

Spectrum of Radiologic Findings in Atypical Pulmonary Metastases

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Article History:

Received: Mar 11, 2022
Revised: July 23, 2022
Accepted: Aug 21, 2022
Available Online: Sep 02, 2022

Author Contribution:

MW conceived idea, JA MW MKZ MKK drafted the study, AA NA collected data, JA AA MKZ MKK did statistical analysis and interpretation of data, JA MW AA critical reviewed manuscript. All approved final version to be published.

Declaration of conflicting interests:

The authors declare that there is no conflict of interest.

How to cite this article:

Arshad J, Waqas M, Khan A, Khan MK, Zia MK. Spectrum of Radiologic Findings in Atypical Pulmonary Metastases. Pak J Chest Med. 2022;28(03):345-356

A B S T R A C T

Background: Atypical pulmonary metastases present a diverse range of radiologic findings in the lungs, deviating from the typical patterns of metastatic disease. These unique radiological characteristics play a pivotal role in their diagnosis and differentiation from other lung pathologies.

Objective: The goal is to show the various imaging patterns for pulmonary metastases from various primary malignancies.

Methodology: This study is a retrospective descriptive analysis in which we examined 30 cases of pulmonary metastasis originating from various primary malignancies. The study was conducted at Radiology departments of Khyber Teaching Hospital, Peshawar and Hayatabad Medical Complex, Mardan between July 2017 and August 2021. Our focus was on identifying and documenting the unique radiologic characteristics associated with metastases originating from different primary cancers.

Results: In our institution, we conducted an analysis of 30 cases of pulmonary metastases. Among these cases, we observed varying patterns of metastatic spread. Specifically, 4 (14%) cases were associated with Renal cell carcinoma, 2 (7%) cases with testicular germ cell tumors, 4 (13%) cases with thyroid cancer, 2 (7%) cases with osteosarcoma, 4 (13%) cases with GI tract adenocarcinoma, 3 (10%) cases with gynecological malignancies, 1 (3%) case with femoral vein leiomyosarcoma, 4 (13%) cases with breast cancer, 1 (3%) case with lymphoma, and 5 (17%) cases with lung carcinoma. These cases exhibited a range of pulmonary metastatic patterns, alongside the typical presentation characterized by multiple soft tissue density nodules.

Conclusion: The usual radiologic signs of lung metastasis are several spherical, variable-sized nodules and widespread interstitial thickening. It is challenging to diagnose lung metastases because of various patterns. Therefore, understanding the various pulmonary metastasis patterns from various primary aids helps in the early detection of metastases.

Keywords: Pulmonary Metastasis; Patterns; Atypical Radiologic Features

Introduction

Pulmonary metastases represent an enduring challenge within the field of oncology, primarily due to the intricate and often perplexing radiologic manifestations they exhibit. These metastatic lesions, when detected in the lungs, can originate from various primary malignancies, making their radiologic appearances highly diverse and complex to decipher.¹ This multifaceted nature of pulmonary metastases poses substantial obstacles to accurate diagnosis and effective treatment planning. It is in this context that atypical pulmonary metastases emerge as a distinct enigma, characterized by a wide spectrum of radiologic features that confound clinicians and radiologists alike. The challenge they present extends beyond mere diagnostic ambiguity; it extends to the burden they place on both patients and healthcare providers. Patients facing atypical pulmonary metastases experience heightened uncertainty about their condition, while healthcare providers grapple with the complexities of tailored treatment strategies.²⁻⁵

In response to this daunting clinical scenario, there exists a compelling and pressing need to deepen our understanding of these unique radiologic patterns associated with atypical pulmonary metastases. Such an understanding is indispensable for ensuring timely and accurate diagnosis. It is this foundation of knowledge that empowers clinicians to craft therapeutic interventions precisely tailored to the individual patient's needs, ultimately leading to improved patient outcomes.^{6,7} In a field where precision and personalized approaches can significantly impact patient well-being, research endeavors aimed at unraveling the intricacies of atypical pulmonary metastases assume critical importance. The pursuit of this knowledge promises to offer a meaningful contribution to the field of oncology, with the potential to enhance the prognosis and quality of life for those confronted with the formidable challenge of atypical pulmonary metastases.

The central objective of this research is to embark on an exhaustive exploration of atypical pulmonary metastases, characterized by their complex and diverse radiologic

presentations. These elusive pulmonary nodules, arising from various primary tumors, present a formidable challenge in the realm of oncology. The study's ambition is to elucidate the myriad imaging patterns and distinctive characteristics associated with atypical pulmonary metastases. By meticulously examining these radiologic findings, the research aims to provide clinicians with a comprehensive understanding of these enigmatic lesions. This deeper understanding is poised to serve as a valuable tool in the clinical arsenal, facilitating early detection, precise staging, and the formulation of tailored treatment strategies. The overarching goal is to empower healthcare professionals to navigate the intricate landscape of atypical pulmonary metastases with greater accuracy and confidence.

In the context of oncology, where the ability to make precise diagnoses and devise individualized therapeutic approaches can profoundly impact patient outcomes, this research assumes paramount importance. It endeavors to make a meaningful contribution to the field by enhancing patient care. Through the insights gained from this study, clinicians will be better equipped to address the complexities of atypical pulmonary metastases, ultimately leading to improved prognoses and enhanced quality of life for individuals grappling with these challenging manifestations. As such, this research not only adds to the body of scientific knowledge but also holds the potential to make a tangible difference in the lives of those confronted with the intricate and often perplexing nature of atypical pulmonary metastases.

