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Case Report

Metastatic Squamous Cell Carcinoma of Lung: An Atypical Presentation in a 65 Years Old Man

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ABSTRACT

Lung cancer stands as one of the most prevalent and fatal malignancies worldwide. It can originate primarily in the lung or manifest as metastases from various organs within the body. Squamous cell carcinoma (SCC) metastases to the lungs account for the majority, constituting 66% of all distant metastases. Distinguishing primary lung cancers from metastatic lung tumors often relies on immuno-histochemical markers such as Napsin A and TTF-1. In this case study, we present the medical history of a 65-year-old male with a history of smoking and occupation as a farmer. He experienced a persistent cough for one year and had been grappling with breathing difficulties for the past three days. Notably, the patient had a previous diagnosis of posterior pharyngeal wall SCC and had undergone chemo-radiotherapy treatment in 2021. Regular follow-up assessments were conducted through annual PET-CT scans, with the latest revealing nodular opacities and cavitations in the left lower lobe of the lung. This article provides a comprehensive account of the histopathological findings obtained from a tiny CT-guided lung biopsy extracted from the left lower lobe mass, alongside its radiological correlation.

Keywords: Squamous cell carcinoma, Immuno-histochemistry, Napsin A, TTF-1

INTRODUCTION

Lung cancer ranks as the second most frequently diagnosed malignancy globally, claiming the foremost position as the leading cause of death. Metastatic malignant neoplasms are typically referred to as secondary lung tumors, with the lung serving as a prevalent site for such metastases. On radiological examinations, secondary tumors commonly manifest as multiple nodules accompanied by malignant hemorrhagic pleural effusion.[1] Patients with lung metastases often present with a range of symptoms, including hemoptysis, coughing, breathlessness, chest pain, and persistent infections.[2]

CASE HISTORY

A 65-year-old male, a long-term smoker with a farming occupation, presented with a chief complaint of a persistent cough lasting one year and recent onset of breathing difficulties over the past three days. The cough was productive, non-foul smelling, and characterized by white mucus. Notably, the cough worsened in the supine position but improved when sitting, with increased coughing episodes occurring during the night.

Upon admission, the patient's vital signs were stable. He had a history of smoking for 35 years and had consumed alcohol and chewed tobacco for the past

decade, but he had successfully quit both habits two years prior after counseling. His diet was varied, and he had no history of fever, breathlessness, hemoptysis, or allergies. Systemic examination of the patient revealed no abnormal findings, and routine laboratory investigations showed no significant changes.

Of note, the patient had a previous diagnosis of posterior pharyngeal wall squamous cell carcinoma (SCC) and had received chemo-radiotherapy in 2021. He had been undergoing yearly follow-up assessments through PET-CT scans, with the latest scan indicating the presence of a few nodular opacities with cavitation in the left lower lobe of the lung, with the largest cavity measuring 2.1x2.0 cm and showing increased radiotracer uptake. An X-ray revealed a well-defined soft tissue lesion with an internal cavity in the left mid zone (Figure 1).

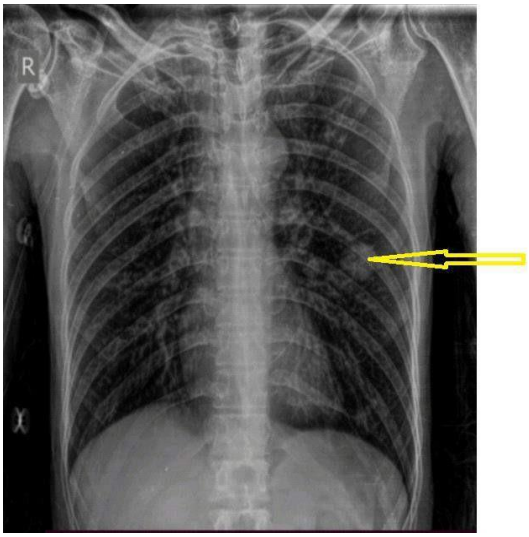

Figure 1: Well defined soft tissue opacity lesion with internal cavity in left mid zone on X-ray chest -PA view

A CT scan further demonstrated a well-defined soft tissue density lesion with a speculated margin and internal cavitation in the superior segment of the left lower lobe, along with multiple nodular opacities in the right middle lobe (Figures 2 and 3). These radiological findings strongly suggested the presence of metastatic bilateral lung lesions, necessitating a biopsy for confirmation.

