Bazex Syndrome (Paraneoplastic Acrokeratosis)

Amor Khachemoune, MD, CWS; Rajesh Yalamanchili, MD; Carlos Rodriguez, BS

GOAL

To understand Bazex syndrome

OBJECTIVES

Upon completion of this activity, dermatologists and general practitioners should be able to:

1. Examine the cutaneous changes observed in Bazex syndrome.
2. Describe the possible pathogenesis of Bazex syndrome.
3. Explain the treatment options for Bazex syndrome.

CME Test on page 304.

This article has been peer reviewed and approved by Michael Fisher, MD, Professor of Medicine, Albert Einstein College of Medicine. Review date: October 2004.

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of Albert Einstein College of Medicine and Quadrant HealthCom, Inc. Albert Einstein College of Medicine is accredited by the ACCME to provide continuing medical education for physicians.

Albert Einstein College of Medicine designates this educational activity for a maximum of 1 category 1 credit toward the AMA Physician's Recognition Award. Each physician should claim only that credit that he/she actually spent in the activity.

This activity has been planned and produced in accordance with ACCME Essentials.

Drs. Khachemoune and Yalamanchili and Mr. Rodriguez report no conflict of interest. The authors report no discussion of off-label use. Dr. Fisher reports no conflict of interest.

Bazex syndrome (paraneoplastic acrokeratosis) is characterized by the presence of hyperkeratotic lesions on the nose, ears, palms, and soles that appear in association with malignancies of the upper aerodigestive tract, most often a squamous cell carcinoma. We present a case of Bazex syndrome and provide a review of the literature.

Cutis. 2004;74:289-292.

Accepted for publication September 9, 2004.

Dr. Khachemoune is a dermatologist from Wellman Laboratories of Photomedicine, Department of Dermatology, Massachusetts General Hospital, Boston. Dr. Yalamanchili is an intern at Austin Medical Education programs, Texas. Mr. Rodriguez is a medical student at the University of Illinois at Chicago College of Medicine.

Reprints: Amor Khachemoune, MD, CWS, Wellman Laboratories of Photomedicine, Department of Dermatology, Massachusetts General Hospital, Harvard Medical School, 55 Fruit St, Boston, MA 02114 (e-mail: amorkh@pol.net).

Psoriasiform dermatitis seen with Bazex syndrome may involve the nose and the helices of the ears in addition to the palms and soles. In most reported cases, the appearance of the characteristic psoriasiform lesions preceded the diagnosis of the associated underlying malignancy. Skin scrapings for potassium hydroxide and fungal cultures should be performed, and skin biopsy of keratotic plaques is recommended to exclude psoriasis.

Case Report

A 70-year-old man with no personal or family history of psoriasis or other skin diseases developed psoriasiform dermatitis of the fingers, toes, and helices of the ears over a period of 3 months. He reported a history of cigarette smoking (1 pack per day) with significant consumption of alcoholic beverages over a period of 30 years. Results from a review of systems revealed progressive hoarseness and dysphagia, with a recent history of a 15-lb weight loss. On physical examination, psoriasiform plaques were seen on the palms and soles, as well as on the helices of the ears (Figure 1) and the tip and dorsum of the nose. There was a yellowish discoloration and dystrophy of all the fingernails and toenails (Figure 2). Results from potassium hydroxide preparations from scrapings of the palms and soles were negative, and fungal culture did not grow any pathogenic fungi.

Six weeks later, the patient developed bilateral cervical lymphadenopathy. Otolaryngologic examination consisted of direct laryngoscopy; imaging studies including magnetic resonance imaging and computed tomography scans; and laryngeal biopsy, which revealed a stage IV squamous cell carcinoma (SCC) confined to the head and neck area. Although the patient did not return for follow-up, management of the laryngeal SCC with surgery and postoperative chemotherapy completely cleared his skin and nail lesions without adjunct dermatologic treatments.

