Groin Eruption in an HIV-Positive Man

Diagnosis: Epidermodysplasia verruciformis (EDV).

MICROSCOPIC FINDINGS AND CLINICAL COURSE

Routine hematoxylin-eosin staining of the biopsy specimens revealed slight epidermal acanthosis, hypergranulosis, and hyperkeratosis (Figure 2). There were characteristic distended keratinocytes with basophilic and finely vacuolated cytoplasm and coarse keratohyaline granules (Figure 3). A biopsy specimen from the right side of the groin was initially interpreted as verruca plana, which was attributed to sampling error. Two additional biopsy specimens from the groin revealed changes consistent with EDV. The results of human papillomavirus (HPV) typing by polymerase chain reaction and restriction fragment length polymorphism analyses were consistent with HPV-8.

DISCUSSION

Epidermodysplasia verruciformis is a widespread eruption that usually begins in childhood and may be sporadic or inherited through an autosomal recessive pattern.[1] Skin manifestations include tinea versicolor–like lesions, red-brown patches on the trunk and upper extremities, and disseminated verruca plana–like lesions on the hands and forearms.[1] Numerous HPV types have been found in EDV skin lesions.[2] Importantly, HPV-5 and HPV-8 have been associated with an increased risk of malignant transformation in EDV lesions, reportedly affecting 30% to 60% of patients.[3] Ultraviolet irradiation may also contribute to the risk of squamous cell carcinoma developing in EDV lesions, as reported cases have occurred most often on sun-exposed surfaces.[1,3] The tumors of EDV develop slowly and are locally destructive but have very weak metastatic potential without cocarcinogens, such as ionizing radiation.[1] The high incidence of cutaneous squamous cell carcinoma in patients with EDV has led to recommendations for frequent cutaneous surveillance in these patients and appropriate protection against UV irradiation.[1]

Abnormal cell–mediated immunity has been described in patients with EDV,[4-6] and there is an increased prevalence of EDV-associated cutaneous HPV infection in immunodeficient states. Epidermodysplasia verruciformis has been reported in association with renal transplantation,[7] Hodgkin disease,[8] systemic lupus erythematosus,[9] and HIV infection.[10,11]

Clinically apparent EDV-like skin disease in HIV-positive patients may be relatively rare, with only a few cases having been reported in the literature.[10-12] In the reported cases, the lesions resembled those seen in classic EDV, ie, flat wart-like papules or tinea versicolor–like macules involving the face, chest, and upper extremities. The site of our patient's lesions was unusual; therefore, the initial differential diagnosis included psoriasis, seborrheic dermatitis, candidal intertrigo, tinea cruris, tinea corporis, and folliculitis.

In contrast to the high incidence of malignant transformation in more classic EDV lesions, recently reported cases of HIV-related EDV have not developed into cutaneous carcinomas (Timothy Berger, MD, and Toby Maurer, MD, e-mail and oral communication, April 1999). Whether HIV-related EDV carries a different risk for malignant transformation from the more classic familial form of EDV remains to be elucidated.

No specific therapy exists for the treatment of EDV. Systemic and intralesional administration of retinoids and interferons have provided only partial responses.[1] Other potential treatment options include destructive modalities (eg, cryotherapy, cantharidin, podophyllin, trichloroacetic acid, and laser ablation), antiviral medications (eg, topical cidofovir), and local immunomodulation (eg, imiquimod).

