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Seeds in Pulmonary Soil: Brief Review and Presentation of a Multitumoral Pulmonary Metastasis Case Series

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Abstract

Pulmonary metastases constitute a common and clinically significant complication of various extrathoracic malignancies. This article presents five illustrative cases—three breast carcinomas, one colorectal adenocarcinoma, and an initially occult colonic primary—that exemplifies the biological, clinical, and therapeutic heterogeneity of this entity. All patients exhibited bilateral nodules, mediastinal lymphadenopathy, and, in two cases, malignant pleural effusion. Early integration of palliative care proved essential in scenarios of sepsis or functional frailty. These findings confirm that prognosis depends on tumor biology, extrapulmonary disease burden, and host response, and they underscore the need for an individualized, multidisciplinary approach that combines tumor-directed therapy, symptom control, and comprehensive support.

Keywords

Pulmonary Metastases, Neoplasms, Radiotherapy, Palliative Care

1. Introduction

Pulmonary metastases constitute a common manifestation in patients with malignancies. Their dissemination follows complex and heterogeneous biological processes modulated by intrinsic characteristics of both the tumour and the host [1]. The modern concept of metastasis is attributed to Stephen Paget, who in 1889 formulated the "seed-and-soil" theory, postulating the selective tropism of certain tumour cells for specific organs [2]. Subsequently, the introduction of X-rays by Wilhelm Röntgen in 1895 enabled the systematic detection of secondary pulmonary lesions, laying the foundations for their clinical and radiological characterisation [3].

Several factors predispose to the development of pulmonary metastases. Among the dissemination pathways, the haematogenous route predominates, given that the systemic venous circulation drains into the pulmonary capillaries, where circulating tumour cells become trapped and extravasate [4]. Other contributory factors—such as vascular invasion, high tumour burden, or a biologically aggressive phenotype (high histological grade or marked migratory capacity)—increase the risk of pulmonary dissemination [5]. Host immunosuppression and systemic inflammation likewise facilitate metastatic colonisation. At the molecular level, phenomena such as over-expression of chemokine receptors—for example, CXCR4, which interacts with its ligand CXCL-12, abundantly expressed in the lung—and of adhesion molecules favour implantation in the pulmonary capillary bed [4] [6] [7]. These alterations, together with the formation of tumour-induced pre-metastatic niches, create a microenvironment conducive to the growth of metastatic foci [4].

A variety of extrathoracic neoplasms metastasise frequently to the lung, whether by anatomical proximity or through a biological tropism that transcends distance [5]. Colorectal cancer produces pulmonary metastases in approximately 6% - 8% of colon tumours and 10% - 18% of rectal tumours, making the lung the second site of dissemination after the liver [8]. Breast carcinoma involves the lung in 20% - 40% of patients, a proportion that rises in aggressive subtypes such as triple-negative disease [9]. Clear-cell renal carcinoma shows a marked predilection for this organ, with pulmonary involvement in 45% - 65% of metastatic cases [10]. Sarcomas, both osseous and soft-tissue, metastasise to the lung in 20% - 40% of cases [11]. These figures underscore the considerable clinical burden posed by pulmonary metastases and the need for specific diagnostic and therapeutic strategies in oncological practice.

The following five clinical cases illustrate different scenarios in which pulmonary metastases arise as the initial presentation, progression, or recurrence of disease, and they provide the basis for the subsequent discussion.

2. Case Presentations

2.1. Case 1

A 51-year-old woman with a history of infiltrating ductal carcinoma of the right breast with a 40% mucinous component, grade III, oestrogen receptor 90%, progesterone receptor 70%, HER2-negative, Ki-67 60%, stage IIB (pT2 pN1 M0 R0)

after modified radical mastectomy and axillary lymphadenectomy presented to the emergency department with progressive dyspnoea and orthopnoea. Thoracic computed tomography showed multiple bilateral nodules and a large pleural effusion, findings compatible with metastatic progression (Figure 1).

