Chapter 2 Spongiotic Dermatitis

Keywords Spongiosis • Spongiotic dermatitis • Eczema • Atopic dermatitis • Contact dermatitis • Nummular dermatitis • Dyshidrotic eczema • Drug eruption • Mycosis fungoides • Pityriasis rosea • Stasis dermatitis • Psoriasiform dermatitis

Spongiotic Dermatitis

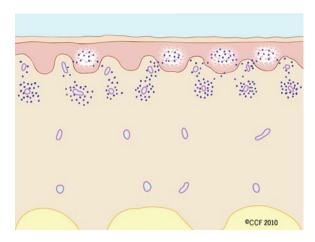
A variety of entities are in this group of inflammatory diseases. This chapter will focus on the group of entities encompassing the eczematous family of dermatitis, but also discuss other important and distinct diseases with spongiosis as its predominant finding.

The spongiotic reaction pattern is characterized by epidermal changes related to the accumulation of intraepidermal edema. The resulting hydrostatic forces cause separation of the keratinocytes revealing the intercellular desmosomal attachments. This appearance has been likened to the cut surface of a sponge, hence the term spongiotic (Fig. 2.1). The epidermal change in spongiotic dermatitis is a dynamic process that evolves over time. It can be divided into three phases: acute, subacute, and chronic. It should be recognized that these divisions are somewhat arbitrary and merely represent a means to conceptualize the histological changes.

Acute Spongiotic Dermatitis

This represents the earliest phase and consequently the least frequently biopsied phase. In the earliest timeframe the epidermis retains its normal basket-weave stratum corneum. The epidermis proper has variable amounts of spongiosis ranging from minimal to spongiotic microvesicles (Fig. 2.2). Spongiotic microvesicles are collections of edema fluid in the epidermis. They form when the hydrostatic pressure from the intraepidermal edema fluid is such that the intercellular junctions between keratinocytes

Fig. 2.1 Schematic presentation of spongiotic pattern. In the spongiotic reaction pattern there is accumulation of edema fluid within the epidermis resulting in the keratinocytes being pulled apart. Typically, there is an associated superficial perivascular inflammatory infiltrate



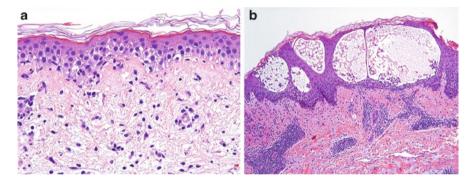


Fig. 2.2 Acute spongiotic dermatitis. (a) In the earliest phase of acute spongiotic epidermis, the epidermis shows spongiosis but does not show spongiotic microvesicles or acanthosis. (b) This case demonstrates spongiotic microvesicle formation

are ruptured. Clinically, this can result in the appearance of blisters. In addition to the intraepidermal spongiosis, there is usually a superficial perivascular inflammatory infiltrate composed of a mixture of lymphocytes, some histiocytes, and often some eosinophils. In some cases, a few neutrophils may be present. The infiltrate is usually concentrated around the superficial vascular plexus, but the pattern of the infiltrate can be somewhat variable. In lesions with an intense infiltrate, it can have the appearance of a more lichenoid pattern. There may also be some extension of the inflammation into the mid-dermis. There is usually some exocytosis of inflammatory cells into the overlying epidermis, usually lymphocytes, but can be other inflammatory cells as well. The superficial dermis usually shows some edema in the earlier phases of the process (Table 2.1).

Table 2.1 Acute spongiotic dermatitis: key microscopic features

- · Normal basket-weave stratum corneum
- Epidermal spongiosis with or without spongiotic microvesicles
- · Variable papillary derma edema
- Superficial perivascular inflammatory infiltrate of lymphocytes and often with admixed eosinophils

Subacute Spongiotic Dermatitis

One of the ways the epidermis reacts to inflammatory insults is by proliferation. This results in additional changes including acanthosis (hyperplasia) and parakeratosis (Fig. 2.3). In subacute spongiotic dermatitis the epidermis has had time to react to the inflammatory process. The epidermis shows variable parakeratosis and acanthosis. There is spongiosis, but it varies. There can be spongiotic microvesicles, but more often, the degree of spongiosis is less than what is seen in acute spongiotic dermatitis. Within the dermis, there is less edema, but otherwise a similar pattern of inflammation (Table 2.2).