Comment

Bazex syndrome (paraneoplastic acrokeratosis) was first described as a clinical entity by Gougerot and Rupp[1] more than 40 years prior to the coining of the disease's current widely used eponym of Bazex syndrome. In 1922, Gougerot and Grupper[1] described a patient with hyperkeratotic lesions on the nose, ears, palms, and soles in conjunction with an SCC on the tongue. Years later, Bazex and colleagues[2] described a patient with an SCC of the pyriform fossa and an associated psoriasiform dermatosis. Since that report, more than 110 cases of Bazex syndrome have been reported, most of which describe the condition as a cutaneous paraneoplastic syndrome characterized by psoriasiform lesions associated with an underlying malignancy of the upper aerodigestive tract (oropharynx, larynx, or esophagus), most often of the SCC subtype.[3-7]

Bazex syndrome can be classified among the cutaneous paraneoplastic disorders that also include acanthosis nigricans maligna, erythema gyratum, necrolytic migratory erythema, and hypertrichosis lanuginosa acquisita.[7] The cutaneous manifestations of Bazex syndrome are paraneoplastic in that the developing skin changes coevolve with an underlying malignancy; these cutaneous hallmarks of the syndrome do not, however, represent metastatic extensions of this malignancy. On the contrary, they may actually serve as harbingers of future oncologic progression.

The cutaneous changes observed in Bazex syndrome have been classified into 3 stages.[3] In the first stage, psoriasiform changes of the fingers, toes, auricular helix, and nose are noted. In addition, the earliest stage of the syndrome is characterized by nail changes, including horizontal and vertical ridging, subungual hyperkeratosis, yellow discoloration, and nail dystrophy. During this stage, the primary tumor is considered asymptomatic. The second stage is primarily typified by proximal extension of the cutaneous changes observed in the first stage to involve the dorsum of the hands and feet, as well as the malar regions of the face. Local symptoms secondary to growth of the primary tumor also may surface during this stage. The third stage in the course of the syndrome is defined by progressive centripetal

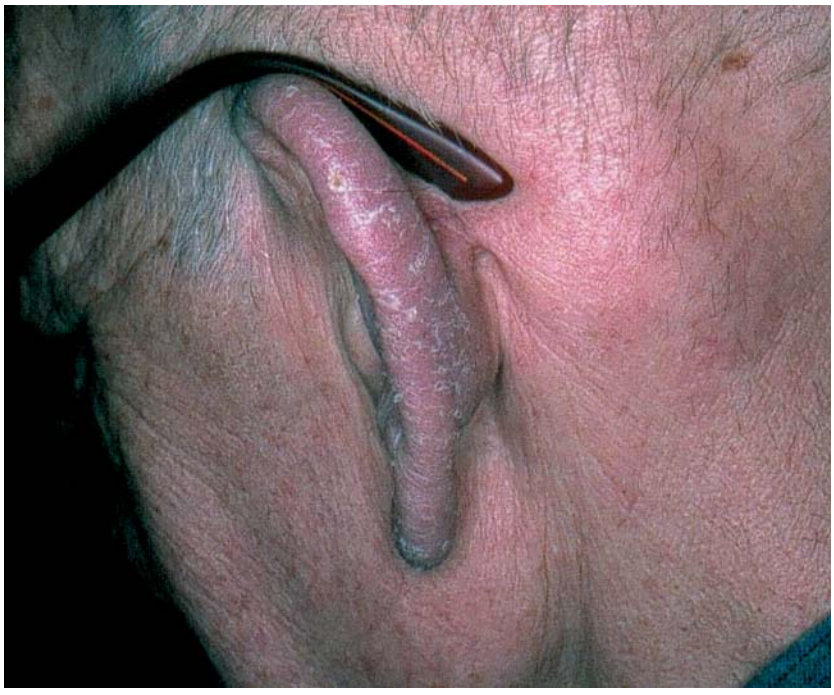

Figure 1. Psoriasiform dermatitis involving the helix of the ear.

extension of the cutaneous disease process to affect regions of the arms and legs (nails, hands, elbows, knees, and feet), scalp, and trunk.[3-7] Other cutaneous changes that have been reported include hyperpigmentation, particularly in individuals with darker skin pigmentation,[6] and development of bullous lesions.[5,8,9]