Objective

The goal is to show the various imaging patterns for pulmonary metastases from various primary malignancies.

Methodology

A considerable clinical problem in the field of cancer is posed by atypical pulmonary metastases and their various radiologic appearances. We undertook a

Table 1. Age Distribution among Study Participants

Age in years	No. of patients	Percentage
<50	9	30.0
50-60	7	23.4
60-70	9	30.0
>70	5	16.6

retrospective descriptive study, concentrating on patients treated at Khyber Teaching Hospital, Peshawar and Hayatabad Medical Complex, Mardan between July 2017 and August 2021, to better comprehend these enigmatic entities. Our main goal was to examine the clinical, imaging, and histopathological records of patients with pulmonary metastases that had been verified by both radiology and histology.

We found eligible individuals by checking the hospital's computer system for instances with the phrase "metastases to lungs." Then, we carefully went over the case files of 40 individuals. Ten patients were not included because there were not enough records available. The rest of 30 patients had their radiologic data thoroughly examined.

It should be noted that because the research was carried out retrospectively, no participants' informed permission

was acquired. A GE OPTIMA 128 SERIAL SLICE CT scanner was used for all imaging procedures in accordance with a set protocol, and all pictures were evaluated on a workstation utilizing data from the picture archiving and communication system (PACS). We certify that our study complied with the requirements of the Institutional Review Boards (IRBs) of Khyber Teaching Hospital, Peshawar and Hayatabad Medical Complex, Mardan for the confidentiality and security of patient data. In order to preserve the confidentiality of patients throughout data analysis, patient names were made anonymous.

Results

In our study of 30 individuals, the age range spanned from 21 to 82 years, with a predominant concentration of

Table 2. Primary Tumor Types and Corresponding Pulmonary Metastases Imaging Patterns

No. of cases	Primary	Imaging pattern of pulmonary metastases
4	Renal cell carcinoma	4 cases showed typical appearance like multiple soft tissue density nodules
2	Testicular germ cell tumor	2 cases showed large peripherally located soft tissue density nodules
4	Thyroid cancer 3- Medullary thyroid carcinoma 1-Papillary thyroid carcinoma	MTC showed Multiple soft tissue density nodules. Papillary thyroid carcinoma showed a miliary pattern.
2	Osteosarcoma	2 cases showed multiple large nodules with extensive central calcification showing a sunburst pattern.
4	GI tract adenocarcinoma	3 cases showed a typical pattern. 1 case showed a consolidation pattern containing an air bronchogram.
3	Gynecological malignancy Endometrial cancer-2 Cervical cancer-1	Cervical cancer showed few cavitory lesions. Endometrial cancer showed multiple soft tissue density nodules.
1	Femoral vein leiomyosarcoma	multiple heterogeneously enhancing soft tissue density nodules in bilateral lung fields.
4	Breast carcinoma	1 case showed endobronchial localization, 3 cases showed multiple pulmonary nodules.
1	Lymphoma	Multiple soft tissue nodules interspersed with background fibro bronchiectatic lung disease with extensive abdominal and mediastinal lymphadenopathy.
5	Lung carcinoma	Multiple sub-centimetric soft tissue density nodules are scattered throughout the opposite lung parenchyma.

Representative cases:

Case 1. Renal cell carcinoma

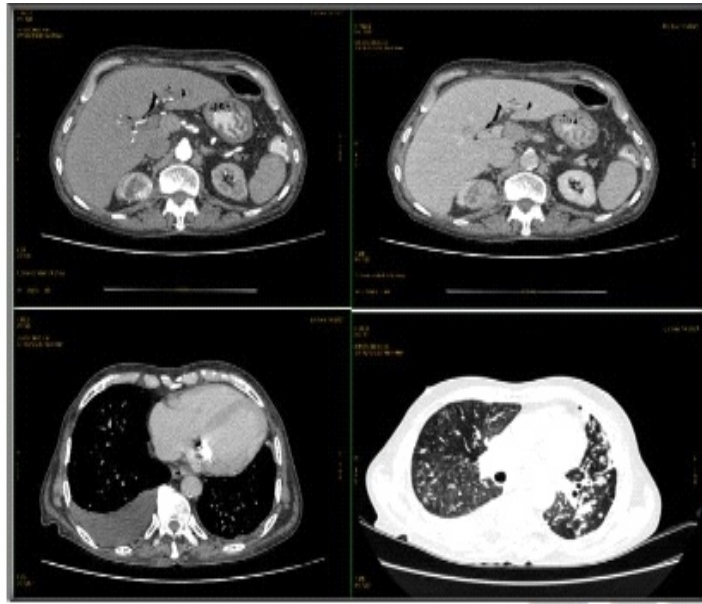


Figure 1. A well-defined hypodense lesion in the right kidney's upper pole that showed variable arterial phase enhancement and wash out in the delayed phase. Few centrilobular nodules and many nodular densities of various diameters in the bilateral lungs.