Fig. 2.3 Subacute spongiotic dermatitis. There is prominent parakeratosis, a diminished granular layer, acanthosis, and mild spongiosis. Within the dermis there is a superficial perivascular infiltrate. The infiltrate generally primarily consists of lymphocytes, but eosinophils are commonly present as well

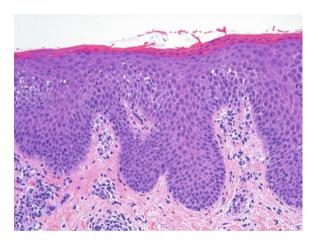


Table 2.2 Subacute spongiotic dermatitis: key microscopic features

- Parakeratosis
- Spongiosis
- Acanthosis
- · Little to no papillary dermal edema
- Superficial perivascular inflammatory infiltrate of lymphocytes and often with admixed eosinophils

Chronic Spongiotic Dermatitis

In chronic spongiotic dermatitis, there is much less spongiosis. The spongiosis is minimal to mild in nature. In this phase, the reactive epidermal changes are more prominent (Fig. 2.4). There is compact hyperkeratosis, variable parakeratosis, thickening of the granular layer, and more pronounced acanthosis. The superficial dermis does not demonstrate evidence of edema and may be slightly fibrotic. The inflammatory infiltrate is less intense but otherwise composed of the same constituent cells (Table 2.3).

Fig. 2.4 Chronic spongiotic dermatitis. In chronic spongiotic dermatitis, there is compact hyperkeratosis with no or minimal parakeratosis. The epidermis is acanthotic and there is little to no apparent spongiosis. The papillary dermis may be fibrotic and there is a variable, usually mild, superficial perivascular infiltrate

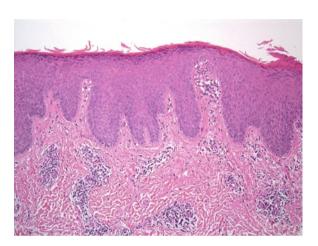


Table 2.3 Chronic spongiotic dermatitis: key microscopic features

- Compact hyperkeratosis and variable parakeratosis
- Acanthosis
- · Minimal spongiosis
- Superficial perivascular inflammatory infiltrate of lymphocytes and often with admixed eosinophils. Usually mild in nature
- · Variable superficial dermal fibrosis

Overlap With Psoriasiform Pattern

In subacute and chronic spongiotic dermatitis, the acanthosis of the epidermis can cause significant overlap with the psoriasiform pattern (Chap. 3). This issue is primarily an issue in construction of the pathology report and will be dealt with at the end of the chapter.

Contact Dermatitis 9

Eczematous Dermatitides

The group of inflammatory disorders in the eczematous family of skin diseases includes a wide range of entities including, atopic dermatitis, nummular dermatitis, contact dermatitis (both allergic and irritant contact dermatitis), dyshidrotic dermatitis (pompholyx), id reaction, and eczematous drug eruptions. Here is one of the secrets of dermatopathology: all of these entities are essentially histologically identical. They all can demonstrate the three patterns of spongiotic dermatitis depending on when the lesion is biopsied. With some of the entities, there can be clues to the diagnosis histologically, but clinical information is often crucial to the diagnosis. With that in mind, it is important to review some of the clinical aspects of these diseases.

Atopic Dermatitis

Atopic dermatitis is a chronic, relapsing, pruritic dermatitis in patients with a familial history of atopy. Atopy is characterized by variable combinations of dermatitis, asthma, sinusitis, and allergic rhinitis. In children, the eruption favors flexural areas such as the antecubital fossa. In adults, the presentation is more variable including very mild periorbital dermatitis to full body erythroderma.

Contact Dermatitis

Contact dermatitis is a result of an exogenous stimulus and can be subdivided into allergic or irritant types. Allergic contact dermatitis is the result of a type IV hypersensitivity reaction that requires exposure to a specific antigen. The prototypical allergic contact dermatitis includes reactions to substances such as poison ivy or latex. Nickel allergies are also common and tend to present where people come into contact with the metal (e.g., earlobes, waistline near blue jeans snaps).

Irritant contact dermatitis results from direct damage to the epidermis from the offending substance rather than an immune mediated response. Detergents are one of the most common causes of irritant dermatitis (so-called dishpan hands). Diaper rash is another prototypical example.