Based on the initial dermatologic manifestations of Bazex syndrome, it is not surprising that the condition is often misdiagnosed as psoriasis or chronic dermatitis. Indeed, histopathologic examination of skin lesions in the syndrome is nonspecific and may mimic psoriasis or other more common dermatoses, demonstrating hyperkeratosis, parakeratosis, acanthosis, vacuolar degeneration of keratinocytes, and/or perivascular lymphohistiocytic infiltrate.[6,7,10] One potential distinguishing feature of Bazex syndrome, however, is specific psoriasiform involvement of the helix of the ear, as opposed to the entire ear, as would be more commonly expected in psoriasis.[7] The tip of the nose also is involved in Bazex syndrome, which is an unusual location for psoriasis.

Extensive reviews of the literature reporting cases of Bazex syndrome demonstrate that most patients have been Caucasian, male, of French descent, and older than 40 years.[6,7] SCCs have accounted for nearly 60% of tumors found in patients with this syndrome, and adenocarcinomas have accounted for less than 10% of malignancies. Furthermore, the majority of the neoplasms have involved the oropharynx and larynx.[7] These neoplasms may be silent and only present with lymph node metastases. Less commonly, primary tumors may occur in the lungs and esophagus. Rare cases of neoplasms of the prostate, liver, stomach, thymus, uterus, vulva, and lymphoid tissues also have been reported.[11] Numerous cases have been described in which the primary tumor could not be identified, and affected patients were diagnosed on the basis of metastases to cervical lymph nodes. In the vast majority of reported cases, the appearance of the characteristic psoriasiform lesions preceded the diagnosis of the associated malignancy.[6,7] Finally, the skin lesions either markedly improved or completely resolved in the great preponderance of patients in whom the underlying malignancy was either treated with chemotherapy and/or radiation therapy or surgical excision.[6,7,10-12] This was true of the patient presented in this report.

The pathogenesis of Bazex syndrome remains a mystery, though several authors have suggested an autoimmune etiology based on the common histologic finding of inflammatory infiltrates along the basal cell layer of affected skin regions.[5,8,9] The immune reaction may be humoral or cellular; the proposed mechanism states that cross reactivity between skin and tumor antigens may produce the characteristic cutaneous changes observed, because antitumor antibodies cross reacting with the epidermis or basement membrane zone could elicit an immunologic response resulting in basal cell layer damage.[13,14] Several authors also have proposed that the tumors may produce a host of growth factors that collectively lead to hyperkeratotic skin changes.[14,15]

Ideal treatment of Bazex syndrome is eradication of the underlying malignancy. Unresectable or

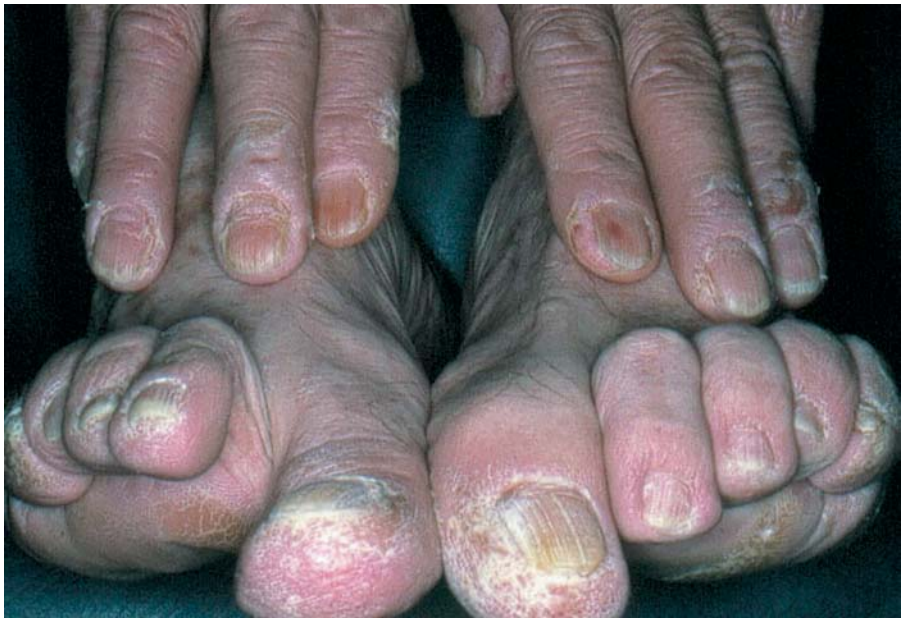

Figure 2. Acral psoriasiform lesions with nail dystrophy.