REFERENCES

1. Majewski S, Jablonska S. Epidermodysplasia verruciformis as a model of human papillomavirus–induced genetic cancer of the skin. *Arch Dermatol.* 1995; 131:1312-1318.
2. Majewski S, Jablonska S. Human papillomavirus–associated tumors of the skin and mucosa. *J Am Acad Dermatol.* 1997;36:659-685.
3. Orth G. Epidermodysplasia verruciformis. In: Salzman HP, Howley PM, eds. *The Papovaviridae.* Vol 2. New York, NY: Plenum Publishing Corp; 1987:199-243.
4. Majewski S, Skopinska-Rozewska E, Jablonska S, et al. Partial defects of cell-mediated immunity in patients with epidermodysplasia verruciformis. *J Am Acad Dermatol.* 1986;15:966-973.
5. Majewski S, Malejczyk J, Jablonska S, et al. Natural cell–mediated cytotoxicity against various target cells in patients with epidermodysplasia verruciformis. *J Am Acad Dermatol.* 1990;22:423-427.
6. Slawsky LD, Gilson RT, Hockley AJ, Libow LF. Epidermodysplasia verruciformis associated with severe immunodeficency, lymphoma, and disseminated molluscum contagiosum. *J Am Acad Dermatol.* 1992;27:448-450.
7. Barr BB, Benton EC, McLaren K, et al. Human papilloma virus infection and skin cancer in renal allograft recipients. *Lancet.* 1989;1:124-129.
8. Gross G, Ellinger K, Roussaki A, et al. Epidermodysplasia verruciformis in a patient with Hodgkin's disease: characterization of a new papillomavirus type and interferon treatment. *J Invest Dermatol.* 1988;91:43-48.
9. Tanigaki T, Kanda R, Sato K. Epidermodysplasia verruciformis (L-L, 1922) in a patient with systemic lupus erythematosus. *Arch Dermatol Res.* 1986;278:247-248.
10. Barzegar C, Paul C, Saiag P, et al. Epidermodysplasia verruciformis–like eruption complicating human immunodeficiency virus infection. *Br J Dermatol.* 1998; 139:122-127.
11. Berger TG, Sawchuk WS, Leonardi C, Langenberg A, Tappero J, Leboit PE. Epidermodysplasia verruciformis–associated papillomavirus infection complicating human immunodeficiency virus disease. *Br J Dermatol.* 1991;124:79-83.
12. Prose NS, yon Knebel-Doeberitz C, Miller S, Milbum PB, Heilman E. Widespread flat warts associated with human papillomavirus type 5: a cutaneous manifestation of human immunodeficiency virus infection. *J Am Acad Dermatol.* 1990; 23:978-981.

Chronic Erythematous Desquamative Plaques of the Eyelids

Diagnosis: Discoid lupus erythematosus (DLE) solely localized to the eyelids.

MICROSCOPIC FINDINGS AND CLINICAL COURSE

Microscopic examination of a biopsy specimen from the cutaneous outer aspect of the eyelids revealed parakeratosis, atrophy, and a subepidermal lymphohistiocytic infiltrate localized around hair follicles, vessels, and muscle fibers. In addition, there were eosinophilic intraepidermal bodies, vacuolar change in the basal layer, and eosinophilic amorphous subepidermal material. The dermis also contained some elanophages, and mucin was noted on staining with alcian blue. Microscopic examination of a biopsy specimen from the mucosal inner aspect of the eyelid showed a lymphohistiocytic, erosive infiltrate at the dermoepidermal junction. Direct immunofluorescence staining from involved skin revealed globular fluorescence along the dermoepidermal junction with C3 and C4. The results of direct immunofluorescence of uninvolved sun-exposed skin were negative. The findings of routine laboratory and autoantibody tests (antinuclear antibody, extractable nuclear antigen, anti-Ro/SSA, and anti-La/SSB) were all normal or negative. Instrumental evaluations did not reveal systemic alterations.

The patient was treated with hydroxychloroquine sulfate (400 mg/d for 8 weeks, followed by 200 mg/d for 8 weeks) and intralesional triamcinolone acetonide (2.5 mg/mL weekly for 6 weeks). He was advised to avoid sun exposure. One month after the initiation of therapy, there was considerable improvement of the disease. One year later, the patient was still asymptomatic and free of disease.

DISCUSSION

Discoid lupus erythematosus is a benign chronic cutaneous disease that is clinically characterized by a malar rash, acute erythema, and discoid lesions with atrophy, telangiectasia, follicular plugging, hypopigmentation or hyperpigmentation, and alopecia. The lesions usually occur in sun-exposed areas. Eyelid involvement is sometimes associated with lesions occurring in other typical cutaneous sites, and it may be the first manifestation of DLE. On the other hand, in long-standing disease, this localization is rarely reported as the sole manifestation.[1]

