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Original Article

Role of High-Resolution Computed tomography in the Evaluation of Pulmonary Metastases: A Tertiary Hospital-Based Study

M. Vijay Kumar, K. Ravindranath Reddy

Department of Radiology, Associate Professor of Radiology, Viswabharathi Medical College and Hospital, R T Nagar, Penchikalapadu, Kurnool, Andhra Pradesh, India

Abstract

Background: Pulmonary metastases constitute 20–54% of extrathoracic malignancies occurring all over the world. Twenty percent of metastatic disease is isolated to the lungs. Development of lung metastases indicates disseminated disease in patients with known malignancies and puts them in stage IV of tumor, node, and metastasis staging system. This otherwise implies an adverse prognosis and alters the management plan. The role of high-resolution computed tomography (HRCT) remains very important in the screening, detection, and staging of pulmonary metastases. Imaging guidance is also used in histologic confirmation of metastatic disease.

Aim of the study: The aim is to study the role of HRCT in the diagnosis of metastases in the lungs using standard methods of HRCT characteristics and cytology/histopathological reports and to calculate the specificity and sensitivity of HRCT in the diagnosis.

Materials and Methods: A total of 46 patients with nodular opacities on plain X-Rays of the chest posteroanterior view, attending the department of radiology, were included in the present study. Among them, 39 patients (Group A) were diagnosed previously and under treatment for primary malignant diseases in the same hospital. The other 7 patients (Group B) were not having any primary malignant disease. They were subjected to HRCT chest to include the apices through the lung bases with an average of 18–20 slices per chest at 2 mm intervals. All the HRCTs were reported by a single radiologist. All the patients were either subjected to image-guided or ultrasound-guided fine-needle aspiration cytology or thoracotomy and biopsy. The HRCT characteristics of the margins of the nodules were classified into four types: (1) Well-defined and smooth margin, (2) well-defined and irregular margin, (3) poorly defined and smooth margin, and (4) poorly defined and irregular margin. The HRCT contrast characteristics were classified as solid, mixed, and ground glass types depending on the contrast enhancement of the lesions.

Observations and Results: Of 46 patients, Group A had 27 males and 12 females with a male-to-female ratio of 1:2.25. The mean age was 53.35 ± 6.70 years. Group B had 5 males and 2 females with a male-to-female ratio of 1:2.5. The mean age was 59.20 ± 3.85 years. All the patients were smokers. Group "A," 25/39 (64.10%), patients had a history of intake of alcohol. In Group B, 4/7 (57.14%) patients had a history of intake of alcohol. In Group A, 10/39 (25.64%) were working as industrial workers (alkali industry and carbide industry), 11/39 (28.20%) were agricultural laborers, and the remaining 7/39 (17.94%) were office goers. In Group B, 2/7 (28. 57%) were working as industrial workers (alkali industry and carbide industry), 3/7 (42.85%) were agricultural laborers, and the remaining 2/7 (28.57%) were office goers. There was no statistical significance between the two groups in regard to demographic information, with $P = 0.341$ ($P < 0.05$). The specificity of HRCT in the diagnosis of pulmonary metastases was 80% and the sensitivity was 90.47%.

Conclusions: HRCT of the chest plays a vital role in the diagnosis of pulmonary metastases either primarily or secondarily. HRCT remains the preferred imaging modality for pulmonary metastases. The technique has some limitations in the detection of pulmonary metastases, especially for nodules <5–6 mm. The specificity of HRCT in the diagnosis of pulmonary metastases was 80% and the sensitivity was 90.47% in the present study.

Key words: Fine-needle aspiration cytology, High resolution computed tomography, Histopathology and thoracoscopy, Primary malignancy, Pulmonary metastases

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INTRODUCTION

The lungs are the organs that are most frequently targeted by metastases from primary malignant tumors. Hence, their assessment remains of paramount importance in the management of oncologic patients.[1] Plain X-ray chest is the standard modality for detection and monitoring, but

Corresponding Author: Dr. K. Ravindranath Reddy, Department of Radiology, Viswabharathi Medical College and Hospital, R T Nagar, Penchikalapadu, Kurnool, Andhra Pradesh, India

