SELÇUK TIP DERGİSİ
SELCUK MEDICAL JOURNAL

DOI:http:/dx.doi.org/10.30733/std.2024.01719
Selcuk Med J 2024;40(2): 98-101

OPEN

OLGU SUNUMU / CASE REPORT

A Case of Lung Cancer Presenting with Paraneoplastic Pruritus

Paraneoplastik Kaşıntı İle Prezente Olan Akciğer Kanseri Olgusu

Oguzhan Yildiz[1], Melek Karakurt Eryilmaz[1], Ali Fuat Gurbuz[1], Fahriye Kilinc[2]

[1]Necmettin Erbakan University, School of Medicine, Department of Medical Oncology, Konya, Türkiye
[2]Necmettin Erbakan University, School of Medicine, Department of Pathology, Konya, Türkiye

ÖZET

Kaşıntı, dermatolojik rahatsızlıklar arasında sıkça görülen ve kişiyi kaşımaya zorlayan hoş olmayan bir duygu olarak tanımlanır. Kronik kaşıntı altı haftadan daha uzun süren kaşıntı olarak tanımlanır. Liken simpleks kronikus (LSC), kronik kaşıntı sonrasında ortaya çıkan kuru, pullu ve kalın cilt lekeleri olarak tanımlanır. Tipik olarak cildin belirli bir bölgesinin alışkanlık olarak kaşınmasının sonucudur. Ayrıca, paraneoplastik kaşıntı, solid tümörlerin erken bir belirtisi olarak ortaya çıkabilir. Bu vaka sunumu, bir cilt biyopsisinin sonucunda doğrulanmış olan LSC tanısı konan 73 yaşındaki bir erkek hastanın tetkik ve tedavi sürecini sunmaktadır. Hastada cilt biyopsi sonrası LSC tanısı almasının ardından yapılan malignite taramasında, akciğerde solid nodül ve karaciğerde multipl metastatik kitleler tespit edildi. Hastaya hem akciğer kitleden hem de karaciğerdeki metastatik kitleden biyopsi yapıldı. Biyopsilerin patolojik değerlendirilmesi sonucunda TTF-1 ve sinaptofizin pozitifti. Hem TTF-1 hem de sinoptofizin pozitif olan hasta Mikst tümör olarak değerlendirildi. Tetkikler sonucunda hastaya, mikst bileşenli akciğer adenokarsinomu ve küçük hücreli akciğer kanseri tanısı konmuştur. Kronik kaşıntı etyolojisini değerlendirmek için, hematolojik hastalıklar, endokrin hastalıklar, karaciğer hastalıkları, enfeksiyonlar ve ilaçlara bağlı etkenler, nörolojik ve psikiyatrik nedenler gibi olasılıklar araştırıldı. Ancak, kronik kaşıntının etyolojisi tam olarak belirlenememiştir. Akciğer kanseri için karboplatin ve etoposid tedavisi başlandıktan sonra, hastanın kaşıntı şikayetinde belirgin azalma olması, kronik kaşıntı ile malignite arasında bir ilişki olabileceğini düşündürmektedir. Ne yazık ki, hasta akciğer kanseri tanısı konulduktan iki ay sonra hipoksi, pnömoni ve multi-organ yetmezliği nedeniyle hayatını kaybetmiştir. Bu vaka, kronik kaşıntının kanser belirtisi olma potansiyelini vurgulamaktadır. Paraneoplastik kaşıntı genellikle hematolojik malignitelerle ilişkilendirilse de, bu durumun solid tümörlerde de görülebileceği unutulmamalıdır.