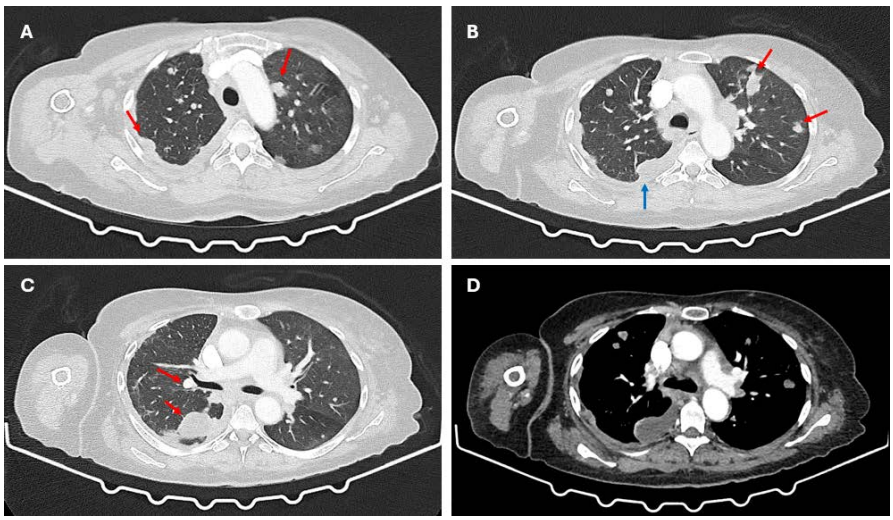

Figure 1. Chest computed tomography: A, B, and C lung window; D mediastinal window. Demonstrates multiple bilateral pulmonary nodules with pleural thickening (red arrow) and a small right-sided effusion (blue arrow); right basal atelectasis; and mediastinal lymphadenopathy.

An evacuative thoracentesis was performed, and a temporary pleural catheter was inserted for continuous drainage. Brain magnetic resonance imaging, requested for headache and photopsia, revealed supratentorial and cerebellar metastases. Whole-brain radiotherapy using 3D-CRT was prescribed at 400 cGy per fraction to a total dose of 2000 cGy to PTV1, with satisfactory initial tolerance. After respiratory and neurological stabilisation, the patient was discharged with an ECOG performance status of 2 and scheduled for a multidisciplinary outpatient oncological follow-up to adjust systemic therapy and optimise symptomatic control.

2.2. Case 2

A 40-year-old woman with a history of right-sided colonic adenocarcinoma, clinical stage T4 N0 M1 at presentation, complicated by intestinal obstruction and non-regional retroperitoneal lymphadenopathy. Initial molecular testing showed wild-type KRAS, NRAS, and BRAF, with low microsatellite instability. During outpatient follow-up, thoracic CT demonstrated progression with infiltrative nodules in the right lower lung field (Figure 2), while abdominal CT confirmed an increase in the size and number of retroperitoneal lymph nodes. These findings indicated systemic progression despite first-line therapy. The case was presented at the multidisciplinary tumour board to evaluate a change of chemotherapy regimen, the inclusion of targeted biological agents, or enrolment in a clinical trial according to molecular profile and functional status.

2.3. Case 3

A 70-year-old woman with left breast carcinoma, clinical stage IIIB (T4B N1 Mx), and a history of right breast carcinoma treated surgically 20 years earlier. Molecular profiling is pending owing to the temporary unavailability of immunohistochemistry. She presented to the emergency department with pain in the right arm, localised to the bicipital region, accompanied by oedema, and sudden-onset dyspnoea with deterioration in functional class. Venous and arterial Doppler ultrasonography of the upper and lower limbs showed no thrombosis but revealed multiple lymphadenopathies. Because the dyspnoea persisted, chest computed tomography (Figure 3) was requested, demonstrating multiple bilateral solid nodules with an infiltrative appearance and mediastinal lymphadenopathy, findings compatible with metastatic progression. The performance of a pleural fluid cytology study via puncture was considered; however, due to the scant volume of fluid, the procedure was ultimately not performed, as the potential risks outweighed the expected benefits.

