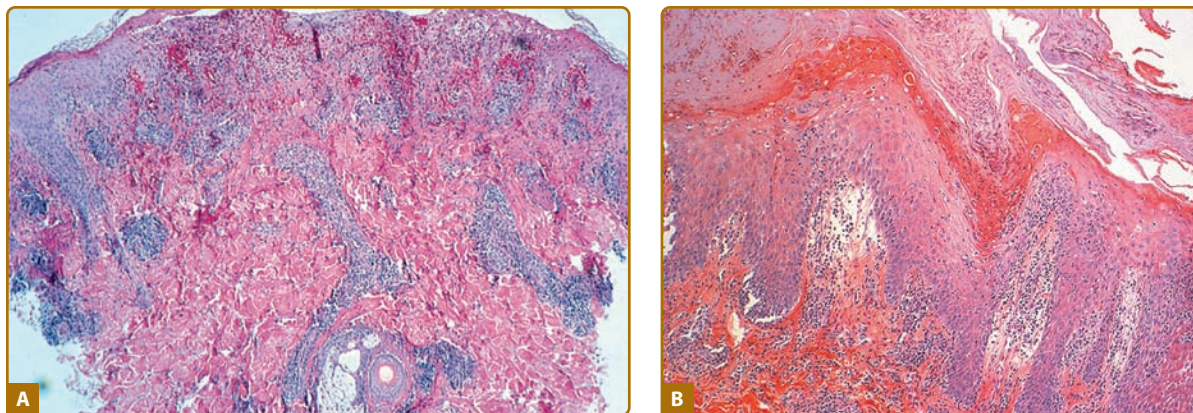


Figure 25-13 Pityriasis lichenoides et varioliformis acuta. **A.** Ulcerated papule with epidermal necrosis, hemorrhage, and superficial and deep perivascular lymphocytic infiltrate. Hematoxylin and eosin (H&E) stain. **B.** Parakeratosis and crust with marked spongiosis and epidermal necrosis. Lymphocyte exocytosis and basal hydropic changes. H&E stain.

Occasional CD30⁺ lymphoid cells and occasional atypical lymphoid cells may be seen as a nonspecific finding in many cutaneous lymphoid infiltrates. The presence of an appreciable numbers of these cells is not consistent with classic pityriasis lichenoides of any type and should raise concern for the lymphomatoid papulosis–CD30⁺ anaplastic large cell lymphoma disease spectrum.³⁰ Other immunohistologic features and the clonality of pityriasis lichenoides are discussed in section “Etiology and Pathogenesis” under section “Pityriasis Lichenoides.”

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of pityriasis lichenoides includes many papular eruptions (Box 25-4). Those that develop crusts, vesicles, pustules, or ulcers are grouped with PLEVA, whereas those that form predominantly scaly papules are grouped with PLC. Most of them can be excluded based on history and typical clinicopathologic features. A few, such as

secondary syphilis and virus-associated lesions, can also be excluded based on serologic tests. Among the most challenging diseases to distinguish from pityriasis lichenoides are lymphomatoid papulosis and macular or papular variants of MF.⁸⁸⁻⁹¹ As detailed earlier, the presence of large atypical lymphoid cells (often CD30⁺) differentiates lymphomatoid papulosis from pityriasis lichenoides.⁸⁴ Macular or papular variants of MF are rare. They exhibit classic histopathological features of MF, including small atypical epidermotropic lymphoid cells with convoluted nuclei and a band-like superficial dermal lymphoid infiltrate.⁹⁰

COMPLICATIONS

Secondary infection is the most common complication of pityriasis lichenoides. PLEVA may be associated with low-grade fever, malaise, headache, and arthralgia. Patients with PLUH/FUMHD can develop high fever, malaise, myalgia, arthralgia, and gastrointestinal