Case 2. Cystic RCC with metastases to lungs

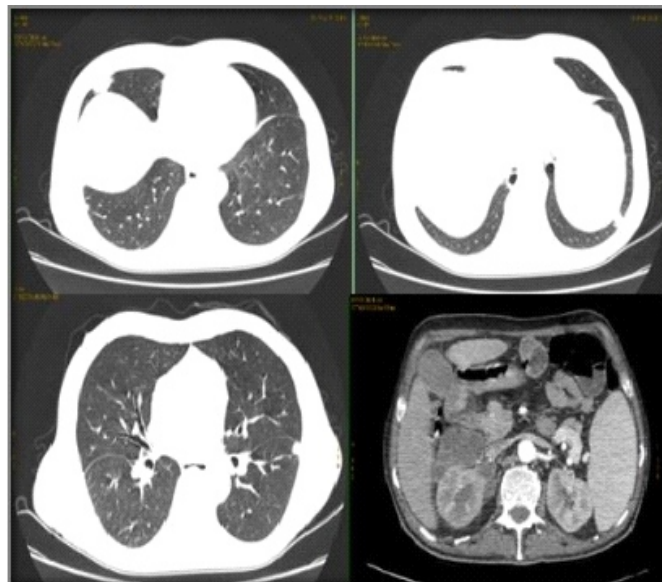


Figure 2. Well-defined loculated peripherally enhancing subcapsular cystic lesion encircling renal hilar vessels. Few sub-pleural nodules in bilateral lungs.

participants in the 50 to 82-year age. This distribution was further detailed as follows: 30% of patients were below 50 years, 23.4% fell within the 50-60 years range, 30% were in the 60-70 age category, and 16.6% were aged over 70 (table 1).

In this research, we present an overview of the diverse imaging patterns of pulmonary metastases across patients afflicted by different primary malignancies. A consistent feature among these patterns is the presentation of soft tissue density nodules in Renal Cell Carcinoma, while Testicular Germ Cell Tumor frequently displays large peripheral nodules. Thyroid cancer, on the other hand, exhibits a mixture of patterns, with Medullary Thyroid Carcinoma characterized by soft tissue density nodules and Papillary Thyroid Carcinoma showcasing a miliary pattern. Furthermore, various other malignancies including Osteosarcoma, GI Tract Adenocarcinoma, Gynecological malignancies, Femoral Vein Leiomyosarcoma, Breast Carcinoma, Lymphoma, and Lung Carcinoma each reveal their own distinct radiologic patterns. These observations underscore the rich diversity seen in the manifestation of pulmonary metastases (Table 2).

Discussion

The various types of breast cancer, identified by Chikarmane et al., (2014) include single or multiple pulmonary nodules, endobronchial localization, air-space consolidation, and lymphangitic carcinomatosis, which may mimic other primaries like pulmonary adenocarcinoma or lymphoma. A unilateral (and ipsilateral to the breast cancer) pleural effusion with no distinguishing characteristics as compared to benign effusions is a common manifestation of pleural localization.¹² In our investigation, of the four patients, three had numerous pulmonary nodules, and one displayed endobronchial location.

A little under 45% of RCC metastases, according to Brufau et al., (2013) were pulmonary metastases. 90% of the time, pulmonary metastases are asymptomatic.¹³ The findings on CT imaging include many nodules (75.6% of cases) or single nodules (30.5% of cases). The typical findings include well-circumscribed, round or oval, less than 2cm, subpleural situated lesions. "Cannonball" metastases, or tumors larger than 5 cm in diameter, are most frequently observed in RCC. RCC lung metastases

Case 3. Testicular germ cell tumour with metastases to lungs

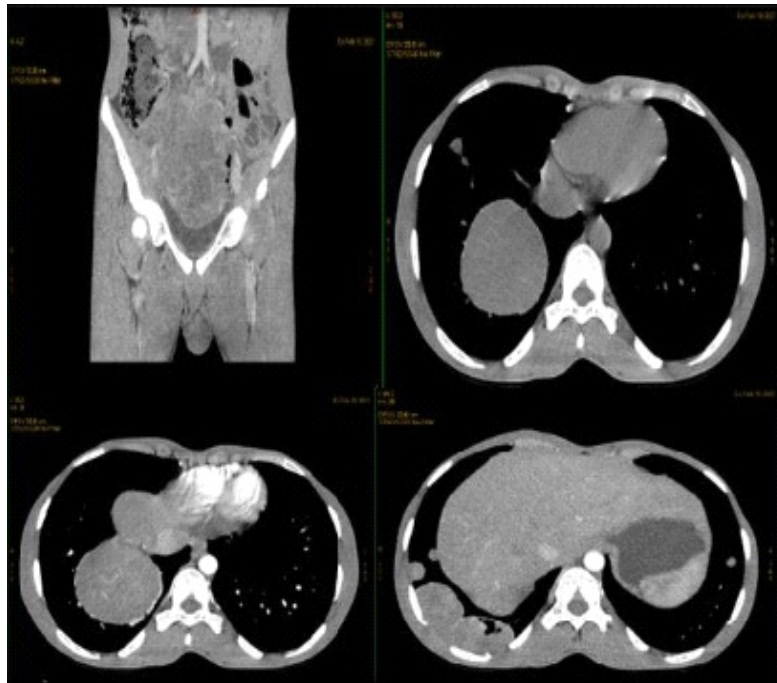


Figure 3. A patient with a right undescended testis has a massive, heterogeneously enhancing mass lesion in the pelvis. Take note of the testis in the left hemi scrotal sac. Large peripherally situated soft tissue density nodules in both lungs that exhibit little contrast enhancement. Testicular seminomatous germ cell carcinoma with lung metastases, according to HPE.