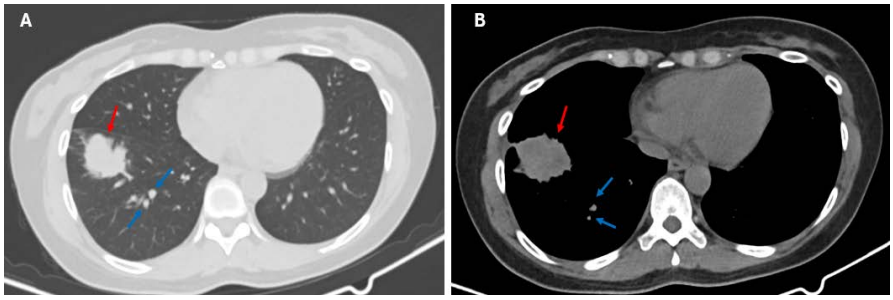

Figure 2. Chest computed tomography: A, lung window; B, mediastinal window. A right basal solid pulmonary mass with an infiltrative appearance is observed (red arrow), along with multiple bilateral basal solid pulmonary nodules of secondary infiltrative appearance (blue arrow).

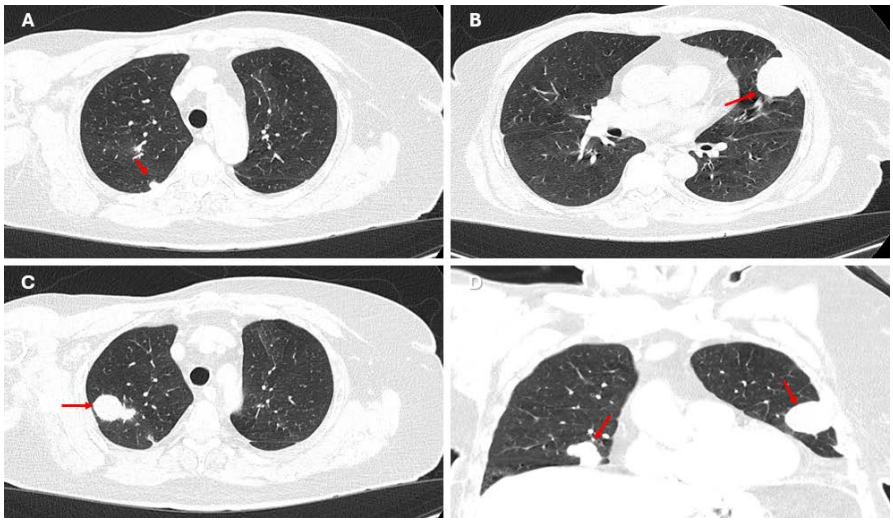

Figure 3. Chest computed tomography: A, B, and C axial plane; D coronal plane. Demonstrates multiple bilateral solid lesions of the lung parenchyma with a secondary infiltrative appearance. Post-mastectomy changes on the right side.

Pain control was optimized and oxygen therapy administered, achieving symptomatic improvement; the patient remained with an ECOG performance status of 2. Given the locally advanced disease and new pulmonary dissemination, the treating team proposed therapy with palliative intent. Discharge was scheduled with an appointment at the multidisciplinary oncology board to define systemic chemotherapy, evaluate the need for biopsy for molecular profiling, and establish supportive and symptom-control strategies.

2.4. Case 4

A 65-year-old man, heavy smoker (60 pack-years), presented with progressive dyspnoea of one month's duration and marked functional decline during the previous week, accompanied by sharp pleuritic chest pain rated 8/10 and a 10-kg weight loss over the past five months. On physical examination he required oxygen via nasal cannula at 3 L/min; vital signs were stable, and oxygen saturation was 92%. Chest computed tomography revealed multiple bilateral infiltrative nodules suggestive of neoplastic dissemination (Figure 4). In the search for an occult primary tumour, tumour markers were measured: carcinoembryonic antigen 325 ng/mL, while prostate-specific antigen, CA 19-9, and alpha-fetoprotein were within normal limits. Pleural fluid cytology was performed via diagnostic thoracentesis, revealing cells suggestive of possible metastatic spread to the lung.