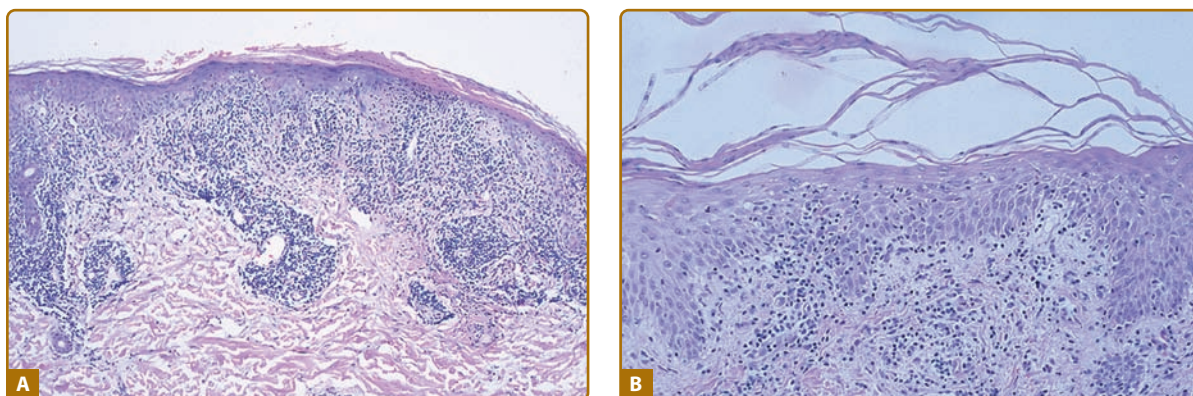


Figure 25-14 Pityriasis lichenoides chronica. **A.** Compact parakeratosis, lymphocytic exocytosis, occasional eosinophilic necrotic keratinocytes, edema, and diffuse lymphocytic infiltrate localizing to epidermal–dermal interface and perivascular sites within the dermis. Hematoxylin and eosin (H&E) stain. **B.** Parakeratosis, spongiosis, and a predominant mononuclear cell infiltrate in the epidermis and dermis with papillary edema. H&E stain.

BOX 25-4 DIFFERENTIAL DIAGNOSIS OF PITYRIASIS LICHENOIDES ET VARIOLIFORMIS ACUTA (PLEVA) AND PITYRIASIS LICHENOIDES CHRONICA (PLC)

Most Likely

- PLEVA
 - Arthropod bites, stings, infestations
 - Leukocytoclastic vasculitis
 - Viral exanthem (e.g., varicella-zoster, herpes simplex)
- PLC
 - Pityriasis rosea
 - Drug eruption
 - Guttate psoriasis

Consider

- PLEVA
 - Folliculitis
 - Rickettsiosis
 - Erythema multiforme
 - Dermatitis herpetiformis
- PLC
 - Spongiotic dermatitis, papular variant
 - Small-plaque parapsoriasis
 - Lichen planus
 - Gianotti-Crosti syndrome

Always Rule Out

- PLEVA
 - Lymphomatoid papulosis
 - Secondary syphilis
- PLC
 - Lymphomatoid papulosis
 - Mycosis fungoides (papular variant)
 - Secondary syphilis

and central nervous system symptoms. Occasionally, debilitated patients may die.^{85,92} PLC has been associated uncommonly with LPP in children.⁴⁴ Despite their sometimes dominant T-cell clonal nature, PLC and PLEVA are considered clinically benign disorders without significant linkage to lymphomas or other malignancies.

PROGNOSIS AND CLINICAL COURSE

Pityriasis lichenoides has a variable clinical course characterized by recurrent crops of lesions that spontaneously resolve. The disorder may resolve spontaneously within a few months or, less commonly, persist for years. PLEVA usually has a shorter duration than PLC. Although the conclusion was not confirmed by subsequent investigation, one report

suggested that the duration of pityriasis lichenoides in children correlated better with its clinical distribution than with the relative abundance of acute and chronic lesions, which often coexisted.⁶⁷ From longest to shortest duration, the distribution of lesions ranged from peripheral (distal extremities) to central (trunk) to diffuse.

