Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Medicine

A Case Report of Synchronous Lung Adenocarcinoma and Systemic Mastocytosis

Hüseyin Döngelli[1*], Ahmet Uğur Akçaoğlu[1], Mustafa Oktay Tarhan[1], İnci Alacacıoğlu[2]

[1]Department of Internal Medicine, Dokuz Eylul University Hospital, Izmir, Turkiye
[2]Department of Hematology, Dokuz Eylul University Hospital, Izmir, Turkiye

DOI: https://doi.org/10.36347/sjmcr.2024.v12i08.023 | **Received:** 14.07.2024 | **Accepted:** 19.08.2024 | **Published:** 21.08.2024

***Corresponding author:** Hüseyin Döngelli
Department of Internal Medicine, Dokuz Eylul University Hospital, Izmir, Turkiye

Abstract **Case Report**

Systemic mastocytosis(SM) is an extremely rare disease and is characterized by clonal proliferation of mast cells in any part of the body. SM patients are prone to developing cancer. Although the relationship between lung adenocarcinoma and SM is unclear, they share similar mutations. A female patient in her 40s presented with complaints of shoulder pain and unexpected weight. Later, the patient was diagnosed with lung adenocarcinoma. Additionally, systemic mastocytosis was detected while investigating her B symptoms and anemia. Induction chemotherapy with carboplatin and paclitaxel was decided as initial treatment. She did not respond to 3 cycles of this chemotherapy regimen. Radiotherapy with etoposide and cisplatin was applied as second-line treatment. Although the size of the lung adenocarcinoma was stable, her anemia, shoulder pain, B symptoms, and cachexia improved after second-line treatment. We present a case of synchronous lung adenocarcinoma and systemic mastocytosis presenting with B symptoms and shoulder pain.

Keywords: Anemia, Lung Carcinoma, Systemic Mastocytosis, Synchronous.

INTRODUCTION

Lung cancer is the most common cause of cancer-related deaths in the world [1]. Although there are no previously published cases of synchronous lung cancer and systemic mastocytosis, hematological malignancies and lung cancer may occur together [2].

Mastocytosis is the clonal overgrowth of mast cells activated by IgE and non-IgE mechanisms, originating mostly from the myeloid lineage found in connective tissue. Generally, the local cutaneous form is more common. There is also systemic mastocytosis involving extracutaneous tissues. Symptoms of systemic mastocytosis are rash, itching, diarrhea, and anaphylaxis caused by cytokine release due to mast cell activation. In a study conducted in Germany, the incidence and prevalence of patients with systemic mastocytosis were found to be 0.9 and 7 per 1 million people [4]. Patients with systemic mastocytosis have a tendency to develop certain cancers such as malignant melanoma.

Although the exact mechanisms in the formation of both diseases are not fully known, they share similar mutations in the tyrosine kinase pathway. KIT D816V mutation is one of the best known mutations in systemic mastocytosis. On the other hand, protein tyrosine kinase mutations have also been detected in lung carcinomas [3].

In this case report, we aimed to emphasize the possible relationship between concurrent systemic mastocytosis and lung adenocarcinoma.

CASE REPORT

A female patient in her 40s was admitted to our clinic with complaints of left shoulder pain, night sweats, fever, fatigue, occasional secretory diarrhea, itching and unexpected weight loss that had been going on for 6 months. She has no known disease or allergies and has been smoking a pack of cigarettes a day for 20 years. In addition to cesarean section, she has a history of lipoma excision from the left axilla and gluteal region. Regarding her family history, her father has liver cirrhosis related to the hepatitis b virus, and her mother was diagnosed with breast cancer.

In her first examination, a hyperpigmented area, cachexia and clubbing were detected on the left shoulder. Additionally, lung percussion revealed dullness in the upper region of the left lung. Routine biochemistry test

and complete blood count resulted as follows: neutrophilic leukocytosis, microcytic anemia, thrombocytosis, elevated acute phase reactants, and decreased albumin. Nutritional parameters such as serum b12, folic acid and ferritin levels related to anemia were in the normal range. Multiple blood samples were taken for culture, and none of them grew pathogens. During inpatient follow-up, a 2g/dL decrease in hemoglobin level was observed in a 24-hour period, and no signs of hemolysis or bleeding, including peripheral blood smear, were found in the examination; Therefore, a bone marrow biopsy was taken and pathological examination revealed systemic mastocytosis with dense mast cell aggregates stained positively with tryptase. In immunohistological examination, mast cells were stained with CD117, and genetic analysis showed KIT D816V mutation as the driver mutation. Additionally, the serum tryptase level was above 20 ng/mL. The patient's B symptoms, itching, diarrhea and abnormal findings in the complete blood count were thought to be due to systemic mastocytosis.

