Letter to Editor

Diagnostic dilemma in patients with lung metastasis

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Sir,

The lungs are the most common site of metastasis for various cancers. Computed tomography (CT) of the lungs is one of the most sensitive modalities to identify lung lesions [1]. However, CT findings of various conditions may overlap, and this can impede diagnosis. We report a case of renal cell carcinoma (RCC) with lung metastases wherein a definitive diagnosis could not be reached using CT thorax and other tests.

An 84-year-old elderly gentleman, known to be hypertensive, came with complaints of bloating, generalized tiredness, and epigastric pain for 1 month. His respiratory rate was 40 breaths/min but other vital parameters were normal. Laboratory investigations, ultrasound abdomen, and electrocardiogram were normal, except for a total leukocyte count of 17,800/mm^3, with 75% neutrophils. A chest roentgenogram showed bilateral patchy air space opacities with multiple nodular opacities in the lungs. He was empirically started on intravenous ceftriaxone (1 g twice daily). High-resolution chest tomography of the thorax showed numerous well-defined, rounded lesions suggestive of metastasis (Fig. 1). A CT oncology study showed signs of a right RCC with mediastinal lymphadenopathy, lung metastases, and moderate right pleural effusion. He underwent right-sided pleurocentesis, and about 1l of blood-tinged fluid was aspirated, whose analysis showed malignant cells. All cultures, including pleural fluid, were negative. A CT-guided right lung biopsy was done, which indicated a clear-cell RCC. The patient was started on target therapy with a tyrosine kinase inhibitor Axitinib 5mg twice daily orally and immunotherapy with a checkpoint inhibitor Pembrolizumab 200 mg intravenous every 3 weeks. He was discharged on the same chemotherapeutic agents and on 2 L/min oxygen through nasal prongs.

The patient was re-admitted after 3 days with complaints of fever, cough, and breathing difficulty. A CT Oncology scan showed an interval increase in the left lung mid- and lower-zone opacification with septal thickening and reticular opacities in both lung fields and re-accumulation of the right pleural effusion. Total leukocyte count was 17,000/mm^3, with 80% neutrophils, but work-up for pneumonia, including multiplex polymerase chain reaction, cultures, serum procalcitonin, and Beta-D-Glucan was negative. He was shifted to the intensive care unit in view of worsening dyspnea and initiated on non-invasive positive pressure ventilation. Chemotherapeutic agents were continued, and pleurocentesis was repeated, draining about 1.5 L of hemorrhagic fluid. He was started on intravenous methylprednisolone (40 mg over 24 h) and aviptadil (150 mg over 12 h). Over the next week, he became hypotensive, requiring vasopressor support, and had worsening respiratory distress, for which he was intubated. Subsequently, he developed an acute kidney injury and succumbed to his illness.

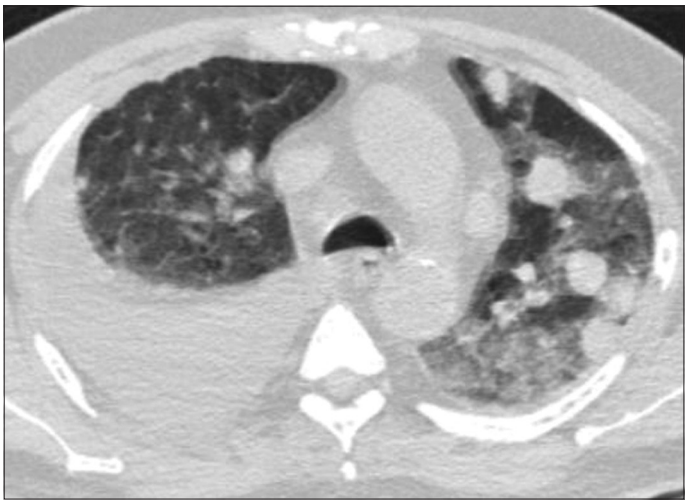

Figure 1: CT oncology scan showing numerous, well-defined, rounded, heterogeneously enhancing lesions scattered in all lobes of both lungs with moderate right sided pleural effusion