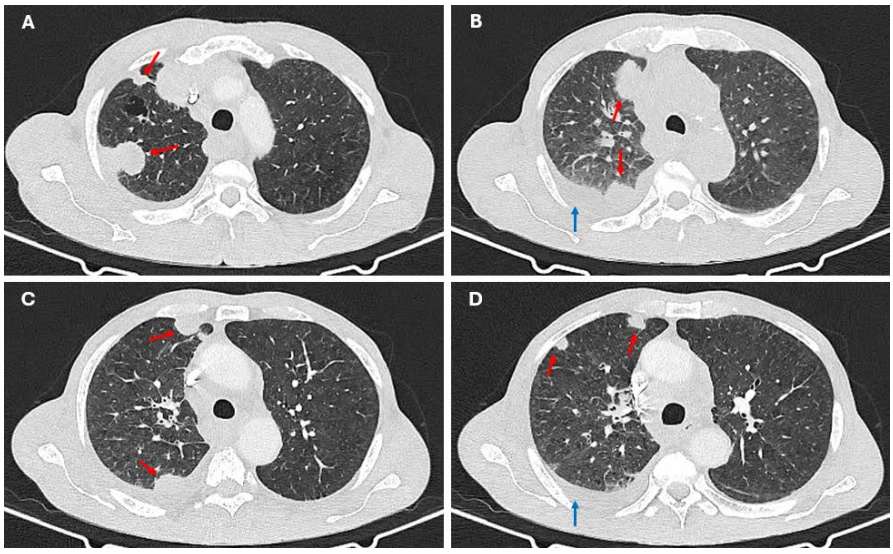

Figure 4. Chest computed tomography: multiple infiltrative pulmonary nodules predominantly in the right lung field (red arrow), associated with a right pleural effusion probably of paraneoplastic aetiology (blue arrow).

Given the suspicion of an occult primary tumour, endoscopic studies were undertaken; colonoscopy identified a 3-cm exophytic lesion in the transverse colon, and multiple biopsy samples were obtained. The patient was stabilized with analgesia, respiratory physiotherapy, and adjustment of oxygen therapy (ECOG 3). A multidisciplinary oncological review was scheduled for one week later to discuss

the histological and immunohistochemical results and to establish a specific therapeutic strategy. However, due to the patient's clinical deterioration (ECOG > 3 and Karnofsky < 20), a purely palliative approach was adopted under the guidance of a pain and palliative care specialist.

2.5. Case 5

A 54-year-old woman with advanced right breast carcinoma, diffuse pulmonary metastases, and bone involvement (vertebral bodies and a proximal femoral fracture) was admitted with septic shock secondary to multiresistant *Serratia marcescens* bacteraemia, which responded favourably to antimicrobial treatment. During her hospital stay she experienced an upper gastrointestinal haemorrhage caused by erosive duodenitis, severe pneumonia with imaging evidence of additional infiltrative lesions (**Figure 5**), and acute kidney injury. Physical examination revealed a rock-hard breast mass, axillary lymphadenopathy, preserved vesicular breath sounds, left coxofemoral deformity, and a grade II sacral pressure ulcer without superinfection. Chest computed tomography was performed to characterise the findings, confirming pulmonary metastases (**Figure 6**).

Despite the interventions undertaken, the patient experienced an unfavourable course with progressive clinical deterioration; accordingly, a multidisciplinary management plan was instituted with the pain and palliative care team, given her limited tolerance of potential systemic chemotherapeutic therapy.