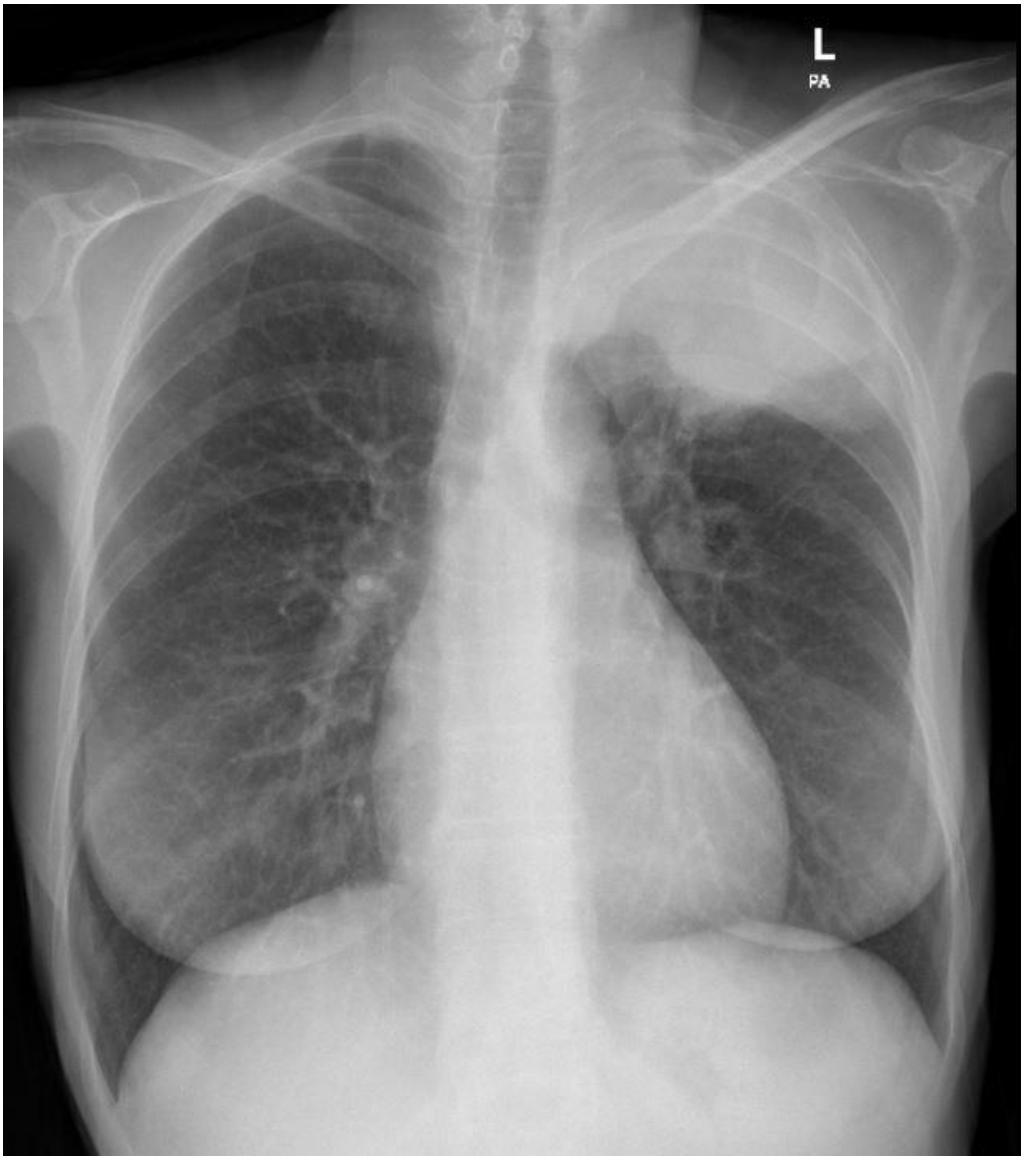

Figure 1: Chest X-Ray revealed opacity in the left upper lung zone

A large mass was detected in the upper region of the left lung on chest radiography (Figure 1). As a result, thoracoabdominal computed tomography (CT) was requested and a 13 cm mass was observed in the apex of the left lung, which was not accompanied by lymph node involvement; It was observed that the mass also invaded the thorax wall (Figure 2). Bronchoscopy was requested to take a biopsy from the tumor, but no results were obtained; therefore, CT-guided percutaneous transthoracic needle biopsy was performed. Pathological examination of the biopsy material revealed lung adenocarcinoma. In the immunohistological examination, driver mutations such as ALK, EGFR, KIT D816V and ROS1 were not found.

