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Case Report

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Fatal Outcome in Lung Cancer with Rare Nasal Metastatic Spread: A Clinical Perspective

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Introduction

Cutaneous metastases to the nose are a rare manifestation of metastatic squamous cell carcinoma (SCC) of the lung. These metastases can present as either solitary or multiple lesions on the skin, and they may appear either fixed or mobile. Reports of cutaneous metastases from lung cancer specifically affecting the nose occur in 1-12% of cases [1]. In some instances, these cutaneous metastases can be the first indication of an underlying solid epithelial malignancy, often associated with a poor prognosis [2]. When these metastases occur on the nasal tip, they are sometimes referred to as "clown nose" due to their resemblance to a red, fake nose.

In this discussion, we present a rare case of a 46-year-old man initially diagnosed with squamous cell carcinoma of the nasal tip. He had no prior symptoms suggesting any systemic involvement. However, after a thorough evaluation, he was found to have primary lung cancer with cutaneous and liver metastases. The patient unfortunately had a fatal outcome, highlighting the fact that in some cases, metastases may be the only presenting symptom, and the patient may have a more sinister underlying pathology.

Case Report

A 46-year-old man, a chronic cigarette smoker for last 10 years, transferred to our tertiary care centre with a diagnosis of squamous cell carcinoma of the tip of the nose. The patient complained of an ulceroproliferative growth on the tip of his nose (Figure 1) that had been present for one and a half months. Initially resembling a small furuncle, the growth gradually increased to its current size of 2 cm x 1.5 cm. It is firm, non-tender, bleeds upon touch and extends from the tip of the nose to the left nasal vestibule.

Figure 1: Ulceroproliferative Growth Over Tip of Nose at the Initial Presentation

Diagnostic nasal endoscopy revealed that the ulceroproliferative growth extended from the left nasal vestibule to the cartilaginous portion of the left nasal septum, while the bony septum, lateral wall, and floor of the left nasal cavity remained uninvolved. The right nasal cavity appeared normal.

Upon arrival at our tertiary care centre, the patient had a stroke, which on evaluation, revealed a right middle cerebral artery infarct, prompting thrombolysis.

Later that same day, the patient had one episode of hematemesis and began experiencing pain in the right hypochondrium. An abdominal ultrasound indicated the presence of a subcapsular bleed in the Liver with evidence of liver metastases and minimal ascites.

Contrast-enhanced computed tomography of the abdomen and pelvis revealed multiple hypoenhancing lesions scattered throughout both lobes of the liver, with the largest lesion measuring 3 x 2.3 cm (AP x TR) located in segment VII. There was also a subcapsular hyperdense collection adjacent to segments V and VI of the liver, suggesting a possible focal breach in the inferior aspect, likely indicating hemoperitoneum (Figure 2).

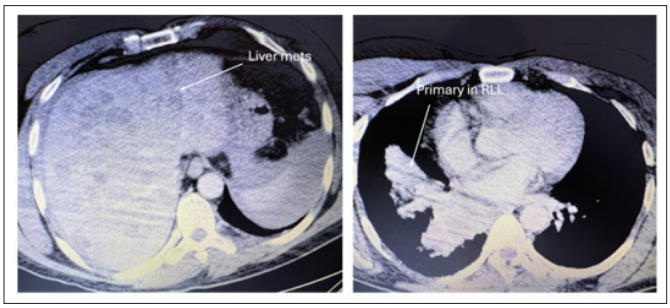

Figure 2: 2a. CECT Abdomen, 2b. CECT Chest

2a: Axial section of CECT abdomen showing multiple hypoenhancing lesions scattered throughout both lobes of the liver

2b: Axial section of CECT Lung showing lesion in the posterior basal segment of the right lower lobe (RLL) in a perihilar location

Contrast-enhanced computed tomography of the lung indicated a heterogeneously enhancing, ill-defined lesion with spiculated margins and surrounding architectural distortion. This lesion measured 4.4 x 6.1 x 3.6 cm (AP x TR x CC) in the posterior basal segment of the right lower lobe (RLL) in a perihilar location. It encased the right interlobar artery and its distal branches without significant luminal narrowing, as well as the right inferior pulmonary vein, also without significant luminal attenuation. The lesion causes the cutoff of the bronchus intermedius, leading to associated consolidation and collapse of the RLL.

Multiple discrete lymph nodes were observed in prevascular, upper/lower paratracheal, retrotracheal, subcarinal, paraesophageal, subaortic, para-aortic, and hilar regions, likely indicative of metastatic disease.

The patient underwent diagnostic/ exploratory laparotomy and approximately 1.5 litres of blood clots were evacuated. The liver was seen studded with multiple nodular lesions, which were likely metastatic deposits. (Figure 3).