Anahtar Kelimeler: Kaşıntı, lichen simplex chronicus, paraneoplastik, karsinom

ABSTRACT

Pruritus, defined as an unpleasant sensation that compels scratching, is a common occurrence in dermatological disorders. Chronic pruritus is defined as itching that persists for a period exceeding six weeks. Lichen simplex chronicus (LSC) is a chronic dermatological condition that presents with dry, scaly, and thickened skin lesions, which typically arise from habitual scratching. Additionally, paraneoplastic pruritus may serve as an early indicator of the presence of solid tumours. This case report outlines the diagnostic and therapeutic process of a 73-year-old male diagnosed with lichen simplex chronicus (LSC), confirmed by skin biopsy. Subsequent malignancy screening revealed the presence of solid nodules in the lungs and multiple metastatic masses in the liver. Biopsies of the lung nodule and liver mass demonstrated positivity for TTF-1 and synaptophysin, leading to a diagnosis of mixed component lung adenocarcinoma and small cell lung cancer. In order to ascertain the underlying cause of the patient's chronic itching, a comprehensive investigation was conducted, which considered a range of potential factors, including haematological diseases, endocrine disorders, liver diseases, infections, drug-related factors, and neurological and psychiatric causes. Despite a comprehensive evaluation, the precise etiology of the chronic itching remained elusive. The initiation of carboplatin and etoposide therapy for lung cancer resulted in a significant reduction in the patient's itching, which may suggest a possible link between chronic itching and malignancy. Unfortunately, the patient succumbed to hypoxia, pneumonia, and multiple organ failure two months post-diagnosis. This case serves to illustrate the potential of chronic pruritus as a symptom of cancer. While paraneoplastic pruritus is often associated with haematological malignancies, this report highlights that it can also occur with solid tumours. It is important for clinicians to be aware of this potential association, as it allows for timely diagnosis and treatment.

Keywords: Pruritus, lichen simplex chronicus, paraneoplastic, carcinoma

Geliş Tarihi/Received: 18 Şubat/February 2024 **Kabul Tarihi/Accepted:** 10 Haziran/June 2024 **Yayın Tarihi/Published Online:** 28Haziran/June 2024

Sorumlu Yazar/Corresponding Author: Oguzhan Yildiz, Necmettin Erbakan University, School of Medicine, Department of Medical Oncology, Konya, Türkiye
e-mail: dr.oguzhan@outlook.com

Atıf yapmak için/ Cite this article as: Yildiz O, Karakurt Eryilmaz M, Gurbuz AF, Kilinc F. A Case of Lung Cancer Presenting with Paraneoplastic Pruritus. Selcuk Med J 2024;40(2): 98-101

Disclosure: *Author has not a financial interest in any of the products, devices, or drugs mentioned in this article. The research was not sponsored by an outside organization. Author has agreed to allow full access to the primary data and to allow the journal to review the data if requested.*

INTRODUCTION

Pruritus, defined as an uncomfortable sensation, is one of the most common clinical findings known for centuries in dermatology (1). Pruritus can be acute or chronic depending on the duration of clinical findings; Chronic pruritus is defined as pruritus lasting longer than 6 weeks (2). Causes of systemic chronic pruritus include hematologic diseases, malignancies, endocrine diseases, liver diseases, postmenopausal pruritus, HIV infection, pregnancy, senile pruritus, brachioradial pruritus, notalgia paresthetica, neuropathic pruritus, and drugs (3). Less than 10% of patients with chronic pruritus can have a malignant disease (4). Lichen simplex chronicus (LSC) is defined as patches of dry, scaly, and thick skin that appear after chronic pruritus. It is typically the result of habitual scratching or rubbing of a particular area of the skin (5). We diagnosed lung small cell carcinoma and lung adenocarcinoma in a patient who presented with LSC after chronic pruritus. In this report, we present this case of paraneoplastic pruritus due to malignancy.

CASE

A 73-year-old male patient was admitted to the hospital in September 2022 with complaints of pruritus all over his body. He had no comorbidities. The patient reported experiencing pruritus for 8-10 months. An investigation into the etiology of chronic pruritus was initiated. Physical examination revealed dry, scaly, and thickened skin patches (Figure 1). A skin biopsy was performed, resulting in a diagnosis of lichen simplex chronicus (LSC) (Figure 2A). These lesions are associated with chronic pruritus. Following pathology results, the investigation into the etiology of chronic pruritus continued. Due to the onset of chronic pruritus at an advanced age, malignancy screening was conducted. Abdominal computed tomography (CT) revealed multiple hypodense lesions, with the largest lesion measuring 3 cm in the liver. Thoracic CT identified a 17 mm solid nodule with irregular borders in the anterior aspect of the right lung upper lobe and an 8 mm nodule in the anteromedial aspect of the right lung upper lobe. Biopsies were performed from both liver and lung masses, and pathological examination of both biopsy materials revealed the presence of areas stained with TTF-1 and synaptophysin, suggesting a dual tumor. Lung adenocarcinoma and small cell lung cancer metastases were considered (Figures 2B,C,D,E,F). The patient underwent screening for hematological diseases, endocrine diseases, liver disease, infection, and drug-related causes of chronic pruritus. No other underlying cause for the chronic pruritus was identified. Chronic pruritus was attributed to malignancy. Treatment with carboplatin and etoposide was initiated for lung cancer. Additionally, the patient received topical antihistamines, topical anesthetics, topical steroids, and oral antihistamines for pruritus. Following chemotherapy, the patient's pruritus and skin lesions improved. However, two months after the lung cancer diagnosis, the patient passed away due to hypoxia, pneumonia, and multiorgan failure.