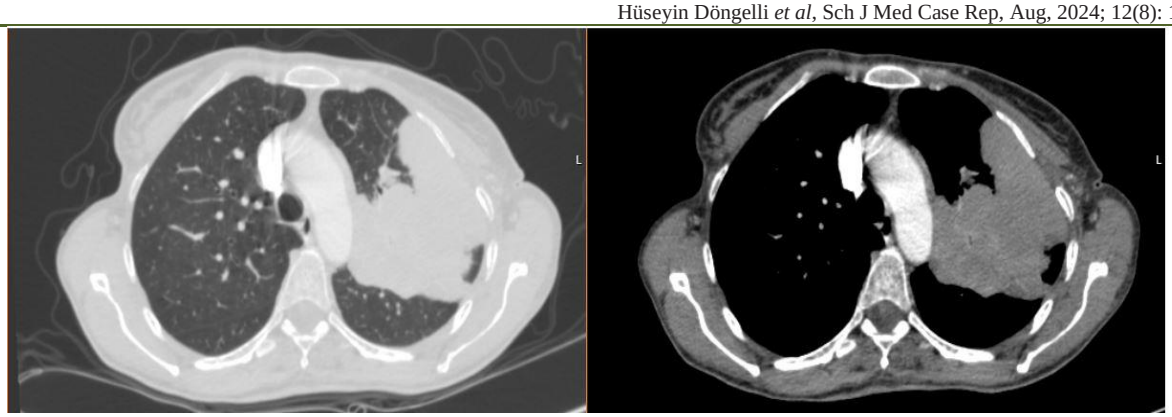

Figure 2: Thorax CT revealed 13 cm size lung mass with thoracic wall invasion

FDG Positron Emission Tomography (PET) was requested to evaluate the spread of the disease and it was revealed that the locally invasive disease was Stage 3A (T4N0M0) (Figure 3). This PET/CT also demonstrated increased diffuse FDG uptake in all bones, consistent with systemic mastocytosis. In a multidisciplinary meeting, induction chemotherapy with carboplatin and paclitaxel was decided as initial treatment. She did not respond to 3 cycles of this chemotherapy regimen and tumor size remained the same without progression. Subsequently, treatment regimen of etoposide plus cisplatin combined with radiotherapy was decided as the second line of treatment; unfortunately, the tumor size still remained after 3 cycles of this second line treatment. Although the size of the lung adenocarcinoma was stable, her anemia, shoulder pain, b symptoms, and cachexia improved after the second line of treatment. Moreover, a second FDG-PET/CT scan was ordered to evaluate the lung carcinoma which revealed metabolic response to the treatment and interestingly diffuse increased FDG uptake in skeletal tissue(bone and bone marrow) in the first PET/CT scan was absent in the second scan correlating with her clinical response (Figure 3).