Case 4. Thyroid Malignancy Metastases to Lungs

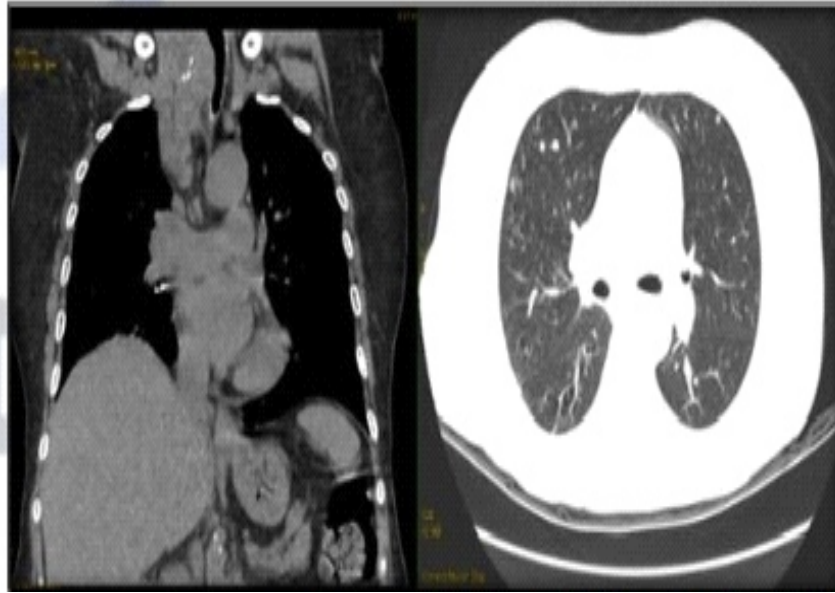


Figure 4. A well-defined, heterogeneously hypodense lesion with few calcific foci is seen. 4x3x4cm (APXTRXCC) in the right thyroid lobe that causes tracheal displacement to the left. Few soft tissue nodules in the bilateral lungs with a density of less than one centimeter. Thyroid medullary cancer has been confirmed by HPE.

Case 5. Osteosarcoma metastases to lungs

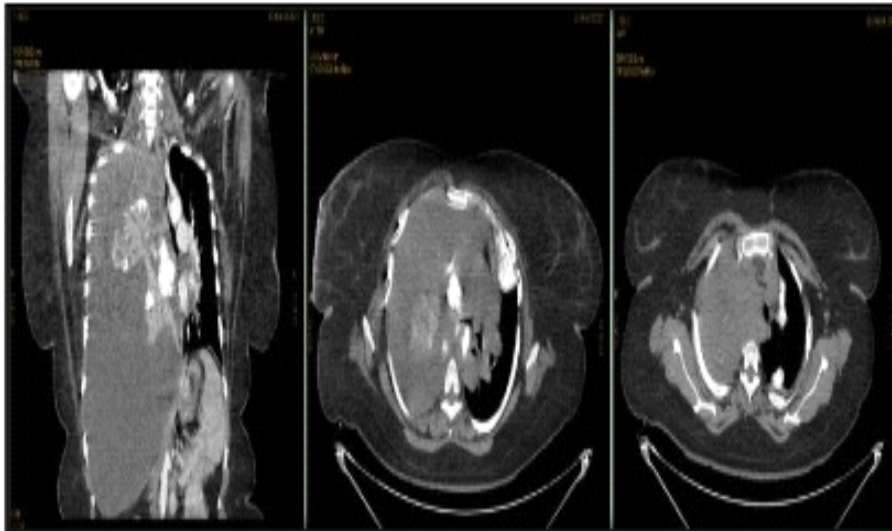


Figure 5. There is a documented instance of a left hip disarticulation due to a high-grade, aggressive osteosarcoma. Right lung collapsed many big nodules with substantial central calcification displaying sunburst pattern and enhancement on post contrast. Similar traits are shared by several big nodules in the left lung. Gross pleural effusion to the right.

Case 6. Pancreatic adenocarcinoma with metastases to lungs

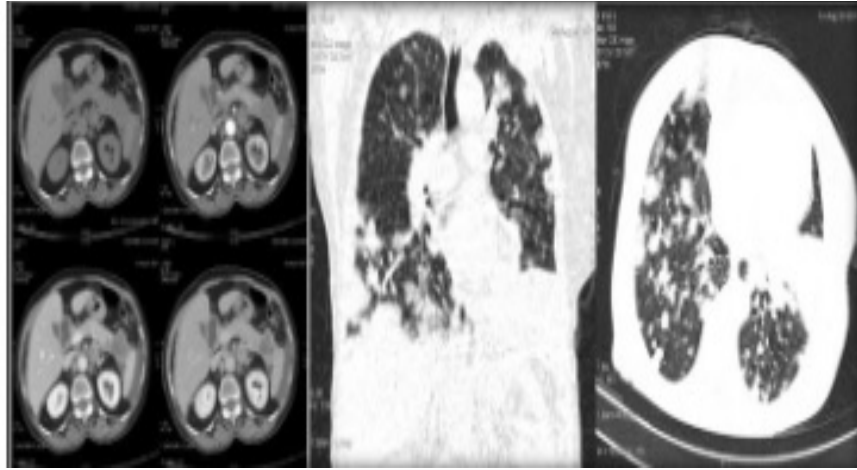


Figure 6. A well-defined multilobulated hypodense lesion with peripheral enhancement and pancreatic tail emergence. Bilateral lungs have many nodular opacities and patchy consolidation zones. Pancreatic adenocarcinoma was verified by HPE.

treated with antiangiogenic treatment may exhibit necrosis and cavitation. Antiangiogenic therapy-induced necrosis and the development of bronchopleural fistulae in metastatic lesions that have extensive contact with the pleura may indicate pneumothorax. In our research Four instances were present, and all four displayed multiple soft tissue density nodules that were primarily subpleural in nature.