Figure 2: Well defined soft tissue density lesion with speculated margin and internal cavitation involving superior segment of left lower lobe

Figure 3: Multiple nodular opacity seen in right middle lobe

Cytological examination of the patient's sputum revealed mature squamous epithelial cells, numerous anucleate squamous cells (Figure 4), and some squamous cells displaying nuclear atypia. The background exhibited a substantial presence of inflammatory cells, primarily neutrophils, along with bacterial colonies (Figure 5). The diagnosis rendered was inflammatory sputum, and a recommendation was made for a lung biopsy.

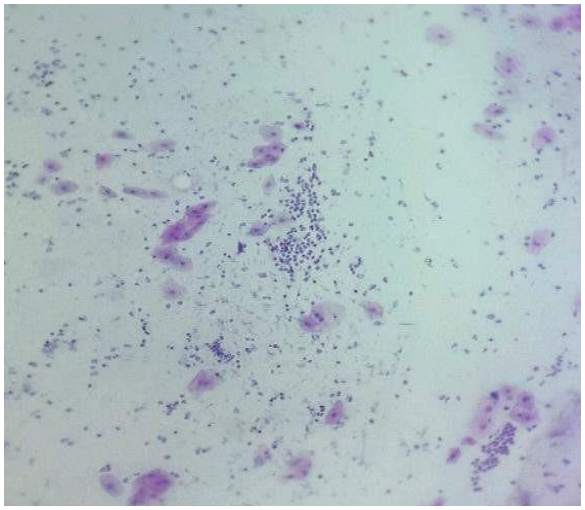

Figure 4: Sputum cytological smear showing squamous cells with inflammatory cells predominantly neutrophils (PAP, X100).

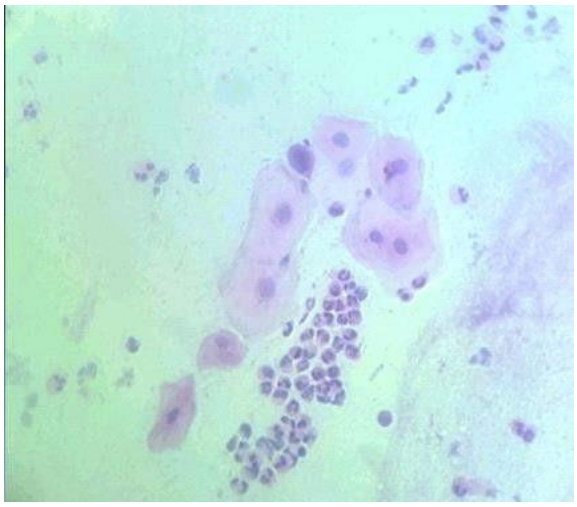

Figure 5: Sputum cytological smear showing clusters of atypical squamous cells with nuclear atypia surrounded by neutrophils (PAP, X400)

Subsequently, a CT-guided biopsy was performed, and the biopsy specimen was sent for histopathological examination. Upon gross examination, we received several small tissue fragments measuring 0.3x0.1x0.1 cm, which appeared gray-white in color. All the tissue was processed in a single block and subjected to formalin fixation and paraffin embedding.

Examination of formalin-fixed paraffin-embedded (FFPE) sections revealed malignant squamous cells arranged in nests, sheets, and occasionally as individual scattered cells. These individual squamous cells exhibited a round to polygonal shape, mild nuclear pleomorphism with a high N:C ratio, vesicular to hyperchromatic nuclei, and some displayed prominent nucleoli. Additionally, moderate eosinophilic cytoplasm was observed, along with areas showing keratin pearl formation. These features collectively supported a diagnosis of Squamous Cell Carcinoma (SCC) of the lung (Figure 6a&b). Given the patient's known history of posterior pharyngeal wall carcinoma and the detection of SCC in the lung, the final diagnosis was established as Metastatic Squamous Cell Carcinoma.

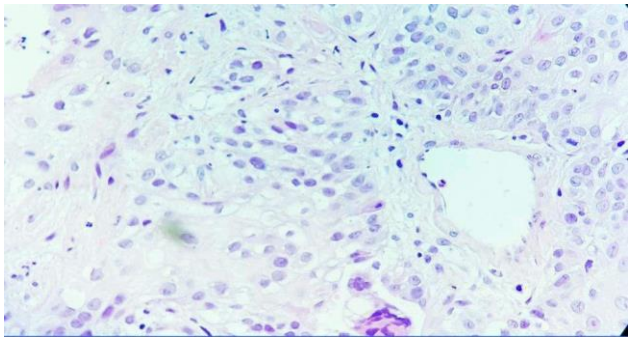

Figure 6a: Microphotograph showing malignant squamous cells arranged in nests, sheets with high N:C ratio (H&E, X400)