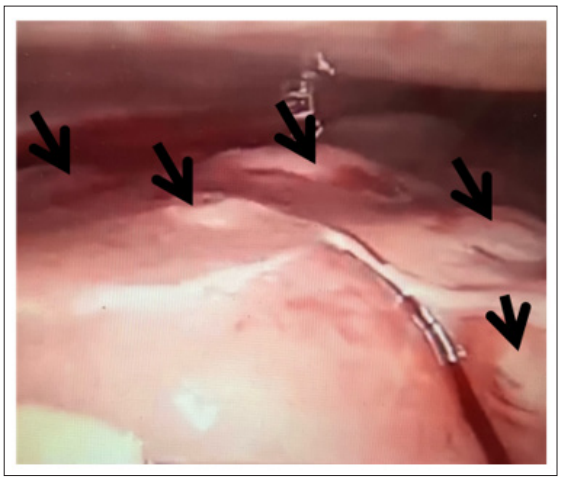

Figure 3: Liver Mets Seen during Diagnostic Laparotomy

The patient underwent fibre-optic bronchoscopy and transbronchial biopsy. A review of the biopsy samples from the tip of the nose indicated squamous cell carcinoma (Figure 4). The transbronchial biopsy report also suggested squamous cell carcinoma (Figure 5). Notably, there was no evidence of overlying dysplasia in the biopsy from the nasal lesion, which implied that it may represent metastasis from the primary lung tumour.

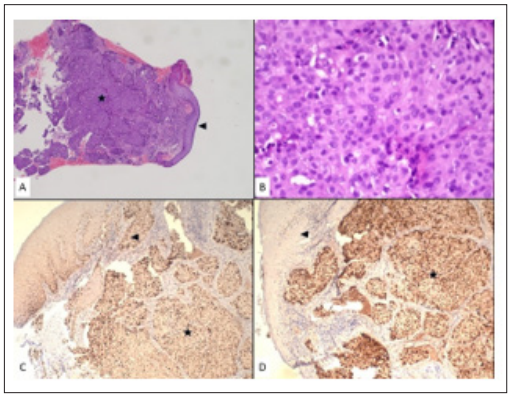

Figure 4: Biopsy from the Tip of the Nose

A: Hematoxylin and eosin stain (40x magnification) Biopsy from the nose with an overlying intact epidermis (arrowhead) with an underlying invasive tumour (star) arranged in islands

B: Hematoxylin and eosin stain (400x magnification) The tumour cells are polygonal and have pleomorphic angulated nuclei with a moderate amount of dense eosinophilic cytoplasm

C: Immunohistochemistry with p40 (clone PRM 155, Ready to use, Pathnsitu) shows nuclear staining in the basal keratinocytes of the epidermis (arrowhead) and the underlying tumour cells (star)

D: Immunohistochemistry with p53 (clone PRM 129, Ready to use, Pathnsitu) shows mutant phenotype in the form of intense nuclear staining in the tumour cells (star), with the keratinocytes of the epidermis being negative.

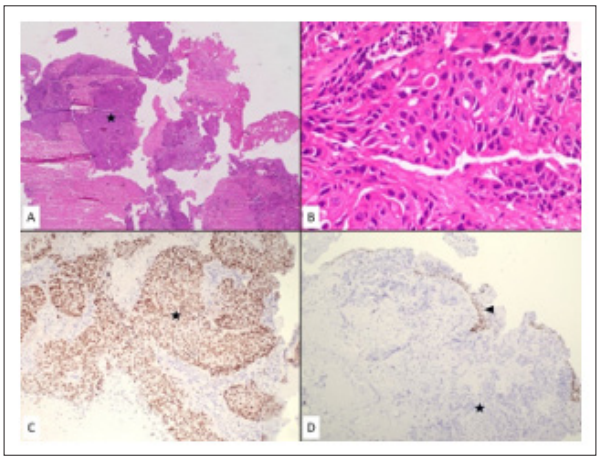

Figure 5: Biopsy from the Lung Mass

A: Hematoxylin and eosin stain (40x magnification) Biopsy from the lung mass shows fragmented tissue with an invasive tumour (star) arranged in islands

B: Hematoxylin and eosin stain (400x magnification) The tumour cells are polygonal and have pleomorphic angulated nuclei with a moderate amount of dense eosinophilic cytoplasm

C: Immunohistochemistry with p40 (clone PRM 155, Ready to use, Pathnsitu) shows nuclear staining in the tumour cells (star)

D: Immunohistochemistry with TTF1 (clone EP229, Ready to use, Pathnsitu) shows preserved nuclear expression in the columnar cells (arrowhead) of the bronchiole with tumour cells being negative.