Histologically, both show features of spongiotic dermatitis. Clinically, there are frequent clues to the diagnosis. For example, in poison ivy, the eruption often has a linear arrangement corresponding to the edge of the offending leaf that brushed along the skin. Depending on the offending agent, there may be peculiar distributions such as with allergic reactions to latex gloves or nickel containing jewelry. A histological clue to the diagnosis of allergic contact dermatitis is the presence of Langerhans cell microabscesses within the epidermis (Fig. 2.5) (not to be confused with the Pautrier's microabscesses of mycosis fungoides which are composed of neoplastic lymphocytes). Langerhans cell microabscesses are not always present in allergic contact dermatitis, and they are not entirely specific. In irritant contact dermatitis,

Fig. 2.5 Langerhans cell microabscess. Allergic contact dermatitis often has Langerhans cell microabscesses, characterized by collections of Langerhans cells within the spongiotic epidermis. Langerhans cells have reniform nuclei and relatively abundant pale eosinophilic cytoplasm

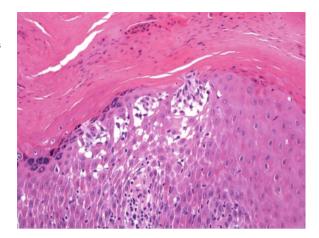
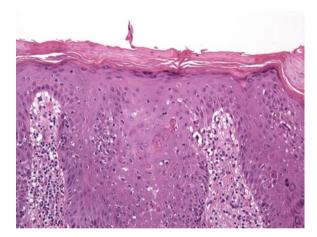


Fig. 2.6 Irritant contact dermatitis. Within the upper epidermis there are scattered dyskeratotic cells. This is a common but nonspecific finding in irritant contact dermatitis



the inflammatory infiltrate tends to be less intense and there may be ballooning degeneration of keratinocytes and/or occasional dyskeratotic keratinocytes in the epidermis, especially the upper half of the stratum spinosum (Fig. 2.6).

Nummular Dermatitis

This is one of the most common types of spongiotic dermatitis that is biopsied. Nummular dermatitis is characterized by round (coin-shaped) to oval patches variably composed of papules and vesicles usually on the extremities. As the eruption evolves, there may be central clearing, clinically resembling dermatophyte infection

(tinea). In patients with atopic dermatitis, they may have flares of their disease presenting as nummular dermatitis. Nummular dermatitis almost always has a component of epidermal acanthosis. Microscopically, it typically has the features of subacute or chronic spongiotic dermatitis. Clinically and histologically the differential diagnosis of nummular dermatitis is psoriasis vulgaris.

Dyshidrotic Eczema (Pompholyx or Palmoplantar Dermatitis)

Dyshidrotic eczema is characterized by a recurrent pruritic, often vesicular, eruption of the palms, soles, or digits. Clinically, the vesicles have a papular appearance. Over time, scaling and cracking can develop. In many patients, this is a manifestation of atopy. A significant proportion of dyshidrotic eczema is the result of an allergic contact dermatitis. Spongiotic vesicles are a very common histologic feature. It is important to always exclude dermatophyte infection, especially in eruptions from the feet. A PAS or GMS stain is recommended to exclude the possibility of an underlying fungal infection.

Id Reactions (Autoeczematization)

Id reactions are the development of an eczematous dermatitis in regions away from the primary inflammatory focus. Dermatophyte infections of the feet (tinea pedis) and stasis dermatitis are two of the most common inciting conditions for id reactions. The patient can develop eczematous dermatitis on the upper extremities, or trunk, far away from the triggering process. In the case of dermatophyte-triggered eczematous dermatitis, no fungi are detectable in the dermatitis representing the id reaction. The id reaction component is difficult to treat without addressing the underlying trigger.

Eczematous Drug Reactions

Drug reactions will be dealt with in more detail in a later section of the book. A minority of drug reactions may be histologically indistinguishable from other forms of eczematous dermatitis. Depending on what sources you read, eczematous drug eruptions can account for <5–10% of all new drug eruptions. In our personal experience, it is relatively uncommon, and the rate is <5%. Association with new medications can help correlation with the diagnosis. In the absence of clinical information implicating a medication, it is not possible to differentiate an eczematous drug reaction from other eczematous dermatitides.

Differential Diagnosis

Eczematous dermatitis is frequently secondarily impetiginized resulting in neutrophils in the stratum corneum. This is also a key feature of a dermatophyte infection. When neutrophils are present in the stratum corneum or upper epidermis, a PAS or GMS should be performed to exclude a possible fungal infection.

Nummular dermatitis and psoriasis may have significant clinical overlap and differentiating these entities is often a diagnostic problem. Nummular dermatitis has more edema fluid in the stratum corneum, less uniform hyperplasia, a retained or thickened granular layer and usually has eosinophils in the dermal infiltrate. These are not features of psoriasis (see Chap. 3).