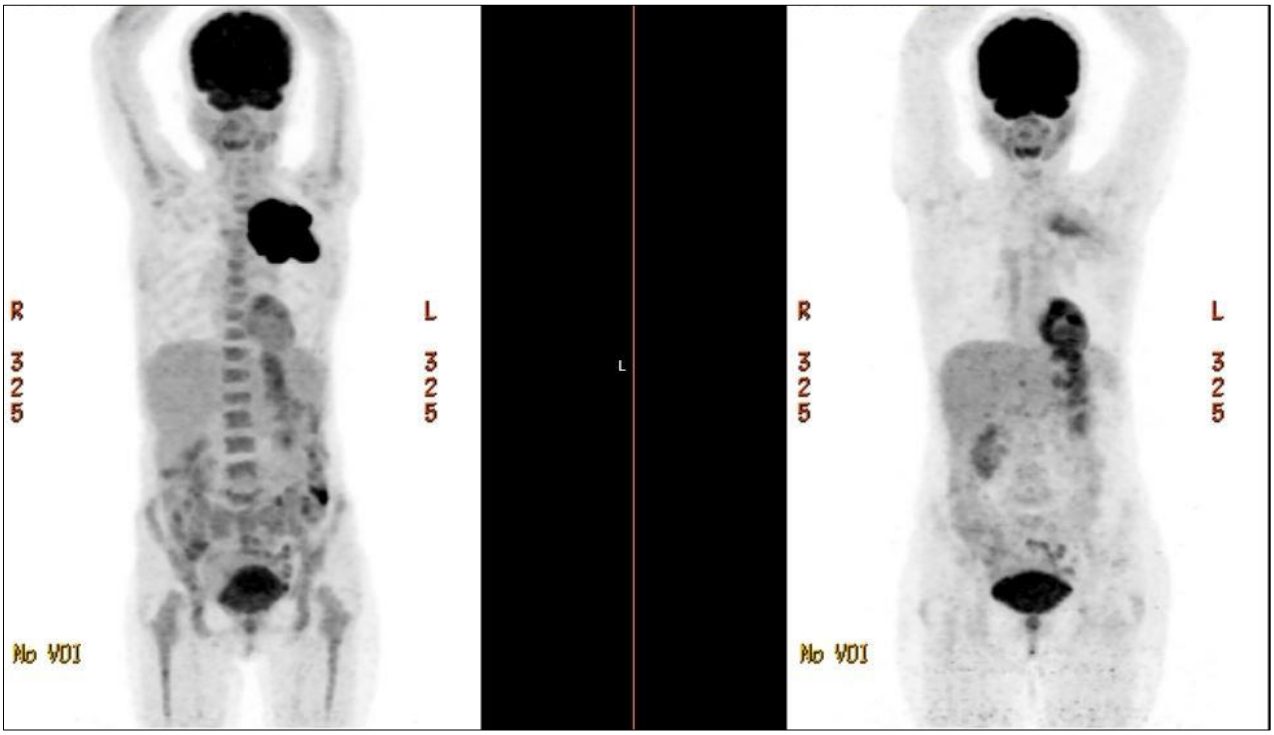

Figure 3: FDG PET/CT scans(the first scan on left and second scan on right with 6 months interval) are showing metabolic response of lung carcinoma and diminished diffuse increased FDG uptake in bones

DISCUSSION

Non-small cell lung carcinoma accounts for approximately 80% of all lung cancers, half of which are adenocarcinomas. The most frequent and important contributing factor is smoking for lung cancer . Our patient only had one risk factor which was smoking and interestingly tumor size at her first evaluation was 12cm without lymph node involvement or metastasis. The most common signs and symptoms at initial presentation are chronic cough(%65), hemoptysis(%33), chest pain(%17,9), dyspnea(%17), lymphadenomegaly(%9,8),

weight loss(%8,3),metastatic pain(%5,9), fatigue(%4,8), fever(%4,3), headache(%1,9) and hoarseness [5]. On the other hand our patient presented with shoulder pain, dullness on the percussion of the lung and constitutional symptoms without pulmonary symptoms. Although Stage III non-small cell lung cancer accounts for approximately 20% of cases at the time of initial diagnosis, the percentage of Stage 3A patients, as in our patient, is quite low [1].

SM has subtypes as follows: indolent SM , aggressive SM , SM with associated clonal hematologic non-MC lineage disease, and mast cell leukemia. Patients with SM have increased risk for some conditions: Venous thromboembolism, stroke, acute coronary syndrome, osteoporosis, fracture, anaphylaxis, urticaria and cancer. The HRs of specific cancer subtypes varied[6,12,13]. There are some case reports mentioning SM patients with solid cancer. Additionally, one study found that the hazard ratio (HR) for all solid cancers was 2.6 (95% CI 1.9–3.6) and most solid cancers were malignant melanoma; however, a non-significant increase in lung cancer risk was detected (HR 1.2, 95% CI 0.5-2.8) [6].

Mutations in the tyrosine kinase gene may be seen in non-small cell lung cancer and systemic mastocytosis; Additionally, tyrosine kinase inhibitors are used in the treatment of both diseases [7]. In this case, the KIT D816V mutation was detected in mast cells but not lung carcinoma cells.

Despite the stable size of her lung carcinoma, the improvement of her anemia and constitutional symptoms following second-line treatment with etoposide plus cisplatin combined with radiotherapy was unexpected. Widespread and homogeneous increased FDG uptake can be observed in hematopoietic tissues such as lymph nodes, bone marrow, spleen and liver in SM patients [8]. In our case, diffuse FDG uptake in the skeletal system on the first PET/CT scan disappeared in the second scan with clinical response after the treatment.

Bonekohn *et al.*, reported that a 71-year-old female patient with SM developed squamous lung carcinoma with the KIT D816V mutation during follow-up [9]. Another case report describes a 58-year-old woman who developed SM and was treated with a KIT inhibitor for metastatic non-small cell lung cancer. The anaphylaxis episode and SM were controlled with this KIT inhibitor treatment [10]. Moreover, no article mentions the simultaneous occurrence of both diseases [9-13]. We present the first case of synchronous lung adenocarcinoma and systemic mastocytosis in the literature.

CONCLUSION

Both diseases share similar genetic abnormalities and there is no established link between them. More research is needed to clarify this. The clinical presentation of our patient is uncommon, and this is the first published case of synchronous systemic mastocytosis and lung adenocarcinoma.

DECLARATIONS

Author Contribution

All authors contributed equally to the concept and design of the study, data collection, analysis and interpretation of results, and preparation of the manuscript.

Acknowledgments: None.

Ethics Approval: Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent: Written informed consent was obtained from the patient for their anonymized information to be published in this article.

Declaration of Conflicting İnterests

The authors declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

Funding: The author(s) received no financial support for the research, authorship, and/or publication of this article.

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