Figure 1. Dry, scaly, and thickened skin patches of the patient

DISCUSSION

Paraneoplastic syndromes are clinical conditions that arise as a result of the influence of cytokines, antibodies, or the immune system's reaction against the tumor, irrespective of the tumor's local or metastatic effects. There is a correlation between the stage of the paraneoplastic syndrome and the size of the tumor. Additionally, it can manifest in early-stage disease (6). Small cell lung cancer (SCLC) is the most common cause of paraneoplastic syndromes (7). Inappropriate Antidiuretic Hormone Syndrome (SIADH) is a common finding in 10% of cases of SCLC (8). Cushing syndrome, which develops due to ectopic corticotropin release in SCLC, is also frequently observed (9). Hypercalcemia in lung cancer may be caused by the secretion of parathyroid hormone-related protein (PTHrP) from the tumor or, less commonly, by bone metastases or primary hyperparathyroidism (10).

Pruritus that lasts for 6 weeks or longer is referred to as chronic pruritus (11). Lichen simplex chronicus (LSC) is defined as patches of dry, scaly, and thickened skin that develop following chronic pruritus. It may manifest as paraneoplastic pruritus. Hematological malignancies are more commonly associated with pruritus than solid tumors (3). The most common hematologic malignancies associated with pruritus include Hodgkin lymphoma, non-Hodgkin lymphoma, polycythemia vera, leukemias, mycosis fungoides, plasma cell dyscrasias, and cutaneous lymphoma (12). In some studies, pruritus was detected in 48-70% of polycythemia vera patients, approximately 30% in Hodgkin's disease, and

