

of Cushing's syndrome. *N Engl J Med* 1991; 325:897-905.

Sheeler LR. Cushing's syndrome. *Urol Clin North Am* 1989; 16:447-455.

Tahir AH, Sheeler LR. Recurrent Cushing's disease after transsphenoidal surgery. *Arch Intern Med* 1992; 152:977-981.

SKIN LESIONS: WHEN TO SUSPECT SYSTEMIC CAUSES

The dermatologic manifestations of systemic disease cover a spectrum that includes autoimmune, neoplastic, and infectious disease. The following are some tips to increase awareness and suspicion of a few of these lesions.

PARANEOPLASTIC PEMPHIGUS

Paraneoplastic pemphigus, a distinct autoimmune disorder associated with neoplasms, was first described only 2 years ago. It produces skin lesions resembling erythema multiforme, lichen planus, or pemphigus vulgaris. Underlying malignancies include lymphoproliferative disorders and bronchogenic carcinoma. To date, eight cases have been reported in the literature, with four additional cases at the Cleveland Clinic (in press). The fact that four cases have occurred at one institution suggests that the disorder is more common than the literature indicates. It has been underrecognized because it was not known how to characterize the syndrome, which often has the appearance of erythema multiforme but is associated with cancer. If a cancer patient has erosive stomatitis, conjunctivitis, polymorphous erythema multiforme, or an eruption resembling bullous lichen planus, paraneoplastic pemphigus should be suspected. The diagnosis can be confirmed with indirect immunofluorescent testing on rat bladder transitional epithelium. The rat bladder test is easily performed, is inexpensive, and has a specificity of 98.9%. Treatment, in addition to managing the underlying tumor, involves immunosuppressive therapy with steroids or azathioprine.

METASTASIS

If a skin lesion proves to be a metastasis, suspect that the primary tumor originates from an organ under the site of the lesion and that the primary cancer is relatively common. In women, the most likely source of metastatic skin lesions is breast cancer. The chest and the abdomen are the most common sites of metastatic skin lesions.

HYPERSENSITIVITY

Erythema nodosum (eg, nodules on the lower legs, possibly tender) is an inadequate diagnosis. Erythema nodosum is really a hypersensitivity response to something else. The possible causes are many, and identification may require an aggressive search. Streptococcal infection is the most common cause, but also consider sarcoidosis, oral contraceptives, sulfonamides, barbiturates, fungal infections, or inflammatory bowel disease. Apart from addressing the underlying cause, treatment with a nonsteroidal anti-inflammatory drug or a steroid may be helpful.

VIRAL INFECTION

Consider herpes simplex virus (HSV) infection when a patient presents with symmetrical erythema multiforme, even when HSV is not clinically evident. In many cases of recurrent disease, testing by polymerase chain reaction will reveal HSV-specific DNA in the lesions. Steroids are of little therapeutic value, but acyclovir may be beneficial.

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SUGGESTED READING

Aslanzadeh J, Helm KF, Espy MJ, et al. Detection of HSV-specific DNA in biopsy tissue of patients with erythema multiforme by polymerase chain reaction. *Br J Dermatol* 1992; 126(1):19-23.

Camisa C, Helm TN, Liu YC, Valenzuela R, Allen C, Bona S, Larrimer N, Korman MJ. Paraneoplastic pemphigus: a report of three cases including one long-term survivor. *J Am Acad Dermatol* 1992; 27:54-553.

Helm TN, Camisa C, Valenzuela R. Perplexing parlance of paraneoplastic pemphigus [letter]. *JAMA* 1992; 268:602.

Helm TN, Camisa C, Valenzuela R, Allen CN. Paraneoplastic pemphigus: a distinct autoimmune vesiculobullous disorder associated with neoplasia. *Oral Surg Oral Med Oral Pathol* (in press).

Liu Y, Valenzuela R, Helm TN, Camisa C. Immunocytometric characterization of lymphocytes in paraneoplastic pemphigus [abstract]. *Am J Clin Pathol* 1991; 96:314.

Liu AY, Valenzuela R, Helm TN, Camisa C, Melton A, Bergfeld WF. Indirect immunofluorescence on transitional rat bladder epithelium: a test with high specificity for paraneoplastic pemphigus. *J Am Acad Dermatol*. In press.

Spencer PS, Helm TN. Skin metastases in cancer patients. *Cutis* 1987; 39(2):119-121.