A minority of cutaneous drug eruptions is eczematous (spongiotic) in nature. They can be indistinguishable from other forms of eczematous dermatitis. Diagnosis requires good correlation with medication history. Unfortunately, some drug eruptions commence months after initiation of a new medication. In that case it is ultimately up to the clinician to sort out the diagnosis; it is beyond the scope of histology in that situation.

Mycosis fungoides can figure into the differential diagnosis of eczematous dermatitis. A detailed discussion of mycosis fungoides is beyond the scope of this text, but references are provided at the end of this chapter. That being said, the differential diagnosis of mycosis fungoides vs. an eczematous dermatitis is relatively common. Lesions of mycosis fungoides have disproportionate amount of intraepidermal lymphocytes within a relatively non-spongiotic epidermis (Fig. 2.7). The intraepidermal lymphocytes have a halo artifact and frequently tag the basal layer of the epidermis. The neoplastic lymphocytes tend to have more irregular, cerebriform nuclei, but this is less helpful in actual practice. Immunostains and clonality studies can also be helpful. A shift in the ratio of CD4 to CD8 positive cells of >4–6:1 in the appropriate context favors mycosis fungoides over eczematous

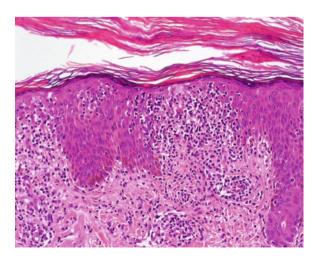


Fig. 2.7 Mycosis fungoides is characterized by epidermotropism of lymphocytes into the epidermis that is disproportionate to the amount of spongiosis

dermatitis. Immunostains for CD4 have to be correlated with immunostains for CD3, as Langerhans cells and histiocytes are also CD4 positive. One should not over interpret a collection of CD4-positive cells as a Pautrier's microabscess when in fact it is a Langerhans cell microabscess. Similarly, a monoclonal population of T-cells can be supportive, but is by no means diagnostic of mycosis fungoides. Eczematous processes can have clonal populations of T-cells. If mycosis fungoides is a strong possibility, assessing clonality from two different biopsies from different locations is useful; identical clones in different locations are supportive of mycosis fungoides. Clinical history can be helpful. A clinical history of long-standing (i.e., years) disease in non-sun-exposed areas on older adults is an important parameter that would also favor mycosis fungoides. Diagnosis of mycosis fungoides often takes many biopsies over time before a diagnosis can be made. Fortunately, it is an indolent disease and so it is best to be cautious and not push too much when confronted with this diagnostic question. See Table 2.4.

Table 2.4 Practical tips: eczematous dermatitis

- · The clinical variants of eczematous dermatitis have essentially the same histologic features
- Acute, subacute and chronic spongiotic dermatitis represent a continuum. It is not important
 to sub-classify spongiotic dermatitis in the line diagnosis
- Use a descriptive diagnosis of "spongiotic dermatitis" (see sample reports at end of chapter)
- · Langerhans cell microabscesses are suggestive of allergic contact dermatitis
- Eliminate where possible more specific entities
- · If neutrophils are the in stratum corneum or epidermis, exclude dermatophytosis or psoriasis
- · Eczematous dermatitis is more spongiotic than mycosis fungoides

Other Forms of Spongiotic Dermatitis

Stasis dermatitis and pityriasis rosea are also in the differential diagnosis. See below for discussion of these entities.

Stasis Dermatitis

Clinical Features

Stasis dermatitis typically presents on the medial aspect of the lower extremities in association with evidence of venous insufficiency. It usually presents in older patients or obese patients. Usually, stasis dermatitis presents as pruritic, scaly plaques. Rarely it presents as a more circumscribed process clinically, and can be confused with a neoplasm. Acroangiodermatitis, a specific form of stasis dermatitis, presents as violaceous macules, nodules or plaques on the dorsal feet. It can be clinically and histologically confused with Kaposi's sarcoma.

Microscopic Features

The epidermis shows features of subacute or chronic spongiotic dermatitis as described above. The key differentiating features are found in the dermis. Within the papillary dermis, there is a lobular proliferation of relatively thick-walled vessels (Fig. 2.8). There may be evidence of tissue edema or, in long-standing cases, fibrosis. There is extravasation of erythrocytes and associated perivascular siderophages to varying degrees. A perivascular lymphocytic infiltrate is present. The infiltrate is variable, but is usually less intense than the infiltrate of the eczematous dermatitides described above (Table 2.5).