3. Discussion

Pulmonary metastasis typically occurs via haematogenous dissemination, whereby tumour cells shed from the primary neoplasm enter the bloodstream and reach the pulmonary circulation [5]. The lungs act as a capillary filter in which these cells may lodge and extravasate into the parenchyma [5]. Less common is lymphatic spread, in which tumour cells travel through the lymph to the thoracic duct and thence to the central venous flow, ultimately reaching the lungs. Transcoelomic seeding to the pleura or lung through contiguity or malignant pleural effusion is also possible, although considered a minor route [1] [12].

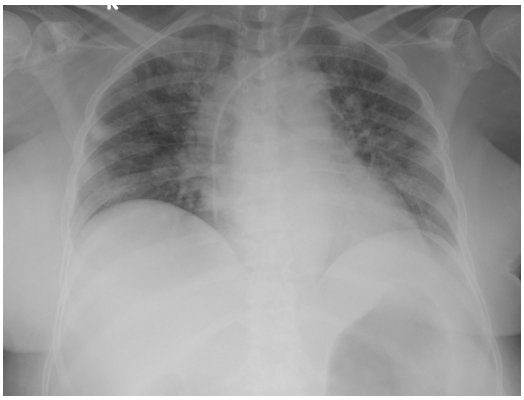

Figure 5. AP Chest radiograph: Bilateral nodular opacities are evident, together with parahilar congestion, cardiomegaly, and a properly positioned central venous catheter.

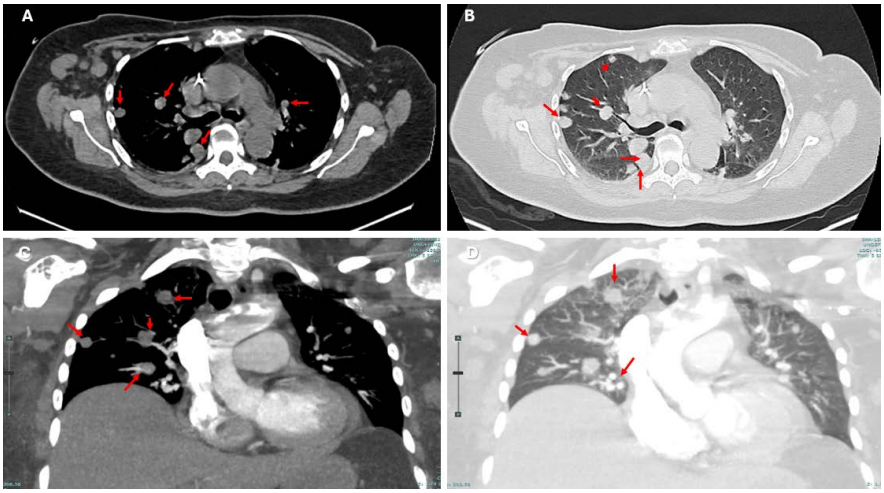

Figure 6. Chest computed tomography: multiple nodular lesions of varying diameters with an infiltrative appearance, suspicious for metastatic disease (red arrow).

For a malignant cell to establish a metastasis, it must complete the metastatic cascade, comprising local tissue and vascular invasion, intravasation into the circulation, survival of haemodynamic and immunological stress in the bloodstream, extravasation into pulmonary tissue, and finally colonization and proliferation in the new environment [2] [4]. Each step is mediated by key molecular alterations; the ability to evade the local immune system through mechanisms such as the expression of inhibitory lymphocyte ligands is crucial for these cells to establish macroscopic, clinically detectable metastatic colonies [4] [5] [7].

The incidence of pulmonary metastases present at the time of diagnosis of the primary cancer is estimated at approximately 17.9 per 100,000 person-years [5] [12]. Population-based registries indicate that about 4% of all new cancer cases present pulmonary metastasis at diagnosis, with very similar frequencies in men (4.13%) and women (3.95%) [8] [12]. Epidemiological series also show that patients with pulmonary metastases tend to be older at diagnosis than those without metastases, reflecting that the risk of dissemination increases with temporal progression of the disease and longer survival in advanced stages [5] [12].