The patient was diagnosed with a case of Squamous cell carcinoma Lung with distant metastasis to the tip of the nose and Liver and staged at cT3N1M1c and Stage IVB

Post-tumour board discussion, the patient received a single dose of immunotherapy with nivolumab (240 mg) and chemotherapy with carboplatin (350 mg) and paclitaxel (160 mg). He also received a single dose of 3 Gy EBRT to Nose. Unfortunately, the patient succumbed to the illness 02 weeks after initiating therapy.

Discussion

Cutaneous metastatic carcinoma of the nose is often misdiagnosed as rhinophyma, rosacea, furuncle, or hemangioma. Cutaneous metastases from lung cancer typically present as single or multiple painless nodules that can be mobile or fixed, hard or flexible [3]. Their colours range from flesh tones to red-purple and blue-black, with diameters varying from 5 mm to 6 cm [4]. Initially, these lesions proliferate but may then slow down, with some undergoing necrosis or ulceration [5]. In some cases, skin metastasis is the first indication of lung cancer before the primary tumour is identified [6]. In a significant series of cases, cutaneous metastasis preceded the diagnosis of primary lung cancer in 14% of instances [7].

The most prevalent histopathological type of cutaneous metastases from lung cancer is adenocarcinoma, followed by squamous cell carcinoma (SCC) or small cell carcinoma, and then large cell carcinoma. Metastatic SCC arising from the lung is often moderately to poorly differentiated [8]. Lung cancer can metastasize to nearly every organ, frequently affecting extrathoracic sites such as the liver, adrenal glands, skeleton, kidneys, brain, abdominal lymph nodes, and gastrointestinal tract. In contrast, skin or cutaneous metastasis is less common.

The mechanisms by which lung cancer metastasizes to the nose are not fully understood. Baston suggests that pulmonary vascular and lymphatic circulation could transport tumour cells to the nose, facilitated by the nearly valveless vertebral venous plexus [9]. The processes of metastasis to these unusual sites remain controversial, with proposed mechanisms including arterial embolism and retrograde venous and lymphatic spread. For pulmonary carcinoma, arterial embolism is the most likely route of dissemination. A tumour embolus may enter the pulmonary veins, gaining access to the systemic circulation through the left atrium and then reaching the cavernous body, thereby supplying blood to the nasal site [10].

Another possible mechanism for metastasis to the nasal tip occurs when intrathoracic pressure increases significantly, allowing blood-borne emboli to travel through venous plexuses and ascend to the venous sinuses of the skull. The pterygoid plexus, cavernous sinus, and pharyngeal plexus communicate with the vertebral system, potentially transporting tumour cells to the nose [11].

The management of cases with metastatic squamous cell carcinoma (SCC) of the lung, including cutaneous metastases, typically involves palliative radiation, combined chemotherapy with radiotherapy, followed by maintenance immunotherapy. Multiple randomized controlled trials and large meta-analyses have confirmed the efficacy of combination chemotherapy and immunotherapy, or single-agent immunotherapy regimens, in treating advanced disease [12].

For advanced cases, treatment should be tailored according to genetic and molecular testing. Targeted therapy is utilized based on mutation status. In patients with advanced SCC of the lung and PD-L1 expression ≥ 50%, preferred first-line treatment options include single-agent pembrolizumab, cemiplimab, or atezolizumab. Other options include the combination of carboplatin with paclitaxel or albumin-bound paclitaxel, along with pembrolizumab, or cemiplimab combined with chemotherapy [12].

In our case, the patient received a single dose of immunotherapy with nivolumab (240 mg) and chemotherapy with carboplatin (350 mg) and paclitaxel (160 mg) with a single dose of EBRT 3 Gy to the nose but succumbed to illness [13].

Conclusion

Cutaneous and subcutaneous metastatic lesions resulting from lung cancer are physically indistinguishable from those caused primarily at the metastatic site resulting in delay in identifying the primary. They occur with enough frequency and in varying locations that lung cancer should always be considered in the differential diagnosis for any patient presenting with rapidly progressing cutaneous lesions, especially in the head and neck region. Squamous cell carcinoma of the lung has the potential to recur and metastasise.

Declarations

- The authors have no relevant financial or non-financial interests to disclose.
- The authors have no competing interests to declare that are relevant to the content of this article.
- All authors certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.
- The authors have no financial or proprietary interests in any material discussed in this article.
- No identification of any patients done in the paper. Appropriate sections covered to hide identity.
- Consent from patient taken.
- Having done for an emergency situation prior sanction not taken and retrospective waiver taken in view of life saving procedure
- Data is available for the journal's perusal

Ethical Statement

1. All the authors mentioned have contributed to the paper
2. No funding has been received for the above study
3. This paper is in accordance with 1964 Helsinki Declaration for compliance with ethical standards
4. There is no conflict of interest for authors' contributing.
5. No identity of the patients has been revealed while writing the paper.

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