RCC accounts for 3% of all adult cancers and 85% of all kidney tumors [2]. The present case highlights the delay in diagnosis due to the absence of suggestive symptoms or laboratory parameters. The most common differentials in cancer patients presenting with breathing difficulty include venous thromboembolism, infection, tumor progression, radiation pneumonitis, drug-induced pneumonitis, including checkpoint inhibitor pneumonitis (CIP), lymphangitis carcinomatosis, alveolar hemorrhage, and pulmonary oedema (Fig. 2). Hematogenous spread from primaries in the head and neck, thyroid, kidneys, adrenals, testes, melanoma, and osteosarcoma accounts for 52.3% of cases of lung metastases, while lymphatic spread from the lung, stomach,

Access this article online

Received - 23 May 2023
Initial Review - 05 Jun 2023
Accepted - 09 Jul 2023

Quick Response code

DOI: 10.32677/ijcr.v9i7.4054

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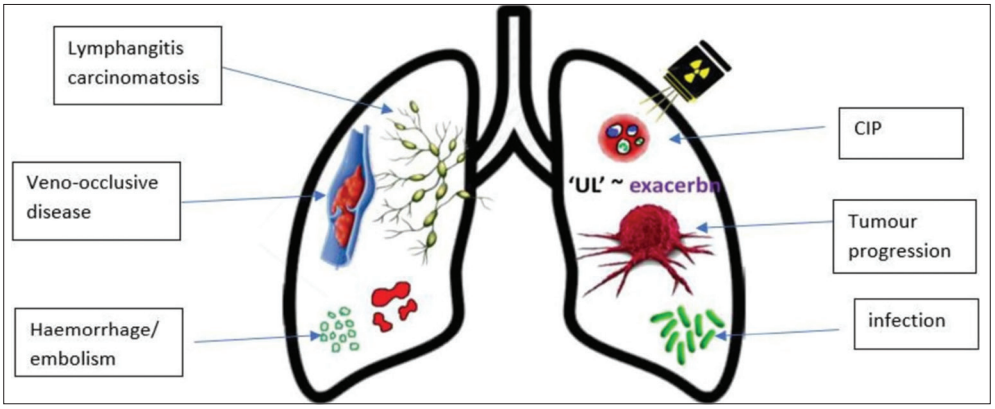

Figure 2: Differential diagnosis in lung lesions in oncology patients

breast, pancreas, uterus, rectum, and prostate, also known as lymphangitis carcinomatosis, account for 26.4% of cases [3,4].

CT scan findings that suggest lung metastasis depend on the primary cancer and include diffuse miliary seedling, cavitation, calcification, and large singular metastases. In hematogenous spread, most metastases are found at the bases and peripheries of the lung [1]. The radiological picture in CIP can range from organizing pneumonia (peribronchovascular and subpleural ground glass opacities in mid and lower zones), non-specific interstitial pneumonia (ground glass and reticular opacities in bases), hypersensitive pneumonitis (diffuse ground glass nodules involving the upper lobe), to acute interstitial pneumonitis (patchy or diffuse ground glass or consolidative opacities) [5]. These features may overlap with the CT features of lymphangitis carcinomatosis, which include septal and interstitial thickening, ground glass opacities, and hilar and mediastinal nodal enlargement. However, the general architecture of the lung is preserved [5,6].

These non-specific clinical and radiological features, as well as ongoing tumor progression and possible superadded infection, may add to the diagnostic challenge even for an experienced radiologist. The ideal approach to diagnosing lung metastasis is by bronchoscopy with transbronchial biopsy, provided that the patient is stable for this procedure.

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Funding: Nil; Conflicts of interest: Nil.

How to cite this article: Shah A, Rangappa P, Jacob I, Reddy N, Rao K. Diagnostic dilemma in patients with lung metastasis. Indian J Case Reports. 2023;9(7):220-221.