TREATMENT

The mainstay of traditional therapy has been a combination of topical corticosteroids and phototherapy (Box 25-5). Systemic antibiotics in the tetracycline and erythromycin families are used primarily for their anti-inflammatory rather than antibiotic effects. One newer option is azithromycin.⁹³ Cases with minimal disease activity may not require any treatment. Photodynamic therapy has been used successfully for PLC.⁹⁴ The more acute the clinical course and the more severe the individual lesions, the more systemic therapy is indicated. Methotrexate is often effective in relatively low doses. Calcineurin inhibitors and retinoids may also be beneficial. Severe cases of PLEVA and PLUH often require systemic corticosteroids or similar drugs to gain control of systemic symptoms. Topical and systemic antibiotics may be needed to treat secondary infections complicating ulcerated skin lesions. These agents are often selected initially to cover Gram-positive pathogens, but subsequent use should be guided by culture results. Bromelain, a pineapple extract, cleared PLC lesions in 8/8 cases.⁹⁵

BOX 25-5 TREATMENT OF PITYRIASIS LICHENOIDES ET VARIOLIFORMIS ACUTA AND PITYRIASIS LICHENOIDES CHRONICA

FIRST LINE

- Topical corticosteroids
- Antibiotics (erythromycin 500 mg PO 2–4 × daily⁹⁶; tetracycline 500 mg PO 2–4 × daily,⁹⁷ minocycline 100 mg PO twice daily; azithromycin 500 mg PO on day 1 and 250 mg PO on days 2–5 bimonthly⁹³)
- Phototherapy (sunbathing, UVB,⁹⁰ UVA + UVB,⁹⁸ narrowband UVB⁹⁹)

SECOND LINE

- Topical tacrolimus^{100,101}
- Prednisone (60/40/20 mg PO taper, 5 days each)¹⁰²
- Methotrexate (10–25 mg PO weekly)^{103,104}
- Phototherapy (UVA1, psoralen + UVA)
- Cyclosporine (2.5–4 mg/kg/day total dose divided into twice-daily PO doses; use the minimum)⁷⁵
- Retinoids (e.g., acitretin 25–50 mg PO daily)¹⁰⁵
- Photodynamic therapy⁹⁴
- Bromelain (pineapple extract)⁹⁵

PREVENTION

There are no known preventive measures.

KEY REFERENCES

Full reference list available at www.DIGM8.com

2. Lambert WC, Everett MA: The nosology of parapsoriasis. *J Am Acad Dermatol* 5(4):373-395, 1981
39. Wood GS et al: Detection of clonal T-cell receptor gamma gene rearrangements in early mycosis fungoides/Sezary syndrome by polymerase chain reaction and denaturing gradient gel electrophoresis (PCR/DGGE). *J Invest Dermatol* 103(1):34-41, 1994
43. Hu CH, Winkelmann RK: Digitate dermatosis. A new look at symmetrical, small plaque parapsoriasis. *Arch Dermatol* 107(1):65-69, 1973
44. Samman PD: The natural history of parapsoriasis en plaques (chronic superficial dermatitis) and pruritic poikiloderma. *Br J Dermatol* 87(5):405-411, 1972
50. Pimpinelli N et al: Defining early mycosis fungoides. *J Am Acad Dermatol* 53(6):1053-1063, 2005
53. Vakeva L et al: A retrospective study of the probability of the evolution of parapsoriasis en plaques into mycosis fungoides. *Acta Derm Venereol* 85(4):318-323, 2005
64. Bowers S, Warshaw EM: Pityriasis lichenoides and its subtypes. *J Am Acad Dermatol* 55(4):557-572, 2006; quiz 573-556
65. Ersoy-Evans S et al: Pityriasis lichenoides in childhood: a retrospective review of 124 patients. *J Am Acad Dermatol* 56(2):205-210, 2007
66. Khachemoune A, Blyumin ML: Pityriasis lichenoides: pathophysiology, classification, and treatment. *Am J Clin Dermatol* 8(1):29-36, 2007
85. Sotiriou E et al: Febrile ulceronecrotic Mucha-Habermann disease: A case report and review of the literature. *Acta Derm Venereol* 88(4):350-355, 2008