Discoid lupus erythematosus of the eyelids was first described in 1875 by Kaposi and Hebra,[2] who stated that the eyelids may be a primary site of typical lesions. Forty-one cases of DLE with eyelid involvement were reported by Donzis et al[3] and Huey et al[4] in the early 1980s. In 17 (43%) of these patients, eyelid lesions were the sole manifestation. In 1989, Burge et al[5] reported that specific eyelid lesions were present in 4 (6%) of 69 patients with chronic cutaneous lupus erythematosus. Later, Cyran et al,[6] reviewing the English-language literature, reported 21 cases of DLE involving or limited to the eyelids. This infrequent localization can lead to misdiagnosis and inappropriate treatment. Diagnosis is difficult because many diseases that need to be differentiated from DLE may also be localized to the eyelids. These diseases include lichen planus of the eyelids, cicatricial pemphigoid, acne rosacea, allergic dermatitis, psoriasis, lymphocytic infiltrates, polymorphic light eruption, facial granuloma, chronic blepharitis, systemic lupus erythematosus, seborrhea, sarcoidosis, tinea faciei, vitiligo, and basal cell carcinoma.[3,4,7] In some previously reported cases, there was a delay of 2 to 3 years before a correct diagnosis was made.[4,6]

Because DLE is usually self-limited, the course of DLE is usually benign; therefore, early recognition and adequate therapy may prevent clinical complications such as permanent scarring, synechiae, entropion, trichiasis, and severe eye impairment.[8] However, since eyelid localization may be the first manifestation of classic DLE,[9] patients in whom it is the only manifestation of disease need to be observed over a long period.

REFERENCES

1. Ziv R, Schewach-Millet M, Trau H. Discoid lupus erythematosus of the eyelids. *J Am Acad Dermatol.* 1986;15:1:112-113.
2. Kaposi M, Hebra F. *On the Diseases of the Skin, Including the Exanthemata.* Vol 4. London, England: New Sydenham Society; 1875.
3. Donzis PB, Insler MS, Buntin DM, Gately LE. Discoid lupus erythematosus involving the eyelids. *Am J Ophthalmol.* 1984;98:32-36.
4. Huey C, Jakobiec FA, Iwamoto T, Kennedy R, Farmer ER, Green WR. Discoid lupus erythematosus of the eyelids. *Ophthalmology.* 1983;90:1389-1398.
5. Burge SM, Frith PA, Juniper RP, Wojnarowska F. Mucosal involvement in systemic and chronic cutaneous lupus erythematosus. *Br J Dermatol.* 1989;121: 727-741.
6. Cyran S, Douglass MC, Silverstein JL. Chronic cutaneous lupus erythematosus presenting as periorbital edema and erythema. *J Am Acad Dermatol.* 1992;26: 334-338.
7. Bettis VM, Vaughn RY, Guill MA. Erythematous plaques on the eyelids: discoid lupus erythematosus (DLE). *Arch Dermatol.* 1993;129:497, 500.
8. Tosti A, Tosti G, Giovannini A. Discoid lupus erythematosus solely involving the eyelids: report of three cases. *J Am Acad Dermatol.* 1987;16:1259-1260.
9. Feiler-Ofry V, Isler Z, Hanau D, Godel V. Eyelid involvement as the presenting manifestation of discoid lupus erythematosus. *J Pediatr Ophthalmol Strabismus.* 1979;6:395-397.

Cutaneous Eruption Limited to Skin Covered by a Swimming Suit

Diagnosis: Mycosis fungoides.

MICROSCOPIC FINDINGS AND CLINICAL COURSE

A bandlike infiltrate of atypical lymphocytes along the dermoepidermal junction was noted, as well as marked epidermotropism and numerous Pautrier microabscesses. Lymphocytes in the epidermis had large hyperchromatic and convoluted nuclei. There was no evidence of spongiosis.

The patient refused any treatment, and she was unavailable for follow-up. Three years later, when she was contacted by telephone, she stated that erythematous patches persisted on her skin, especially on the buttocks, although her general condition remained good. She again refused any treatment.