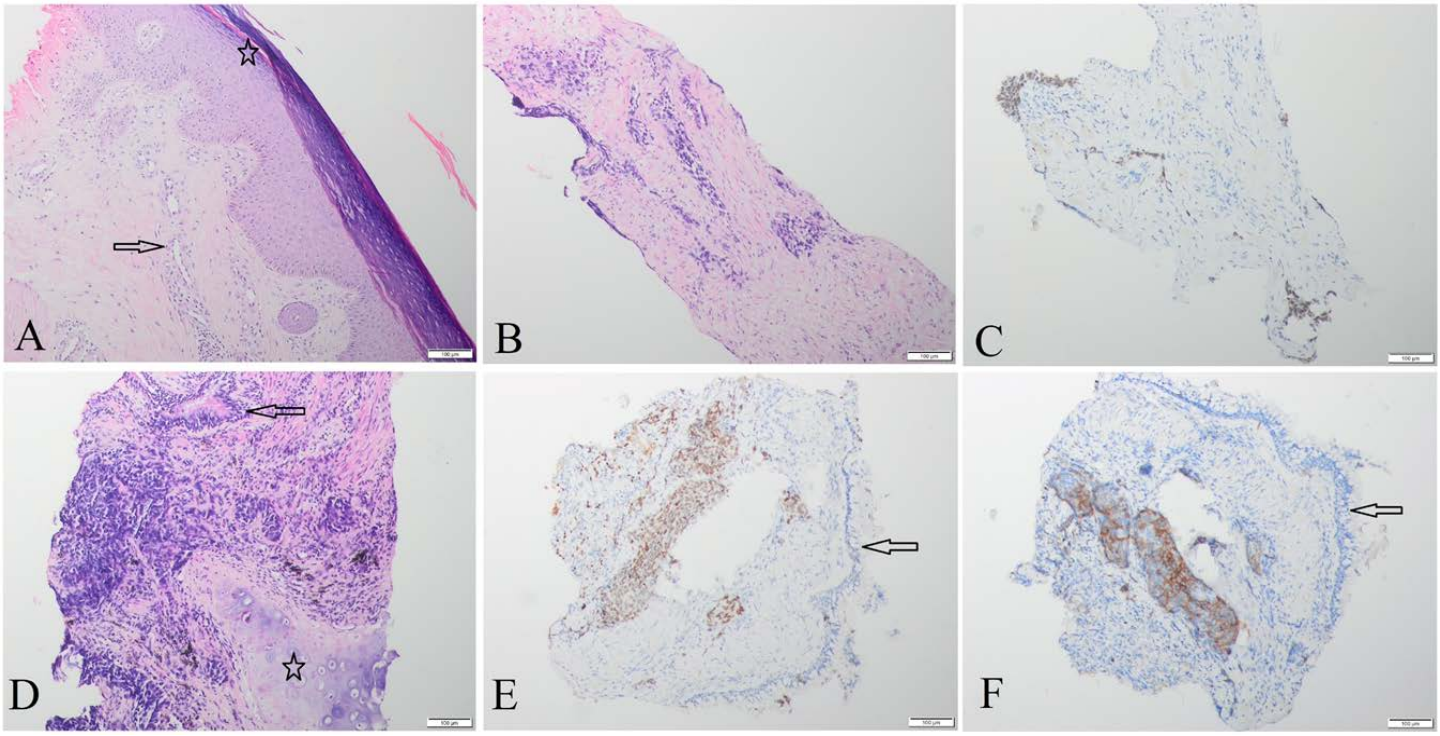

Figure 2. A) In the skin tissue, hypergranulosis (asterisk), irregular acanthosis in the epidermis, hyperkeratosis on the surface, perivascular lymphocytes and rare eosinophils (arrow) in the dermis are observed. B) In the biopsy sample taken from the liver, infiltrative tumor cells forming groups within the fibrotic stroma are observed. C) Nuclear TTF-1 positivity is observed in tumor cells observed in the liver. D) In the lung biopsy sample, tumoral infiltration is observed within the fibroinflammatory stroma (chondroid tissue of the bronchial wall is marked with an asterisk). E) Nuclear TTF-1 positivity is observed in tumor cells observed in the lung. F) Cytoplasmic Synaptophysin positivity is observed in some of the tumor cells (Arrows in D, E and F point to the bronchial surface epithelium) (A, B, D: Hematoxylin&Eosin, 100x magnification; C, E: Immunohistochemical TTF-1, 100x magnification; F: Immunohistochemical Synaptophysin, 100x magnification).

approximately 3% in other hematological malignancies. Chronic pruritus has also been reported in breast cancer, non-melanoma skin cancer, biliary tract cancer, and gastric carcinoid tumors. (13,14). Treatment of LSC aims to reduce pruritus and minimize existing lesions. Rubbing and scratching increase LSC. Pruritus and inflammation can be treated with a lotion or steroid cream applied to the affected area of the skin (15). Jaxon et al. investigated pruritus in more than 25,000 patients with solid cancer during follow-up and treatment. A total of 203 patients were included in the study. The most common tumor associated with pruritus was breast cancer at 36.5%, followed by lung cancer at 23.2%. In this study, pruritus was evaluated during the cancer treatment process, and no data were provided on the rate of pruritus etiology at the time of diagnosis. Our patient had chronic pruritus and had no additional disease other than the underlying cancer, and her pruritus was relieved after chemotherapy. In this study, pruritus was assessed during the treatment process, but patients diagnosed due to pruritus were not reported (16). In paraneoplastic pruritus, pruritus decreases or disappears with the treatment of the underlying malignancy. If the malignant disease recurs, the pruritus may also recur (4).

In conclusion, chronic pruritus can be a symptom of paraneoplastic syndrome. It is most commonly associated with hematological malignancies. However, it should be kept in mind that, although rare, it may be due to underlying solid malignancies. Therefore, patients with chronic pruritus should be screened for malignancy.

Conflict of interest: *Author declares that there is no conflict ofinterest between the authors of the article.*

Financial conflict of interest: *Author declares that he did not receive any financial support in this study.*

Address correspondence to: *Oguzhan Yildiz, Necmettin Erbakan University, School of Medicine, Department of Medical Oncology, Konya, Türkiye*

e-mail: *dr.oguzhan@outlook.com*

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