The five analyzed cases confirm the biological and clinical heterogeneity of pulmonary metastases and underscore the need for an individualized, multidisciplinary approach. Although the lung acts as a "capillary filter" for most neoplasms, the dissemination pattern depends on tumour biology, disease burden, and host immune status [4] [7]. The patients with breast carcinoma (Cases 1, 3, and 5) illustrate three distinct scenarios: oligometastatic progression with pleural effusion, pulmonary relapse without available molecular profile, and multiorgan disease with associated sepsis [9] [13]. In all, positive hormone-receptor status conferred endocrine options, but the high Ki-67 and potential triple-negative status in Case 3 anticipate a more aggressive course and the need for early chemotherapy.

The colorectal adenocarcinoma in the 40-year-old patient (Case 2) and the occult primary in the male smoker (Case 4) highlight the importance of molecular

characterization. The absence of RAS/BRAF mutations and low microsatellite instability limit the use of immunotherapy and oblige optimization of cytotoxic chemotherapy or exploration of clinical trials [8]. The late finding of the colonic lesion in the smoker underscores that a markedly elevated carcinoembryonic antigen and multiple pulmonary nodules should prompt a systematic search for the primary tumour, even in the presence of risk factors for lung cancer.

From a diagnostic standpoint, high-resolution computed tomography remains the reference tool for delimiting number, size, and location of lesions, as shown in **Figures 1-6** [14] [15]. Nevertheless, cerebral magnetic resonance imaging (Case 1) and colonoscopy (Case 4) remain essential to rule out extrathoracic disease and guide the therapeutic sequence. Thoracentesis with positive cytology, placement of a pleural catheter, and biopsy of metastatic tissue allow confirmation of tumoural nature and, when possible, genomic profiling to guide targeted therapies.

Therapeutic management must balance systemic control and local palliation. Whole-brain 3D-CRT radiotherapy (Case 1) and immediate pleural drainage procedures proved effective in relieving symptoms and gaining time before initiating systemic treatment; depending on the scenario, specific surgical interventions such as metastasectomy may also be offered [16]. By contrast, the patient in Case 5 exemplifies a setting in which metastatic burden, opportunistic infections, and overall frailty necessitate shifting oncological intent to palliative care focused on quality of life.

The concomitant presence of mediastinal lymphadenopathy (Cases 1, 2, and 3) and the pathological fracture (Case 5) confirm that lymphatic and haematogenous spread can coexist, increasing treatment complexity. These findings support evidence that the number of lesions, their bilaterality, and the presence of extrapulmonary metastases are independent prognostic factors that determine the feasibility of metastatic resection and overall survival.

4. Conclusion

Pulmonary metastases represent the terminal stage of a biological cascade encompassing invasion, intravasation, circulatory survival, extravasation, and colonization, driven by molecular alterations that promote organ tropism and immune evasion. The five cases analyzed illustrate this diversity: all exhibited bilateral nodular dissemination, mediastinal lymphadenopathy, or pleural effusion, highlighting the utility of high-resolution computed tomography as a first-line investigation. Effective management demands a balance between systemic control—chemotherapy, hormone therapy, or targeted agents—and locoregional palliation through palliative chemotherapies, resolution of acute decompensations, and, when appropriate, surgical resection of lesions in selected patients. The need for early integration of palliative care is evident in individuals with a high metastatic burden, sepsis, or functional frailty. Taken together, these findings confirm that prognosis depends on tumour biology, extrapulmonary disease extension, and the host inflammatory response, reinforcing the relevance of individualized strategies

and continuous multidisciplinary coordination.

Consent

The study was funded with personal resources. Patient confidentiality and anonymity were guaranteed, respecting their autonomy, dignity, and fundamental rights. Prior informed consent was obtained for the use of clinical data, with clear explanations provided regarding the study' objectives.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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