Pustular Bazex Syndrome with Flexural Localization Associated with Metastatic Lung Carcinoma: Case Report

Fleksüral Bölgelerde Lokalize, Metastatik Akciğer Karsinomu ile İlişkili Püstüler Bazex Sendromu

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ABSTRACT A 60-year-old male who had been diagnosed with metastatic lung carcinoma six years previously and had not accepted the a treatment was evaluated due to rash in his body. The patient's history revealed that the rash started six months ago on the back of the hand and extended to the upper extremities and his ear. Dermatological examination of the patient revealed erythematous-squamous plaques spread on flexural areas, bilateral upper limbs and ears, and pustules with peripheral location around the plaques. Histopathologically, there was hyperkeratosis, focal parakeratosis, small pustular change and perivascular lymphocytic infiltrate in the papillary dermis. Based on the clinical manifestation, presence of carcinoma and histopathologic evaluation, the patient was diagnosed as Bazex syndrome. In the present study, we have reported a very rare atypical form of Bazex syndrome due to psoriasiform lesions with acral and flexural location, accompanied by numerous pustules. This is the first case of acrokeratosis paraneoplastica in the literature that associated with metastatic lung carcinoma.

Key Words: Carcinoma, non-small-cell lung; paraneoplastic syndromes

ÖZET Altı yıl önce metastatik akciğer karsinomu tanısı alan ve her türlü tedaviyi kabul etmeyen 60 yaşında erkek hasta vücudunda döküntü yakınması ile başvurarak değerlendirildi. Hastanın anamnezine bakıldığında, döküntünün altı ay önce el sırtında başladığı, daha sonra üst ekstremiteler ve kulağa yayıldığı öğrenildi. Yapılan dermatolojik muayenede fleksüral alanlarda, her iki üst ekstremitede ve kulaklarda yayılma gösteren eritematöz, skuamöz plaklar ve plakların etrafında periferik yerleşimli püstüller gözlendi. Histopatolojik incelemede papiller dermisde hiperkeratozis, fokal parakeratozis, küçük püstüler değişiklikler ve perivasküler lenfosit infiltrasyonu mevcut idi. Klinik bulgular, karsinom varlığı ve histopatolojik değerlendirme sonuçları göz önüne alındığında hastaya Bazex sendromu tanısı kondu. Bu çalışmada, Bazex sendromunun, akral ve fleksüral yerleşim gösteren psöriazis benzeri lezyonlardan dolayı çok nadir ve atipik olduğu düşünülen, çok sayıda püstülün eşlik ettiği bir formu sunulmuştur. Bu olgu, literatürde, metastatik akciğer karsinomu ile ilişkili olan ilk akrokeratozis paraneoplastika olgusudur.

Anahtar Kelimeler: Karsinom, küçük hücre dışı; paraneoplastik sendrom

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Bazex syndrome is first defined as the cutaneous sign of supra-diaphragmatic malignancies in 1965.[1] It is a very rare disease that usually seen in Caucasian males over 40 years of age.[2]

Squamous cell carcinoma of the upper aerodigestive tract, and other tumours with cervical or mediastinal lymph node metastases are the most common neoplasms associated with Bazex syndrome.[3,4] However it has al-

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so been described in combination with a variety of other malignant neoplasms, such as gastric adenocarcinoma, colon adenocarcinoma, small cell lung carcinoma, lung adenocarcinoma, Hodgkin's disease, T-cell lymphoma, multiple myeloma, hepatocarcinoma, thymoma, cutaneous squamous cell carcinoma, prostate adenocarcinoma, vulvar, uterine, bladder carcinoma and retroperitoneal liposarcoma.[2,3,5,6-12] In the present study, we report an atypical form of acrokeratosis paraneoplastica with an atypical location, and it is the first case in the literature associated with metastatic lung carcinoma.