treatment-resistant tumors, however, pose a significant challenge for the clinician. Numerous studies have been conducted demonstrating equivocal efficacies of various standard dermatological therapies in the treatment of skin lesions occurring in this syndrome. Unfortunately, in the vast majority of patients, such treatment options as topical tar, topical and systemic corticosteroids, UVB irradiation, antifungals, and antibiotics have proven to be of little use.[6,7] Gill and colleagues[9] have reported that oral psoralen–UVA phototherapy may offer some promise of effective treatment in these patients. However, larger studies are required to further investigate the therapeutic benefits of this treatment option. Although the management of treatment-resistant cutaneous lesions in Bazex syndrome may prove problematic, it is clear that the clinician must be astute in recognizing this disease process in its earlier stages to identify and effectively treat any underlying malignancy as expeditiously as possible.

Acknowledgment—The authors wish to thank Dr. Eric Ehrsam for his assistance with the preparation of this manuscript.

REFERENCES

1. Gougerot H, Grupper C. Dermatose érythématosquameuse avec hyperkératose palmoplantaire, porectasies digitales et cancer de la langue latent. *Paris Méd*. 1922;43:234-237.
2. Bazex A, Salvador R, Dupré A, et al. Syndrome paranéoplasique à type d'hyperkératose des extrémités. Guérison après le traitment del'épthélioma laryngé [letter]. *Bull Soc Fr Dermatol Syphiligr*. 1965;72:182.
3. Bazex A, Griffiths A. Acrokeratosis paraneoplastica: a new cutaneous marker of malignancy. *Br J Dermatol*. 1980;103:801-805.
4. O'Brien TJ. Bazex syndrome (acrokeratosis paraneoplastica). *Australas J Dermatol*. 1995;36:91-93.
5. Bolognia JL, Brewer YP, Cooper DL. Bazex syndrome (acrokeratosis paraneoplastica): an analytic review. *Medicine (Baltimore)*. 1991;70:269-280.
6. Bolognia JL. Bazex syndrome: acrokeratosis paraneoplastica. *Semin Dermatol*. 1995;14:84-89.
7. Sarkar B, Knecht R, Sarkar C, et al. Bazex syndrome (acrokeratosis paraneoplastica). *Eur Arch Otorhinolaryngol*. 1998;255:205-210.
8. Handfield-Jones SE, Matthews CAN, Ellis JP, et al. Acrokeratosis paraneoplastica of Bazex. *J R Soc Med*. 1992;85:548-550.
9. Gill D, Fergin P, Kelly J. Bullous lesions in Bazex syndrome and successful treatment with oral psoralen phototherapy. *Australas J Dermatol*. 2001;42:278-280.
10. Wareing MJ, Vaughan-Jones SA, McGibbon DH. Acrokeratosis paraneoplastica: Bazex syndrome. *J Laryngol Otol*. 1996;110:899-900.
11. Buxtorf K, Hübscher E, Panizzon R. Bazex syndrome. *Dermatology*. 2001;202:350-352.
12. Hsu YS, Lien GS, Lai HH, et al. Acrokeratosis paraneoplastica (Bazex syndrome) with adenocarcinoma of the colon: report of a case and review of the literature. *J Gastroenterol*. 2000;35:460-464.
13. Pecora AL, Landsman L, Imgrund SP, et al. Acrokeratosis paraneoplastica: report of a case and review of the literature. *Arch Dermatol*. 1983;119:820-826.
14. Jean LB, Yvelise PB, Dennis LC. Bazex syndrome (acrokeratosis paraneoplastica): an analytic review. *Medicine*. 1991;70:269-280.
15. Politi Y, Ophir J, Brenner S. Cutaneous paraneoplastic syndromes. *Acta Derm Venereol (Stockh)*. 1993;73:161-170.