there is an increasing use of high-resolution computed tomography (HRCT) or positron-emission tomography (PET) CT scan which is more sensitive in imaging technique for better identification of metastases.[2] In the daily radiological practice staging and regular follow up of patients with malignant diseases remains a challenge to the radiologist; the extensive knowledge about the pathophysiology and imaging features of metastatic disease, differential diagnosis, and the impact of the diagnosis on patients' management are major concerns for the radiologist.[3] Malignancies of the head and neck, thyroid, adrenals, kidneys, testes, melanomas, and osteosarcomas spread through hematogenous route directly to the lungs.[1] The other common primary malignancies included in adults are breast carcinoma and colorectal carcinoma.[4] The less common primaries metastasizing to the lungs are choriocarcinoma and Ewing's sarcoma.[5] Among children, the common primaries are rhabdomyosarcoma, esthesioneuroblastoma, Wilm's tumor, Ewing's sarcoma, and osteosarcomas. Secondaries in the lungs are usually asymptomatic, with or without constitutional symptoms related to disseminate metastatic disease and/or primary tumor dominating.[6] Sometimes pulmonary metastases may present with haemoptysis and pneumothorax. CT scan features of secondaries in the lung are classified into four types: (1) Well-defined and smooth margin, (2) well-defined and irregular margin, (3) poorly defined and smooth margin, and (4) poorly defined and irregular margin.[7] If the margin is sharp and distinct and separated from the surrounding normal lung, it is considered well defined. If the margin of the nodule is hazy or indistinct with its edge merging imperceptibly into the surrounding lung, then it is considered as poorly defined.[8] Lung metastases on CT scan may also present as diffuse miliary seeding in medullary carcinoma of the thyroid, as large singular metastases in choriocarcinoma, melanoma, and hypernephroma, as calcification of metastases (osteosarcomas, adenocarcinoma, and secondary to chemo- and radiation therapy), and as cavitation of pulmonary metastases in squamous cell carcinoma of the head and neck and from the genitourinary tract in women.[9] Pulmonary metastatic disease will also appear as lymphangitic carcinomatosis in tumors of the stomach, breast, pancreas, uterus, rectum, and prostate.[10] Using thin-section HRCT (i.e., 2 mm slice thickness), the rate of detection of the non-calcified pulmonary nodules was found to be 75% in patients with extrapulmonary malignant tumors.[11] In the present study, the role of HRCT in the diagnosis of metastases in the lungs was analyzed using standard methods of CT scan characteristics and cytology/histopathological reports. There was also an attempt to calculate the specificity and sensitivity of CT scan in the diagnosis.

Type of the Study

This was a progressive, cross-sectional, and analytical study.

Period of Study

The study duration was from January 2013 to December 2015.

Institute of Study

The study was conducted at the Department of Radiology, Viswabharathi Medical College and Hospital, R T Nagar, Penchikalapadu, Kurnool, Andhra Pradesh.

MATERIALS AND METHODS

A total of 46 patients with nodular opacities on plain X-Rays of the chest posteroanterior (PA) view, attending the Department of Radiology, were included in the present study. Among them, 39 patients (Group A) were diagnosed previously and were under treatment for primary malignant diseases in the same hospital. The other seven patients (Group B) were not having any primary malignant disease. An Institutional Ethical Committee Clearance was obtained before the commencement of the study. An ethical committee cleared consent form was used during the study.

Inclusion Criteria

1. Patients aged >25 years and <80 years were included.
2. Patients belonging to both the genders were included.
3. Patients with nodular opacities on plain X-rays of chest PA view were included.
4. Patients with or without established primary malignancy were included.

Exclusion Criteria

1. Patients <25 years and >80 years were excluded.
2. Patients who are already confirmed the diagnosis of secondary metastases of lug by biopsy were excluded.
3. Patients with debilitating illnesses or immunodeficiency were excluded. All the patients were subjected to HRCT chest to include the apices through the lung bases with an average of 18–20 slices per chest at 2 mm intervals. Scans were viewed on a 320 × 320 matrix at varying window widths and density settings. Small nodules were distinguished from vessels on end by serially tracing the latter through multiple contiguous cuts.

All the HRCT scans were reported by a single radiologist. All the patients were either subjected to image-guided or ultrasound-guided fine-needle aspiration cytology (FNAC) or thoracotomy and biopsy. At the time of operation, the locations of all pulmonary nodules were recorded. The HRCT characteristics of the margins of the nodules were

classified into four types: (1) Well-defined and smooth margin, (2) well-defined and irregular margin, (3) poorly defined and smooth margin, and (4) poorly defined and irregular margin. A margin was considered well defined if the nodule was sharply and distinctly separated from the surrounding normal lung and as poorly defined if it was hazy or indistinct, with its edge merging imperceptibly into the surrounding lung. The shape of the metastatic nodules was noted and classified as round, polygonal, and complex. The CT scan contrast characteristics were classified as solid, mixed, and ground glass types depending on the contrast enhancement of the lesions. The FNAC and histopathological findings of the nodules were classified as: (1) Expanding type: The tumor merely displaces the surrounding normal structures; (2) alveolar space-filling type: The tumor invades and fills alveolar spaces; (3) alveolar cell type: The tumor grows along the alveolar walls, continuously covering them; and (4) interstitial proliferation type: The tumor invades the interstitium. All the data were analyzed using standard statistical methods.

