

Pulmonary Adenocarcinoma and Bazex Syndrome (Paraneoplastic Acrokeratosis)

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Bazex syndrome, or paraneoplastic acrokeratosis, is a rare psoriasis-like paraneoplastic skin disease, characterized by erythema and scaling, which is accompanied by hyperkeratotic lesions. The tumors most frequently associated with Bazex syndrome are squamous cell carcinomas of the upper respiratory and digestive tracts, whereas lung cancers, particularly adenocarcinomas, are rarely associated. We present a case in which both pulmonary adenocarcinoma and Bazex syndrome were present.

Key words: *Pulmonary adenocarcinoma. Paraneoplastic acrokeratosis. Bazex syndrome.*

Adenocarcinoma de pulmón y síndrome de Bazex (acroqueratosis paraneoplásica)

El síndrome de Bazex o acroqueratosis paraneoplásica es una rara afectación paraneoplásica cutánea, psoriasiforme y eritematodescamativa, que se acompaña de lesiones hiperqueratósicas. Los tumores más frecuentemente asociados a este síndrome son los epidermoides del tracto aerodigestivo superior. Los carcinomas de pulmón, y concretamente los de estirpe adenocarcinoma, se asocian raramente a este síndrome. Presentamos un caso en el que se describen ambas entidades.

Palabras clave: *Adenocarcinoma de pulmón. Acroqueratosis paraneoplásica. Síndrome de Bazex.*

Introduction

Between 7% and 15% of neoplastic diseases are associated at some point in their progression with some form of paraneoplastic syndrome. In lung cancer, the percentage can be as high as 10% of patients and may involve various organs and systems. Of these, the most frequently described are the nervous system¹ (myasthenic syndrome, neuropathy, encephalitis, or retinopathy) and the endocrine system² (syndrome of inappropriate secretion of antidiuretic hormone, ectopic corticotropin production, or hypercalcemia).

The incidence of cutaneous paraneoplastic syndrome in bronchogenic carcinoma is low.³⁻⁵ On many occasions, the recognition and assessment of the associated signs and symptoms lead to early suspicion of a tumor. We describe a rather uncommon case of cutaneous paraneoplastic syndrome associated with lung adenocarcinoma.

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Clinical Observations

A 78-year-old male, an ex-smoker (50 pack-years), had been diagnosed 3 years earlier with advanced idiopathic pulmonary fibrosis, with chronic respiratory insufficiency. In the course of a clinical and radiologic examination a 2.5-cm pseudonodular lesion was observed in the upper left lobe, associated with a small pleural effusion, with no hemoptysis, constitutional symptoms, or indications of other organ involvement. The physical examination showed scaly erythematous to violaceous pruriginous lesions on his hands and feet, as well as hyperkeratosis and thickening in the periungual regions of both extremities, together with erythema of the palms and soles (Figures 1 and 2) and ear helices. The patient reported that the lesions had appeared some 4 months earlier. No significant abnormal laboratory findings were recorded. Fiberoptic bronchoscopy revealed a lesion with submucosal invasion at the entrance to the upper left lobe. Several biopsies were performed, demonstrating adenocarcinoma.

Discussion

The carcinomas most frequently associated with paraneoplastic acrokeratosis, or Bazex syndrome, are those that affect the upper respiratory and digestive



Figure 1. Erythema and scaly hyperkeratotic plantar lesions.



Figure 2. Subungual hyperkeratosis and onycholysis.

tracts.^{5,6} A review of the literature by Sarkar et al⁷ showed that of 112 cases, nearly half of the associated tumors were located in the oral cavity, pharynx, and larynx, and that most were squamous cell carcinomas. These authors described 19 cases of lung cancer (only 3 of them adenocarcinomas⁸), 18 of which were of unknown origin with a positive lymph node biopsy. Some exceptional cases have been described of Bazex syndrome associated with prostate, gastric, endometrial, or vulvar epidermoid adenocarcinoma, hepatocarcinoma, bronchial carcinoid tumors,⁹ and breast cancer.¹⁰ From the clinical perspective, patients tend to be white males and the average age is about 60 years. At the time of diagnosis, they generally present metastatic lymph node involvement, although cutaneous manifestations may precede those of the tumor itself by several months.

According to the initial 1965 description by Bazex and Griffiths,¹¹ the syndrome consists of 3 stages: the first stage is characterized by a symmetrical scaly erythematous pruriginous rash in the distal regions of the fingers and toes, followed by involvement of the ears and nose. Subsequently there is hyperkeratosis of the periungual region and dystrophy of the nails, with associated onycholysis. At this stage the neoplastic disease is usually asymptomatic, as skin manifestations usually precede cancer symptoms by 2 to 6 months. In the second and third stages, there is lymph node involvement with progression of the skin lesions, with centripetal spread toward the rest of the extremities and the trunk. From the histologic perspective, the lesions correspond to hyper- and parakeratosis, acanthosis, and the vacuolar degeneration of keratinocytes, with predominantly lymphomonocytic perivascular infiltration of the papillary dermis.^{5,10,12} Direct immunofluorescent assay may show local deposits of immunoglobulins, C3 components, or fibrin in the basement membrane.^{5,6,10} Diagnosis is usually clinical and is based on the patient's medical history and on the characteristic

distribution of the lesions. In this way, other diseases such as acral psoriasis, pityriasis rubra pilaris, erythematous lupus, and familial hyperkeratosis of the palms and soles can be ruled out.^{4,12-14}

The pathogenesis of the syndrome is unclear. Several authors⁷ suggest an autoimmune mechanism in which cancer cells and epidermic cells may share a common antigen. Other explanations implicate stimulated expression of transforming growth factor α ^{6,15} by the tumor as the pathogenic mechanism in skin, which is mainly evident as hyperkeratosis. This skin disease does not respond to steroid or keratolytic therapy, and in 90% of the cases the lesions clear up (either totally or partially) with effective cancer therapy, although some cases of partial improvement with retinoid (etretinate) therapy have been described.¹⁵ Nail alterations improve more slowly and may persist after the tumor is treated.¹⁶ In view of our patient's advanced idiopathic pulmonary fibrosis underlying the manifestations and his poor functional status, we chose not to resort to chemotherapy or surgery. The patient died a few months later due to the progression of the neoplastic disease.

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