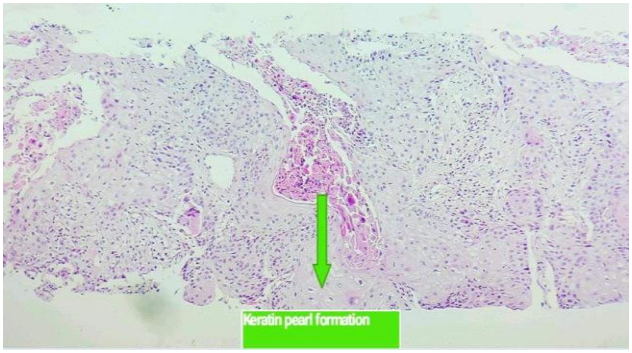

Figure 6b: Microphotograph showing sheets of malignant squamous cells with keratin pearl formation (H&E, X100)

DISCUSSION

Histopathologically, lung cancers are categorized into two primary types: 1) Small cell lung carcinoma and 2) Non-small cell lung carcinoma (including SCC, Adenocarcinoma, and Large cell carcinoma).[2] Radiological imaging stands as the frontline investigational tool crucial for managing lung cancer patients.[3]

In the general population, SCC is the second most common carcinoma of the lung, following adenocarcinoma. SCC comprises approximately 30-35% of all lung cancers and is predominantly associated with heavy smoking. Notably, SCCs are more frequently encountered in male smokers, while adenocarcinoma is more prevalent among female smokers.[4] SCC tumors tend to manifest in the central regions of the lung or in the main airways, such as the left or right bronchi.[5]

A diagnosis of SCC is established when a minimum of 10% of the tumor bulk in resected samples displays keratinization or intracellular bridges. Furthermore, SCC can be differentiated as well, moderately, or poorly differentiated based on how closely the tumor resembles normal histology. Squamous IHC biomarkers, such as p63 and p40 proteins, are often utilized for confirmation.[5]

The World Health Organization (WHO) revised its classification in 2015 to recognize three SCC variants based on histological examination:[5]

- Keratinizing
- Non-keratinizing
- Basaloid

The detection of metastasis signifies rapid disease progression and an advanced stage of lung cancer.[6] In our case, the patient had primary posterior pharyngeal wall SCC with subsequent lung metastases. The lung is the most common site for distant metastases, and it is also the most likely site for a metachronous primary tumor to arise outside of the head and neck region in oropharyngeal squamous cell carcinoma (OPSCC).[7]

Our patient had a previous history of posterior pharyngeal wall squamous cell carcinoma (SCC) and had received treatment, with yearly follow-up assessments conducted through PET-CT scans. The latest radiological scans indicated the presence of a few nodular metastatic opacities, which were subsequently confirmed by a CT-guided lung biopsy as metastatic SCC. This presentation was atypical in our case.

In patients with a history of OPSCC, distinguishing between distant recurrence and metachronous lung primary has important implications for accurate registry data, prognostic assessments, and potential alterations in therapeutic options, including eligibility for oncology studies. Initial diagnostic examination is typically performed using standard histologic techniques. While OPSCC is traditionally characterized as non-keratinizing, these morphological features can overlap with poorly differentiated primary lung SCC and are insufficient for clear differentiation.[7]

Metastatic lung tumors are typically not curable, but palliative treatments aim to prevent further spread. The presence of distant metastases significantly impacts survival. Factors such as the primary tumor's location, initial T and N stages, and the presence or absence of regional control above the clavicle all influence the likelihood of distant metastases.[3]

Tumors in advanced stages in the hypopharynx, oropharynx, and oral cavity are associated with the highest incidence of distant metastases. The majority of distant metastases in SCC (66%) occur in the lungs. Distinguishing pulmonary metastases from a new primary tumor can be challenging, especially if a solitary lesion is present.[3] In our case, collective radiological assessments (CT lung, PET scan, and X-ray chest) revealed bilateral lung metastases. However, only the left lung lesion was biopsied, leading to a diagnosis of SCC. The right lung lesion remained unbiopsied.

Napsin A and Thyroid transcription factor 1 (TTF1) are valuable immunohistochemical markers that are positive in primary lung cancer but negative in metastatic lung tumors. Both IHC markers tested negative in our case.

CONCLUSION

In view of the patient's history of posterior pharyngeal wall squamous cell carcinoma, the collective findings point towards a diagnosis of metastatic and metachronous squamous cell carcinoma in the left lung mass. Immunohistochemistry, in conjunction with PET/CT scans and clinical correlation played a pivotal role, as histomorphology alone cannot reliably differentiate between primary lung SCC and metastatic SCC in the lung.

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