DISCUSSION

Mycosis fungoides is a cutaneous T-cell lymphoma that usually evolves through 3 well-known clinical stages: patches, plaques, and tumors. Histopathologically, it is characterized by a variably dense bandlike infiltrate of lymphocytes along the papillary dermis and dermoepidermal junction. Often, lymphocytes can be seen within the epidermis ("epidermotropism"). The histopathologic findings tend to vary according to the different clinical stages of the disease.[1]

At first glance, our patient seemed to have an allergic contact dermatitis due to some allergen that was present in her swimming suit or in another similar item of clothing. However, based on the cutaneous biopsy findings, the diagnosis of lymphomatoid contact dermatitis[2-4] was considered. Histopathologically, differentiating mycosis fungoides from its spongiotic simulants,[5] including lymphomatoid contact dermatitis, can be difficult, because collections of lymphocytes are present in discrete foci within the epidermis in both conditions. However, in authentic mycosis fungoides, the intraepidermal collections consist of atypical lymphocytes, which tend to be closely crowded, resulting in Pautrier collections. In contrast, the intraepidermal collections that are seen in inflammatory dermatoses are composed not only of lymphocytes but also of Langerhans cells, keratinocytes, and, sometimes, eosinophils. This mixture of cells is not seen in Pautrier collections of mycosis fungoides.[6(pp105-108)] Furthermore, intraepidermal lymphocytes in lesions of mycosis fungoides are larger than those within the dermis,[6(pp125-128)] and there is no associated spongiosis.[6(pp117-120)] However, in lymphomatoid contact dermatitis, the results of cutaneous patch testing for the suspected allergen are positive, and the lesions disappear after adequate treatment and avoidance of the allergen. In our patient's case, the results of all patch tests were negative, and the eruption persisted only on the area of skin that was covered by the swimming suit. Moreover, poikilodermatous skin changes such as those seen in our patient are not usually present in allergic contact dermatitis. Another differential diagnosis that should be considered is seabather's eruption,[7] but features such as the long history of the eruption, the absence of pruritus, the poikilodermatous appearance of the lesions, and, chiefly, the histopathologic findings of stereotypical mycosis fungoides made this diagnosis in our patient.

In short, our patient had mycosis fungoides with poikilodermatous skin lesions. The eruption remained limited to the area of skin that had been covered by the swimming suit, probably because of the therapeutic effect of the sun during the summer at the beach, which cleared the lesions on the sun-exposed areas and delineated the silhouette of the swimming suit on sun-protected skin.

REFERENCES

1. Horiuchi Y, Tone T, Umezawa A, Takezaki S. Large cell mycosis fungoides at the tumor stage: unusual T8, T4, T6 phenotypic expression. *Am J Dermatopathol.* 1988;10:54-58.
2. Gomez Orbaneja J, Iglesias Diez L, Sanchez Lozano JL, Conde Salazar L. Lymphomatoid contact dermatitis: a syndrome produced by epicutaneous hypersensitivity with clinical features and a histopathologic picture similar to that of mycosis fungoides. *Contact Dermatitis.* 1976;2:139-143.
3. Ecker RI, Winkelmann RK. Lymphomatoid contact dermatitis. *Contact Dermatitis.* 1981;7:84-93.
4. Wall LM. Lymphomatoid contact dermatitis due to ethylenediamine dihydrochloride. *Contact Dermatitis.* 1982;8:51-54.
5. Ackerman AB, Breza TS, Capland L. Spongiotic simulants of mycosis fungoides. *Arch Dermatol.* 1974;109:218-220.
6. Ackerman AB, Jacobson M, Vitale P. *Clues to Diagnosis in Dermatopathology I.* Chicago, Ill: ASCP Press; 1991:105-108, 117-120, 125-128.
7. Wong DE, Meinking TL, Rosen LB, Taplin D, Gogan DJ, Burnett JW. Seabather's eruption: clinical, histologic, and immunologic features. *J Am Acad Dermatol.* 1994;30:399-406.

Alopecia, Hypohidrosis, and Ulcerations in a Man

Diagnosis: Mycosis fungoides.

MICROSCOPIC FINDINGS AND CLINICAL COURSE

Histologic examination showed a dense lichenoid dermal infiltrate with marked epidermotropism of highly atypical, convoluted lymphocytes. Atypical lymphocytes surrounding and infiltrating the wall of small to medium-size vessels in the dermis and subcutaneous tissue were noted in the biopsy specimen from the area near an ulceration. There was epidermotropism into sweat glands, with epithelial proliferation and loss of the lumen. A biopsy specimen from the scalp showed perifollicular infiltrates of atypical lymphocytes with epidermotropism. These findings are consistent with mycosis fungoides.