According to a study led by Martínez et al., (2014) gynecological malignancies exhibit distinct patterns of pulmonary metastases. Endometrial cancer, encompassing Type 1 to Type 3, tends to present with multiple soft tissue density nodules and subpleural metastases in the lungs.¹⁴ Ovarian cancer, on the other hand, often leads to pleural metastases, appearing as either nodules or effusions, due to the transdiaphragmatic spread of perit-

Case 7. Cervical cancer showing cavitary metastases

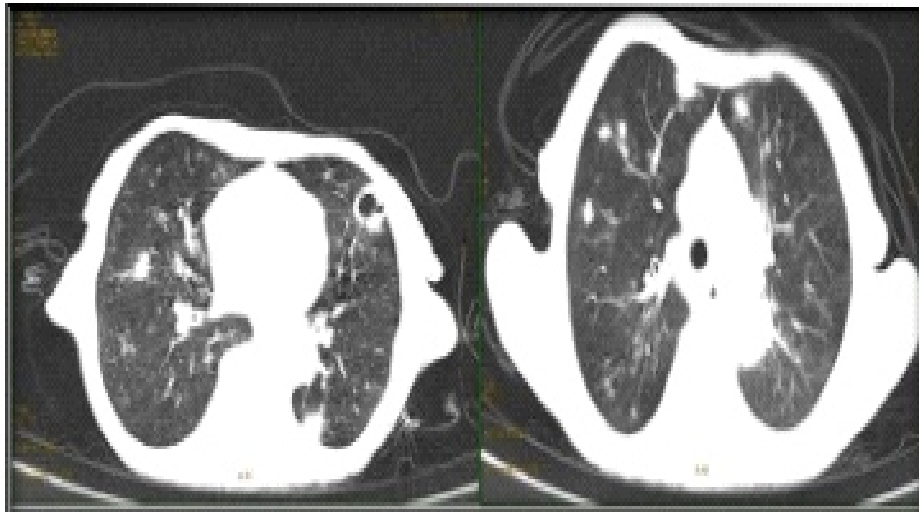


Figure 7. Multiple nodular opacities and cavitary changes noted in bilateral lungs with known case of cervical cancer.

Case 8. Soft tissue sarcoma with metastases to liver and lungs

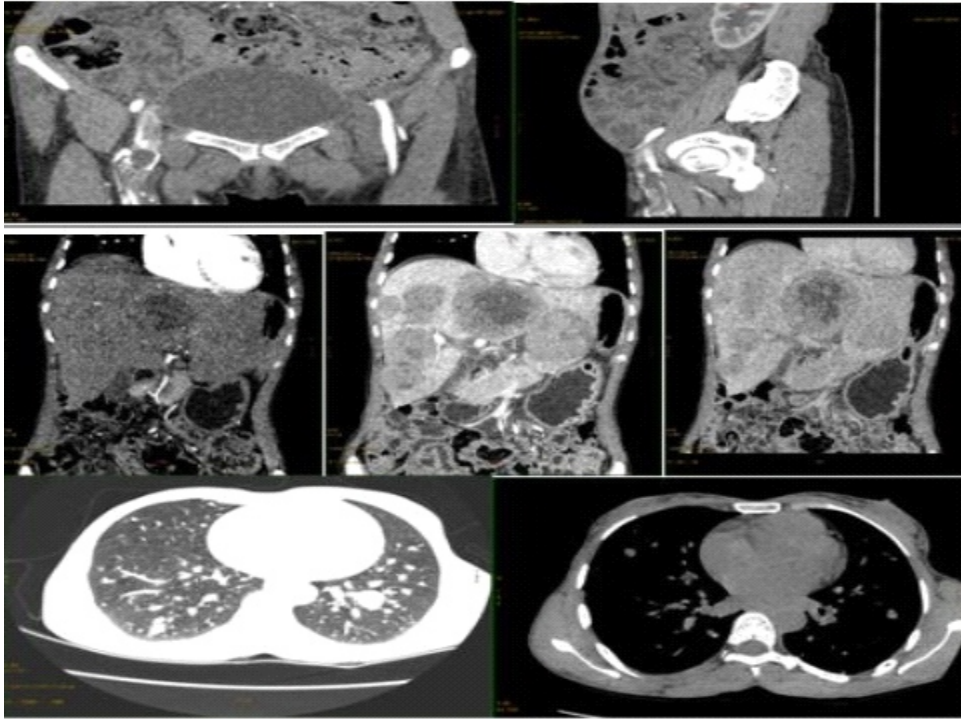


Figure 8. A massive, well-defined lesion in the right thigh that arises from the femoral vein causes the vein to enlarge and eventually replace itself. Leiomyosarcoma of the femoral vein. A tumor thrombus is indicated by a heterogeneously enhancing linear filling defect on the right side that extends from the tumor site to the external iliac vein. In both liver lobes, there are numerous well-defined heterogeneous hypodense lesions that exhibit peripheral heterogeneous enhancement in the arterial phase with few arterial feeders from the hepatic artery and progressive enhancement in the following phases with internal non-enhancing necrotic areas without any washout. Nodules with a high soft tissue density in both lungs.