CASE REPORT

A 60-year-old male was evaluated in the oncology clinic upon our consultation request due to lesions in his body. The patient's history revealed that he had presented to the chest polyclinic in 2001 with complaints of weight loss, fever, shortness of breath, chest pain, sputum production and swelling in the testes. He had been diagnosed with metastatic lung carcinoma on the basis of his lung x-ray, thoraco-abdominal tomography, testicular and abdominal USG, and cytological examination of the sample taken from his pleural effusion. The patient, who had rejected the treatment, been discharged from the hospital upon his request. The patient, who was not followed until 2006, presented to our oncology clinic complaining of shortness of breath, and rash. The rash had started six months previously on the back of the hand and extended to the upper extremities, ear helices and neck. Dermatological examination of the patient revealed erythematous-squamous plaques spread on flexural sites, in particular, as well as axilla, inguinal area, gluteal area, neck, popliteal site, bilateral upper limbs and ear helices and pustules with peripheral location around the plaques. In addition, palmoplantar hyperkeratosis, paronychia, subungal hyperkeratosis, yellow discoloration and onycholysis on nails were accompanied (Figure 1, 2). The patient was photographed with patient's approval. In the laboratory analyses, those parameters were not in the normal limits: LDH: 178 U/L (248-414), ALP: 169 U/L (30-120), GGT: 154 U/L (0-55), total protein: 5.8 gr/dl (6.6-8.7), albumin: 2.9 gr/dl (3.5-5.3) and Calcium: 7.2 mg/dl (8.5-10.5).

Histopathologically, there was hyperkeratosis and a focal parakeratosis on the top of the epidermis. Epidermal changes included spongiosis and basal vacuolazation. There was small pustular changes in the epidermis and perivascular lymphocytic infiltrates in the papillary dermis (Figure 3). Based on the clinical manifestation, the presence of carcinoma and histopathologic evaluation, the patient was diagnosed as Bazex syndrome. Topical corticosteroid treatment was started. However, the patient died in the course of treatment due to cardiopulmonary arrest.

DISCUSSION

In Bazex syndrome, the skin changes occur before discovery of underlying tumor (67%), after clinical manifestation of tumor (15%) or concurrently with tumor discovery (18%). Removal of neoplasm leads to remission of dermatosis, recurrence of tumor will trigger a relapse.[3-5] In our case, the patient was diagnosed as Bazex syndrome five after the diagnosis of carcinoma.

Bazex syndrome is most commonly co-present with these the first three carcinomas: oropharynx-larynx, lung and cancers with an unknown primary site. Cancers that are rarely co-present with Bazex syndrome include prostate, urinary bladder, liver, stomach, colon, thymus, uterus, vulva as well as myelomas.[13] Our case had Bazex syndrome associated with metastatic lung carcinoma with an indefinite primary site. According to our present knowledge, there is no reports in the literature that mentioned a case of Bazex syndrome associated with metastatic lung carcinoma.

The most frequently involved areas in Bazex syndrome include ears (79%), nails (75%), nose (63%), palmar area (58%), and plantar area (51%). Acrokeratosis paraneoplastica of Bazex typically exhibits three clinical stages[2,3,5,6,13] as follows:

Stage 1, the skin lesions are not well-defined and involve helices of ears, nose, fingers, toes and nails. The tumor is said to be asymptomatic in this stage.

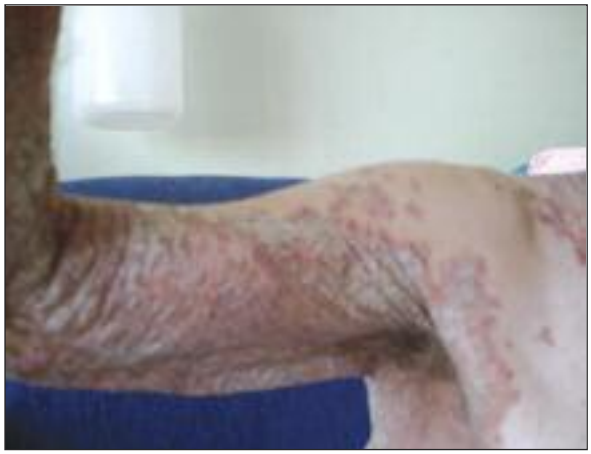

FIGURE 1: Erythematous and squamous plaques starting from the hand dorsum and extending to axilla and neck, and pustules with peripheral location around the plaques.

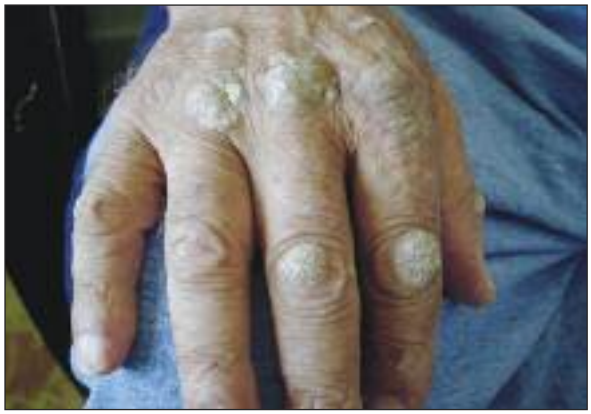

FIGURE 2: Erythematous-squamous plaques on the patient's right hand dorsum.