The patient was referred to the M. D. Anderson Cancer Center, Houston, Tex, for treatment. A partial remission, including healing of the skin ulcers, was achieved in 6 months with interferon alfa therapy combined with extracorporeal photopheresis and antiobiotic therapy.

DISCUSSION

Mycosis fungoides can present as patches, plaques, tumors, erythroderma, or other variants. Plaques, tumors, and erythroderma can arise de novo, or they can follow previous skin involvement with patch stage or one of the other clinical variants of mycosis fungoides. Patients often have chronic dermatitis for 10 to 20 years before the disease is diagnosed. Patch-stage lesions, which are described clinically as scaly, erythematous, or poikilodermatous, are typically located on the breasts and buttocks, but they can occur anywhere and may be asymptomatic or pruritic. The plaque-stage variant presents as erythematous to violaceous, scaly, indurated lesions that may mimic the appearance of other dermatoses, such as psoriasis, eczema, lichen planus, or tinea.

Tumors in mycosis fungoides present as reddish brown or purplish red nodules that can ulcerate. Erythroderma, when present, is usually generalized, and it is associated with intense pruritus. Patients with mycosis fungoides can also present with anhidrosis and alopecia due to infiltration of the adnexal structures in the dermis by abnormal lymphocytes.[1-3] A male patient with mycosis fungoides who presented with generalized anhidrosis, progressive alopecia, pruritus, and Sjögren syndrome without skin lesions has also been described.[4] He had some of the typical features of mycosis fungoides, but he also had some unusual clinical features. He had generalized alopecia, hypohidrosis, and many erythematous reticulated patches mimicking livedo vasculitis, with multiple punched-out ulcerations on his buttocks, thighs, and arms. Ulceration that is not associated with necrosis of tumors is rare in mycosis fungoides. In 1994, Zelger et al[3] described a patient with mycosis fungoides who had 4 brownish red patches and plaques, one of which was ulcerated.

Although the histologic appearance of cutaneous T-cell lymphoma varies widely, according to Shapiro and Pinto[5] the diagnosis can be established by the presence of 2 or more of the following features in a biopsy specimen: Pautrier microabscesses, epidermotropism with slight or no spongiosis, lining up of lymphocytes along the basal layer, a lichenoid infiltrate that spares the dermoepidermal junction, and the clear presence of lymphocytes that are slightly large and hyperconvoluted. Microscopic involvement of blood vessels and adnexal structures is an unusual feature of mycosis fungoides.

When making the diagnosis of cutaneous T-cell lymphoma, the histologic findings must be correlated with the clinical presentation.[5] The clinical presentation in the case reported herein correlated well with the histopathologic finding of atypical hyperconvoluted lymphocytes involving hair follicles, sweat glands, and blood vessels in addition to dermis and epidermis.

REFERENCES

1. Hitchcock MG, Burchette JL, Olsen EA, Ratech H, Kamino H. Eccrine gland infiltration by mycosis fungoides. *Am J Dermatopathol.* 1996;18:447-453.
2. Kossard S, White A, Killingsworth M. Basaloid folliculolymphoid hyperplasia with alopecia as an expression of mycosis fungoides (CTCL). *J Cutan Pathol.* 1995; 22:466-471.
3. Zelger B, Sepp N, Weyrer K, Grunewald K, Zelger B. Syringotropic cutaneous T-cell lymphoma: a variant of mycosis fungoides? *Br J Dermatol.* 1994;130:765-769.
4. Dubin DB, Hurowitz JC, Brettler D, et al. Adnexotropic T-cell lymphoma presenting with gereralized anhidrosis, progressive alopecia, pruritus, and Sjögren's syndrome. *J Am Acad Dermatol.* 1998;38:493-497.
5. Shapiro PE, Pinto FJ. The histologic spectrum of mycosis fungoides/Sezary syndrome (cutaneous T-cell lymphoma): a review of 222 biopsies, including newly described patterns and the earliest pathologic changes. *Am J Surg Pathol.* 1994; 18:645-667.