oneal disease. Cervical cancer's pulmonary metastases manifest as cavitary lung lesions, setting it apart from other gynecological malignancies. Choriocarcinoma is characterized by hemorrhagic lung metastases, featuring a characteristic "halo" sign on CT scans. Finally, benign metastasizing leiomyomatosis (BML) typically results in asymptomatic patients with multiple solid lung nodules, often linked to a previous history of hysterectomy. In their study, among three cases of gynecological malignancies, two were attributed to endometrial cancer, showing multiple soft tissue density nodules as the prominent pulmonary metastatic feature. In contrast, the sole case of cervical cancer presented with only a few cavitary lesions in the lungs.

Metastatic adenocarcinoma in the lungs can exhibit a lepidic growth pattern, similar to bronchoalveolar carcinoma, and may present radiologically in a way that resembles pneumonia. According to a study by Joon et al., (2001), six out of 65 patients with adenocarcinoma

originating in the gastrointestinal tract displayed this particular metastatic pattern.¹⁵ Radiological findings associated with such metastases include focal or extensive ground-glass opacities, consolidations with air bronchograms, airspace nodules, and nodules featuring CT halo signs. In our own study, among four cases of gastrointestinal tract adenocarcinoma metastases, one case demonstrated a consolidation pattern containing an air bronchogram.

As per the research conducted by Wood et al., (2020) a macronodular pattern, often referred to as the "cannonball" appearance, characterized by distinct and well-defined margins, is a common feature in Medullary carcinomas of the thyroid.¹⁶ While pulmonary micronodular patterns are more frequently associated with metastatic papillary thyroid cancer, they are also observed in cases of Medullary thyroid cancer. It's important to note that granulomatous diseases like tuberculosis, histoplasmosis, or sarcoidosis typically

Case 9. Breast carcinoma metastases to lungs

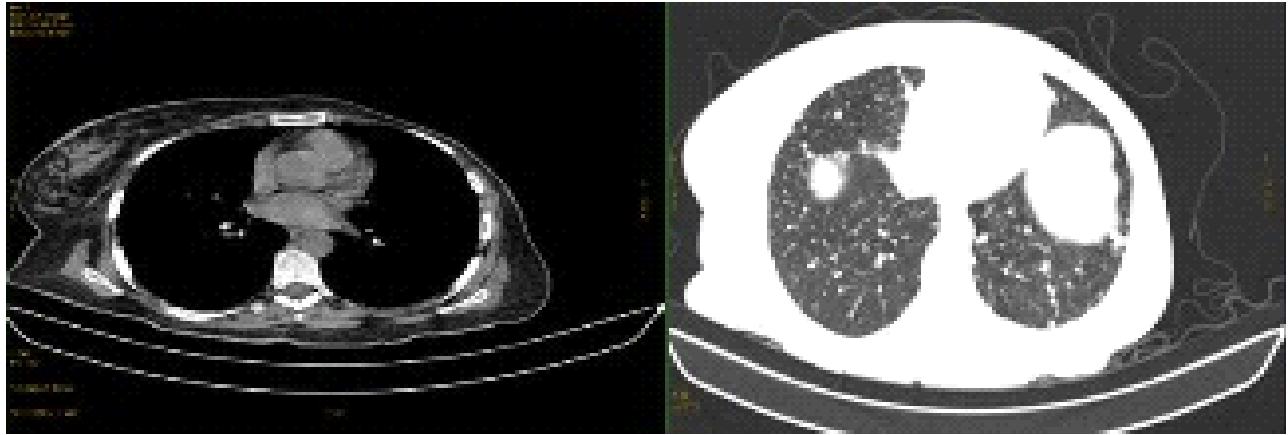


Figure 9. A known example of breast cancer underwent a mastectomy on the left breast. Soft tissue density nodules in the bilateral lungs, dispersed widely.

manifest as a micronodular pulmonary pattern, making diagnosis challenging at times. Additionally, reticulonodular perihilar lesions and calcified pulmonary metastases have been documented in the literature. Notably, very few instances of micronodular patterns in Medullary thyroid cancer have been reported in a comprehensive literature

review. In our study, which involved four cases, three were identified as medullary thyroid carcinoma, and one was papillary thyroid carcinoma. Among the medullary thyroid carcinoma cases, three showed the presence of multiple soft tissue density nodules. In contrast, the case of papillary thyroid carcinoma exhibited a miliary pattern of