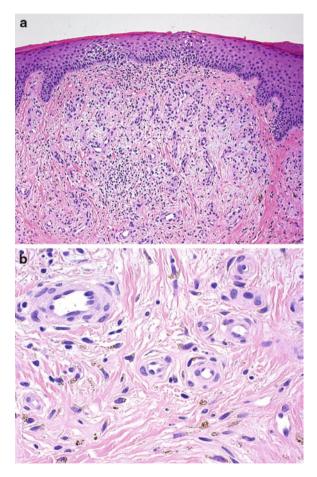


Fig. 2.8 Stasis dermatitis. (a) The epidermis shows variable spongiosis and acanthosis. Within the dermis there is a lobular proliferation of relatively thick-walled blood vessels and a perivascular lymphocytic infiltrate. (b) Higher power view of papillary dermal blood vessels with surrounding siderophages, a frequent finding in long-standing cases of stasis dermatitis

Table 2.5 Key microscopic findings: stasis dermatitis

- · Variable acanthosis and spongiosis
- · Lobular proliferation of relatively thick-walled vessels in superficial dermis
- · Extravasation of erythrocytes and siderophages common

Differential Diagnosis

The differential diagnosis of most cases includes the forms of spongiotic dermatitis in the eczematous dermatitis group outlined above. In some cases, there may be a combination of eczematous dermatitis superimposed on underlying stasis change. In rare cases, the vascular proliferation is so prominent as to mimic a vascular neoplasm such as Kaposi's sarcoma. This form of stasis dermatitis is referred to as acroangiodermatitis (Fig. 2.9). Careful attention to histological features allows distinction. Acroangiodermatitis does not have the dense proliferation of spindled endothelial cells with slit-like vascular spaces, lacks the promontory sign of early Kaposi's sarcoma and does not express latent nuclear antigen of HHV-8. Recognition of more conventional areas of stasis change can be helpful (Table 2.6).

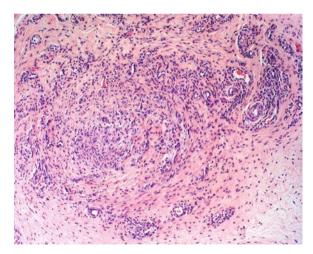


Fig. 2.9 Acroangiodermatitis. The reactive vascular proliferation due to stasis can sometimes be quite prominent and cause confusion with a vascular neoplasm

Table 2.6 Practical tips: stasis dermatitis

- · Keep a high index of suspicion on biopsies from the lower legs
- · The vascular changes are the most important feature
- Patients can have an eczematous dermatitis superimposed on underlying stasis change
- Occasionally stasis dermatitis can clinically mimic a neoplasm and the clinician may submit
 with a clinical diagnosis of squamous cell carcinoma

Pityriasis Rosea

Clinical Features

Pityriasis rosea usually presents in young adults, though a wide age range may be affected. The eruption starts as a salmon-colored herald patch that in the next 7–14 days is followed by a widespread, symmetric eruption of numerous small pink to red scaly plaques. The eruption usually starts on the trunk and then spread to the abdomen and proximal extremities.

Microscopic Features

The most characteristic feature of pityriasis rosea is the presence of discrete mounds of parakeratosis in the stratum corneum (Fig. 2.10). The epidermis shows mild spongiosis and mild acanthosis. Within the dermis, there is a superficial perivascular lymphocytic infiltrate. Eosinophils are rarely present. There may be extravasation of erythrocytes in the papillary dermis and exocytosis of erythrocytes into the overlying epidermis and, when present, is a helpful feature (Table 2.7).

Fig. 2.10 Pityriasis rosea. In the stratum corneum, there are discrete mounds of parakeratosis. The epidermis is mildly spongiotic and acanthotic. The dermal infiltrate is predominately composed of lymphocytes. Extravasation of erythrocytes is commonly seen in the papillary dermis, and frequently there is exocytosis of erythrocytes into the epidermis

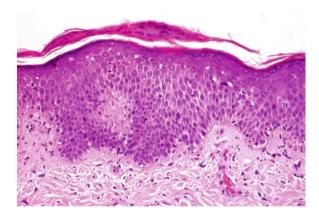


Table 2.7 Key microscopic findings: pityriasis rosea

- · Discrete mounds of parakeratosis
- · Spongiosis
- · Papillary dermal hemorrhage common
- · Mild perivascular lymphocytic infiltrate

Differential Diagnosis

The differential diagnosis includes subacute spongiotic dermatitis and it is often not possible to distinguish without clinical history. Guttate psoriasis (see Chap. 3) also resembles pityriasis rosea. Classically, guttate psoriasis has mounds of parakeratosis

surmounted by collections of neutrophils. Neutrophils are not a feature of pityriasis rosea (Table 2.8).