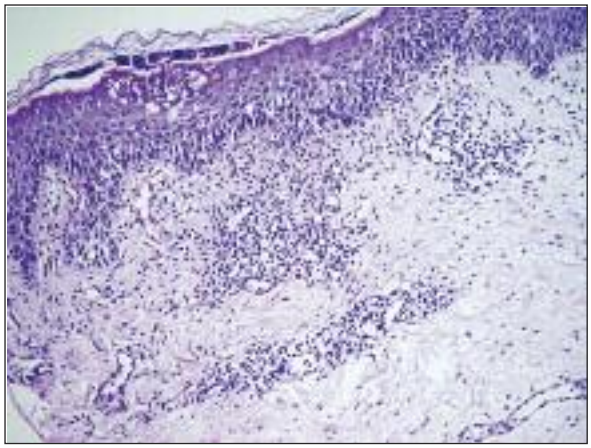

FIGURE 3: Hyperkeratosis, epidermal spongiosis, basal vacuolar change, epidermal pustule and dermal infiltration (Hematoxilin eosin X400)

Stage 2, the lesions tend to spread to additional sites, such as palms and soles. This stage is characterized by appearance of local symptoms referable to the tumor.

Stage 3, if the tumor remains untreated, areas of erythema and scaling begin to develop on the elbows, knees and trunk. As it is seen, the lesions may spread to elbows, knees and trunk in untreated patients. The literatures include one case with flexural involvement. Ali et al. reported a case of Bazex syndrome with flexural location caused by tonsillar adenocarcinoma.[14] The lesions of our patient started from the acral area and extended to axilla, inguinal area and even to the neck. We think that this resulted from our patient's refusal of anticancer treatment for a long period of time, namely five years.

Classical cutaneous signs of Bazex syndrome include papulosquamous lesions, hyperpigmentation, keratoderma, erythematous or villous, well-demarcated patches and plaques with acral location.[2,3,5,6,13] Changes in nails are paronychia, subungal hyperkeratosis, yellow discoloration and onycholysis.[2,3,5,6,13] The literature includes only a few cases of Bazex syndrome accompanied by bullous lesions.[3,15,16] Gill et. al. reported a Bazex syndrome case who had susceptible bullae on the lateral aspects of feet caused by squamous cell carcinoma and who was successfully treated with oral psoralen phototherapy.[16] Our case had, in addition to papulosquamous lesions with acral location, occasional pustules surrounding erythematous squamous plaques at flexural sites like the axilla and inguinal area. We did not encounter a case of Bazex syndrome with a pustular form in our literature examination search. Our patient also had palmoplantar hyperkeratosis, as well as paronychia, subungal hyperkeratosis, yellow discoloration and onycholysis on the nails.

The issue of how the characteristic eruptions in Bazex syndrome occur is still open to dispute. According to one theory, antibodies enter a cross reaction with the tumor, surround keratinocytes or basal membrane antigens, and cause damage to the epidermal or basal membrane. The histopathological changes in the affected skin are nonspecific. A

mild degree of acanthosis is often seen with hyperkeratosis and focal parakeratosis. There is usually a lymphocytic infiltrate in the upper dermis. Dyskeratotic keratinocytes, vacuolar degeneration, band-like infiltration and melanin incontinence may be rarely seen.[5,6,13,17] Our case histopathologically had hyperkeratosis, parakeratosis, acanthosis and perivascular lymphohistiocytic infiltration. In addition, spongiosis, basal vacuolization, and especially small pustular changes that were not seen in the similar cases in the previous literature were observed.

Clinical manifestation, presence of underlying cancer and histopathology are diagnostic in Bazex syndrome. The main differential diagnosis should include psoriasis. The distinguishing clinical feature, which is nearly always present in Bazex syndrome, is involvement of the helices of the ears and the tip of the nose. In psoriasis, the palms and soles are more frequently involved more than the dorsum. In Bazex syndrome histologically, some psoriasiform features are present including hyperkeratosis, parakeratosis, and a superficial lymphohistiocytic infiltrate, but other nonpsoriasiform changes also exist. These include vacuolar degeneration with melanin-containing macrophages in the dermis and dyskeratotic keratinocytes. In addition, pytiriasis rubra pilaris, lupus erythematodes, Reiter's disease, hyperkeratotic hand and foot eczema, mycosis of the nails or tinea of the hands and feet and hereditary palmoplantar keratosis are considered at differential diagnosis. The patient's history as well as the characteristic distribution, non-specific histologic findings of the skin lesions and positive fungal cultures are useful at differential diagnosis.