Case 10. Carcinoma of lung with multiple metastases

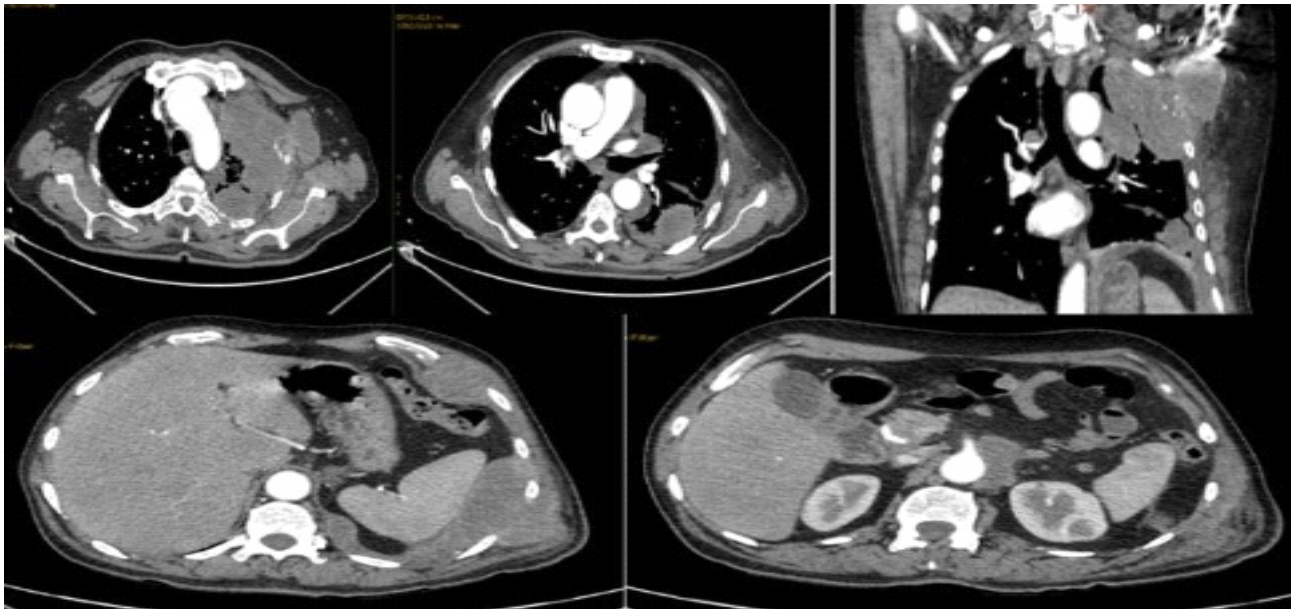


Figure 10. In the left hemithorax, left lateral chest wall, left anterior and posterolateral abdominal walls, intra and retroperitoneal regions with corresponding rib destructions, mediastinal and mesenteric metastatic lymphadenopathy, there are numerous well-defined conglomerate soft tissue density lesions. Several soft tissue lumps with subcentimetric

Case 11. Lymphoreticular malignancy like lymphoma metastases to lungs

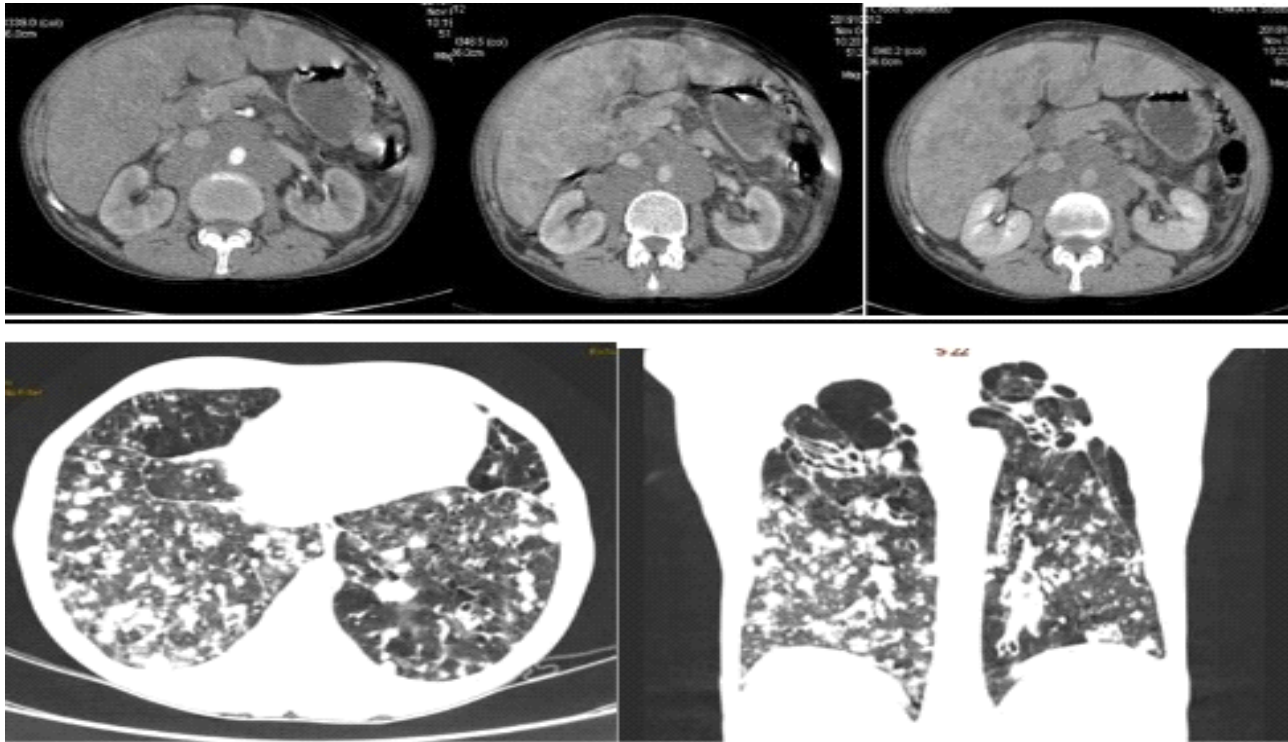


Figure 11. Multiple well defined hypoenhancing lesions can be found in the liver's two lobes. Conglomerate hypoenhancing lymph nodes covering the IVC, bilateral renal arteries, and the aorta in the prevertebral area from L2 to L5. Background fibrobronchiectatic lung disease is interlaced with many soft tissue density nodules.

metastases, which sets it apart from the others in terms of radiological presentation.