Table 2.8 Practical tips: pityriasis rosea

- Discrete mounds of parakeratosis are the key histologic feature
- · A specific diagnosis of pityriasis rosea is not possible without the appropriate clinical history
- In the absence of a sufficient history, the case should be signed out descriptively as "spongiotic dermatitis" (see sample reports at the end of the chapter)

Vesicular Dermatophytosis

Dermatophyte infections can sometimes present with prominent spongiosis. Usually, there are neutrophils in the stratum corneum and eosinophils are found as part of the dermal infiltrate. Dermatophyte infection will be discussed in more detail in Chaps. 3 and 12. As a general rule, a PAS or GMS stain should always be considered when examining a spongiotic dermatitis involving the feet.

Sample Reports: Spongiotic Dermatitis NOS (Eczematous Dermatitis)

Example 1:

Clinical history: Rule out psoriasis.

Diagnosis: Spongiotic dermatitis, see comment.

Comment: The epidermis shows parakeratosis with irregular acanthosis, a

maintained granular layer and diffuse mild spongiosis. Within the dermis, there is a superficial perivascular mixed inflammatory infiltrate of lymphocytes and scattered eosinophils. The degree of spongiosis, intact granular layer, and presence of eosinophils in the infiltrate argue against the possibility of psoriasis. The histological features are most consistent with an eczematous dermatitis such as nummular dermatitis. Clinicopathologic correlation is

recommended.

Example 2:

Clinical history: Rule out dermatitis, drug eruption, etc.

Diagnosis: Spongiotic dermatitis, see comment.

Comment: The epidermis shows parakeratosis, some hyperkeratosis, spon-

giosis, and occasional Langerhans cell microabscesses. Within the dermis, there is a superficial predominantly perivascular mixed infiltrate of lymphocytes and eosinophils. The histological features are compatible with an eczematous dermatitis. The presence of Langerhans cell microabscesses in the epidermis

suggests the possibility of a contact dermatitis. Clinicopathologic correlation is recommended.

Example 3:

Clinical history: Rule out mycosis fungoides.

Diagnosis: Spongiotic dermatitis, see comment.

Comment: The biopsy demonstrates parakeratosis overlying an epidermis

with irregular acanthosis, and spongiosis. There is some exocytosis of lymphocytes, but no Pautrier's microabscesses. The histological features are most compatible with an eczematous dermatitis. The degree of spongiosis argues against the diagnosis of mycosis fungoides. That being said, if this eruption persists or progresses, additional biopsies over time may be indicated to evaluate for the possibility of mycosis fungoides.

Clinicopathologic correlation is recommended.

Sample Report: Stasis Dermatitis

Clinical history: Rash on legs.

Diagnosis: Spongiotic dermatitis, see comment.

Comment: The epidermis is spongiotic with hyperkeratosis and parakeratosis.

Within the dermis there is a lobular proliferation of relatively thick blood vessels in association with a mild perivascular lymphocytic infiltrate, and some dermal hemorrhage. The histologic features are consistent with stasis dermatitis. Clinicopathologic correlation

is recommended.

Sample Report: Pityriasis Rosea

Clinical history: Rash on trunk.

Diagnosis: Spongiotic dermatitis, see comment.

Comment: There are focal mounds of parakeratosis overlying a mildly

spongiotic epidermis. Within the dermis, there is a mild superficial perivascular lymphocytic infiltrate with focal extravasation of erythrocytes. Given the pattern of parakeratosis, pityriasis rosea should be considered. An eczematous dermatitis could also be considered. Clinicopathologic correlation is recom-

mended.

Selected References 19

General Comment: Spongiotic Versus Psoriasiform

As mentioned previously, the epidermis may have significant acanthosis in many of the forms of spongiotic dermatitis. Therefore, most of the above examples could have "psoriasiform dermatitis" as the diagnosis. However, the comment would remain essentially the same. This underscores the fact that the comment is more important in many ways than the top line diagnosis.

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