Treatment of the syndrome primarily involves eradication of the underlying malignancy with surgery, chemotherapy or radiotherapy.[5,6,17] If the tumour is unresectable or resistant to treatment, etretinate (0.75-1 mg/kg/day) is the drug of choice. Additionally, topical and systemic steroids, salicylic acid, topical vitamin D analogues, and PUVA are used in treatment.[5,6,16,17] Our case died shortly after starting topical corticosteroid treatment and the treatment could not be evaluated.

In conclusion, we present the first case of acrokeratosis paraneoplastica, which developed in association with metastatic lung carcinoma, had a flexural location and was in the pustular form.

REFERENCES

1. Sharma V, Sharma NL, Ranjan N, Tegta GR, Sarin S. Acrokeratosis paraneoplastica (Bazex syndrome): case report and review of literature. Dermatol Online J 2006; 12 (1): 11.
2. Pecora AL, Landsman L, Imgrund SP, Lambert WC. Acrokeratosis paraneoplastica (Bazex' syndrome). Report of a case and review of the literature Arch Dermatol 1983;119 (10):820-6.
3. Bolognia JL, Brewer YP, Cooper DL. Bazex syndrome (acrokeratosis paraneoplastica). An analytic review. Medicine (Baltimore) 1991;70 (4):269-80.
4. Bolognia JL. Bazex syndrome: acrokeratosis paraneoplastica. Semin Dermatol 1995;14 (2): 84-9.
5. Valdivielso M, Longo I, Suárez R, Huerta M, Lázaro P. Acrokeratosis paraneoplastica: Bazex syndrome. J Eur Acad Dermatol Venereol 2005; 19(3):340-4.
6. Hsu YS, Lien GS, Lai HH, Cheng YS, Hu CH, Hsieh MC, et al. Acrokeratosis paraneoplastica (Bazex syndrome) with adenocarcinoma of the colon: report of a case and review of the literature. J Gastroenterol 2000;35(6):460-4.
7. Lucker GP, Steijlen PM. Acrokeratosis paraneoplastica (Bazex syndrome) occurring with acquired ichthyosis in Hodgkin's disease. Br J Dermatol 1995;133(2):322-5.
8. Chave TA, Bamford WM, Harman KE. Acrokeratosis paraneoplastica associated with recurrent metastatic thymic carcinoma. Clin Exp Dermatol 2004;29(4):430-2.
9. Hara M, Hunayama M, Aiba S, Suetake T, Watanabe M, Tanaka M, et al. Acrokeratosis paraneoplastica (Bazex syndrome) associated with primary cutaneous squamous cell carcinoma of the lower leg, vitiligo and alopecia areata. Br J Dermatol 1995;133(1):121-4.
10. Obasi O, Garg SK. Bazex paraneoplastic acrokeratosis in prostate carcinoma. Br J Dermatol 1987;117(5):647-51.
11. Arregui MA, Ratón JA, Landa N, Izu R, Eizaquirre X, Díaz-Pérez JL. Bazex's syndrome (acrokeratosis paraneoplastica)--first case report of association with a bladder carcinoma. Clin Exp Dermatol 1993;18(5):445-8.
12. Sator PG, Breier F, Gschnait F. Acrokeratosis paraneoplastica (Bazex's syndrome): association with liposarcoma. J Am Acad Dermatol 2006;55(6):1103-5.
13. Sarkar B, Knecht R, Sarkar C, Weidauer H. Bazex syndrome (acrokeratosis paraneoplastica). Eur Arch Otorhinolaryngol 1998;255 (4): 205-10.
14. Ali M, Keir M, Dodd H, Cerio R. Flexural Bazex syndrome associated with tonsillar adenocarcinoma. J Drugs Dermatol 2004;3(5):557-9.
15. Mutasim DF, Meiri G. Bazex syndrome mimicking a primary autoimmune bullous disorder. J Am Acad Dermatol 1999;40(5 Pt 2):822-5.
16. Gill D, Fergin P, Kelly J. Bullous lesions in Bazex syndrome and successful treatment with oral psoralen phototherapy. Australas J Dermatol 2001;42(4):278-80.
17. Stone SP, Buescher LS. Life-threatening paraneoplastic cutaneous syndromes. Clin Dermatol 2005;23(3):301-6.