According to the research conducted by Seo et al., (2001) the presence of calcification within a lung nodule is typically associated with benign lesions such as granulomas or hamartomas.¹⁵ However, it's important to note that calcification can also occur in metastatic nodules from osteosarcoma or chondrosarcoma. The literature reports sarcomas like osteogenic sarcoma, chondrosarcoma, synovial sarcoma, and giant cell tumor as entities that can give rise to calcified lung metastases. Moreover, papillary and mucinous adenocarcinomas are among the metastatic tumors most likely to develop calcified lung metastases. Additionally, calcification may occur in various tumors after undergoing antineoplastic therapy. Different mechanisms of calcification, such as ossification of tumor cartilage, mucoid calcification, and dystrophic calcification, are observed in metastases from different primary sources. It's worth emphasizing that while calcification is a common finding in benign lesions, a level of suspicion is warranted when evaluating calcification within a pulmonary nodule for potential metastases.

In our specific study, we observed two cases originating from osteosarcoma, both of which displayed multiple large nodules characterized by extensive central calcification, forming a distinctive sunburst pattern.

According to a study by Angirish et al., (2020) and her colleagues, approximately 15% of patients diagnosed with Non-Seminomatous Germ Cell Tumors (NSGCT) present with pulmonary metastases at the time of their initial diagnosis.¹⁷ In comparison to seminomas, NSGCT patients are approximately 20 times more likely to develop intrathoracic metastases. These metastases from seminomas tend to appear as larger nodules, measuring at least 1 to 2 cm, with a more uniform density. Conversely, NSGCT patients often exhibit small, peripheral, and bilateral pulmonary nodules.

The primary mode of pulmonary metastasis is through hematogenous dissemination, although there is also a possibility of lymphatic spread via the thoracic duct, which can lead to involvement of the left supraclavicular nodes and subsequently the lungs. Depending on the histology of the tumor, the pattern of mediastinal spread varies. NSGCTs tend to spread less consistently to the

anterior mediastinum, aortopulmonary window, and hilar, supraclavicular, and cervical lymph nodes. They frequently spare the posterior mediastinum and subcarinal regions. In contrast, seminomas tend to disseminate via the thoracic duct to the posterior mediastinum in a nearly contiguous manner, and approximately 70% of metastatic testicular seminomas display mediastinal involvement. In our specific study, we observed two cases originating from seminomatous germ cell tumors of the testis. These cases featured large, peripherally located soft tissue density nodules within the lungs.

In accordance with the findings presented by Purandare et al., (2015) and her research team, lung involvement in lymphoma can manifest through various patterns, including the presence of large masses, mass-like consolidations, nodules with or without cavitation, ground glass opacities, and the appearance of a lymphangitis or perilymphatic pattern.¹⁸ In our study, we encountered a particular case of diffuse lymphoma, which exhibited multiple soft tissue nodules within the lung parenchyma, interspersed within a background of fibrobronchiectatic lung disease. This case was further notable for the presence of extensive abdominal and mediastinal lymphadenopathy, adding to the complexity of its radiological presentation. Within the context of this study, we observed a single case of pulmonary metastases originating from leiomyosarcoma of the right femoral vein. This particular case presented with multiple soft tissue density nodules that exhibited heterogeneous enhancement, evident in both bilateral lung fields.

As per the research conducted by Martínez et al., (2014), it is noteworthy that over 50% of lung cancer patients initially present with metastatic disease, and the common sites for these distant metastases include bones, adrenals, the brain, and the liver.¹⁴ This metastatic disease is further classified into M1a, indicating intrathoracic metastasis, and M1b, signifying extrathoracic metastases. It's important to recognize that M1a cases generally have a more favorable prognosis when compared to M1b. The M1a category encompasses malignant pleural effusion, pleural metastases, pericardial disease, and pulmonary nodules in the contralateral lung. On the other hand, M1b comprises metastases to distant sites such as bones, adrenals, liver, brain, and any other extra-thoracic locations. In our own study, we identified five cases of pulmonary metastases originating from lung carcinoma, characterized by the presence of multiple subcentimetric soft tissue density nodules dispersed throughout the bilateral lung parenchyma.

Conclusion

Characteristic radiological findings of pulmonary metastasis often include the presence of multiple, round, and variably sized nodules, along with the diffuse thickening

of the lung interstitium. The diversity in these patterns can complicate the accurate diagnosis of pulmonary metastases, making it essential to understand the distinct patterns associated with metastases from various primary sources. This knowledge of the different pulmonary metastatic patterns originating from diverse primaries proves invaluable in facilitating early diagnosis of metastases and their respective primary malignancies.

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