72 Skin Manifestations of Internal Disease

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It is a generally accepted concept in medicine that the skin can develop signs of internal disease. Therefore, in textbooks of medicine, one finds a chapter describing in detail the major systemic disorders that can be identified by cutaneous signs. The underlying assumption of such a chapter is that the clinician has been able to identify the specific disorder in the patient and needs only to read about it in the textbook. In reality, concise differential diagnoses and the identification of these disorders are actually difficult for the nondermatologist because he or she is not well-versed in the recognition of cutaneous lesions or their spectrum of presentations. Therefore, this chapter covers this particular topic of cutaneous medicine not by simply focusing on individual diseases, but by describing the various presenting clinical signs and symptoms that point to specific disorders. Concise differential diagnoses will be generated in which the significant diseases will be distinguished from the more common cutaneous disorders that have minimal or no significance with regard to associated internal disease. The latter disorders are reviewed in table form and always need to be excluded when considering the former. For a detailed description of individual diseases, the reader should consult a dermatologic text.

PAPULOSQUAMOUS SKIN LESIONS

(Table 72-1) When an eruption is characterized by elevated lesions, either papules (<1 cm) or plaques (>1 cm), in association with scale, it is referred to as *papulosquamous*. The most common papulosquamous diseases—*tinea*, *psoriasis*, *pityriasis rosea*, and *lichen planus*—are primary cutaneous disorders (Chap. 71). When psoriatic lesions are accompanied by arthritis, the possibility of psoriatic arthritis or reactive arthritis (formerly known as Reiter's syndrome) should be considered. A history of oral ulcers, conjunctivitis, uveitis, and/or urethritis points to the latter diagnosis. Lithium, beta blockers, HIV or streptococcal infections, and a rapid taper of systemic glucocorticoids are known to exacerbate psoriasis. Comorbidities in patients with psoriasis include cardiovascular disease and metabolic syndrome.

Whenever the diagnosis of pityriasis rosea or lichen planus is made, it is important to review the patient's medications because the eruption may resolve by simply discontinuing the offending agent. Pityriasis rosea–like drug eruptions are seen most commonly with beta blockers, angiotensin-converting enzyme (ACE) inhibitors, and metronidazole, whereas the drugs that can produce a lichenoid eruption include thiazides, antimalarials, quinidine, beta blockers, and ACE inhibitors. In some populations, there is a higher prevalence of hepatitis C viral infection in patients with lichen planus. Lichen planus–like lesions are also observed in chronic graft-versus-host disease.

In its early stages, the mycosis fungoides (MF) form of *cutaneous T cell lymphoma* (CTCL) may be confused with eczema or psoriasis, but it often fails to respond to the appropriate therapy for those inflammatory diseases. MF can develop within lesions of large-plaque parapsoriasis and is suggested by an increase in the thickness of the lesions. The diagnosis of MF is established by skin biopsy in which collections of atypical T lymphocytes are found in the epidermis and dermis. As the disease progresses, cutaneous tumors and lymph node involvement may appear.

In *secondary syphilis*, there are scattered red-brown papules with thin scale. The eruption often involves the palms and soles and can resemble pityriasis rosea. Associated findings are helpful in making the diagnosis and include annular plaques on the face, nonscarring alopecia, condyloma lata (broad-based and moist), and mucous patches as well as lymphadenopathy, malaise, fever, headache, and myalgias. The interval between the primary chancre and the secondary stage is usually 4–8 weeks, and spontaneous resolution without appropriate therapy occurs.

TABLE 72-1 SELECTED CAUSES OF PAPULOSQUAMOUS SKIN LESIONS

1. Primary cutaneous disorders
   a. Tinea[a]
   b. Psoriasis[a]
   c. Pityriasis rosea[a]
   d. Lichen planus[a]
   e. Parapsoriasis, small plaque and large plaque
   f. Bowen's disease (squamous cell carcinoma in situ)[b]
2. Drugs
3. Systemic diseases
   a. Lupus erythematosus, primarily subacute or chronic (discoid) lesions[c]
   b. Cutaneous T cell lymphoma, in particular, mycosis fungoides[d]
   c. Secondary syphilis
   d. Reactive arthritis (formerly known as Reiter's syndrome)
   e. Sarcoidosis[e]

[a]Discussed in detail in **Chap. 71**; cardiovascular disease and the metabolic syndrome are comorbidities in psoriasis; primarily in Europe, hepatitis C virus is associated with oral lichen planus. [b]Associated with chronic sun exposure more often than exposure to arsenic; usually one or a few lesions. [c]See also Red Lesions in "Papulonodular Skin Lesions." [d]Also cutaneous lesions of HTLV-1-associated adult T cell leukemia/lymphoma. [e]See also Red-Brown Lesions in "Papulonodular Skin Lesions."

ERYTHRODERMA

(Table 72-2) *Erythroderma* is the term used when the majority of the skin surface is erythematous (red in color). There may be associated scale, erosions, or pustules as well as shedding of the hair and nails. Potential systemic manifestations include fever, chills, hypothermia, reactive lymphadenopathy, peripheral edema, hypoalbuminemia, and high-output cardiac failure. The major etiologies of erythroderma are (1) cutaneous diseases such as psoriasis and dermatitis (Table 72-3); (2) drugs; (3) systemic diseases, most commonly CTCL; and (4) idiopathic. In the first three groups, the location and description of the initial lesions, prior to the development of the erythroderma, aid in the diagnosis. For example, a history of red scaly plaques on the elbows and knees would point to psoriasis. It is also important to examine the skin carefully for a migration of the erythema and associated secondary changes such as pustules or erosions. Migratory waves of erythema studded with superficial pustules are seen in *pustular psoriasis*.

Drug-induced erythroderma (exfoliative dermatitis) may begin as an exanthematous (morbilliform) eruption (Chap. 74) or may arise as diffuse erythema. A number of drugs can produce an erythroderma, including penicillins, sulfonamides, carbamazepine, phenytoin, and allopurinol. Fever and peripheral eosinophilia often accompany the eruption, and there may also be facial swelling, hepatitis, myocarditis, thyroiditis, and allergic interstitial nephritis; this constellation is frequently referred to as *drug reaction with eosinophilia and systemic symptoms* (DRESS) or *drug-induced hypersensitivity reaction* (DIHS). In addition, these reactions, especially to aromatic anticonvulsants, can lead to a pseudolymphoma syndrome (with adenopathy and

TABLE 72-2 CAUSES OF ERYTHRODERMA

1. Primary cutaneous disorders
   a. Psoriasis[a]
   b. Dermatitis (atopic > contact >> stasis [with autosensitization] or seborrheic)[a]
   c. Pityriasis rubra pilaris
2. Drugs
3. Systemic diseases
   a. Cutaneous T cell lymphoma (Sézary syndrome, erythrodermic mycosis fungoides)
   b. Other lymphomas
4. Idiopathic (usually older men)

[a]Discussed in detail in **Chap. 71**.