OBSERVATIONS AND RESULTS

A total of 46 patients presenting with nodular opacities on plain X-ray of the chest were included in the present study. Among them, 39 patients (Group A) were diagnosed previously and under treatment for primary malignant diseases in the same hospital. The other seven patients (Group B) were not having any primary malignant disease. In Group A, there were 27 males and 12 females with a male-to-female ratio of 1: 2.25. The youngest patient was aged 35 years and the eldest patient aged 71 years with a mean age of 53.35 ± 6.70 years. In Group B, there were 5 males and 2 females with a male-to-female ratio of 1:2.5. The youngest patient was 41 years old and the eldest patient was aged 77 years with a mean age of 59.20 ± 3.85 years. There was a history of smoking in all the patients of both the groups. In Group "A," 25/39 (64.10%) patients had a history of intake of alcohol. In Group B, 4/7 (57.14%) had a history of intake of alcohol. In Group A, 10/39 (25.64%) were working as industrial workers (alkali industry and carbide industry), 11/39 (28.20%) were agricultural laborers, and the remaining 7/39 (17.94%) were office goers. In Group B, 2/7 (28. 57%) were working as industrial workers (alkali industry and carbide industry), 3/7 (42.85%) were agricultural laborers, and the remaining 2/7 (28.57%) were officegoers [Table 1]. There was no statistical significance between the two groups with $P = 0.341$ ($P < 0.05$).

In Group A, 39 patients were presenting with different variety malignancies, such as lymphomas - 9, renal cell carcinoma - 3, hepatic cell carcinoma - 2, osteosarcomas - 6, testicular carcinoma - 04, nephroblastoma - 3, laryngeal and hypopharyngeal carcinomas - 6, oral cavity squamous cell carcinoma – 3, and rhabdomyosarcoma and Ewing's sarcomas - 3. Their occurrence of laterality, presentation of number of nodules and whether the metastatic nodules were centrally placed or diffuse were tabulated in Table 2. Overall there were 94 nodules which were observed among the 39 patients of Group A.

In Group "A" patients, features of pulmonary metastatic nodules in terms of size, shape, contrast uptake, and the margins are observed and tabulated in Table 3.

The Group B patients with nodular opacities on plain X-Ray chest PA view were further investigated with HRCT. All the lesions were subjected to image-guided FNAC and combined with the Group A patients

Table 1: The age, gender incidence, and the demographic data of the study group (*n*-46)

Group	Male	Female	Smokers	Alcohol consumers	Industrial workers	Agricultural laborers	Officegoers	Mean Age	Male: Female
A-39	27	12	27	25	10	11	7	53.35±6.70	1:2.25
B-07	5	2	7	4	2	3	2	59.20±3.85	1:2.50

Table 2: The CT scan characteristics in the Group "A" patients (*n*-39)

Primary Diagnosis of malignancy	Unilateral	Bilateral	2–6 nodules	6 nodules	Central	Diffuse
Lymphomas - 9	2	7	2	7	2	6
Renal - 3	1	2	0	2	1	2
Hepatic - 2	1	1	1	1	0	2
Bone - 6	3	5	4	2	3	3
Gonads - 4	1	3	1	3	1	3
Trophoblastic - 3	1	2	1	2	0	3
Head and neck - 6	4	2	4	2	4	2
Oral cavity - 3	2	1	2	1	1	2
Sift tissue sarcomas - 3	0	3	1	2	1	2

CT: Computer tomography

for analysis. The HRCT types were compared with results obtained from the FNAC and histopathological examinations. FNAC was done in 21/46 (45.65%) of the patients, and biopsy (by thoracotomy) followed by histopathological examinations of the tissues was done in 12/46 (26.08%) patients in this study. Only 6/12 (50%) patients who underwent thoracotomy and biopsy had undergone FNAC also. Overall 27/46 (58.69%) patients were classified according to the cytology/pathology reports (in other words, 27 nodules). Among these 27 nodules, 13/27 (48.14%) were each <5 mm in diameter and identified on HRCT scans and were studied separately. There was a correlation between CT scan reports and cytology/histopathological studies in 19/27 of the patients (70.37%) (true positive). There were 01/27 (07.40%) false positive pathology reports, 04/27 (18.51%) true negative reports, and 02/27 false negative reports. The specificity and sensitivity of CT scan findings in the diagnosis of secondaries in the lungs were calculated and found that the sensitivity was 90.47% and specificity was 80%. In this study, CT scan could be used as a diagnostic tool in the final diagnosis of secondaries in the lungs [Table 4].

DISCUSSION

The incidence of pulmonary metastatic disease in patients who have primary malignant disease or have died of an extra-thoracic malignancy is reported as 20–54%.[12] The indications for chest radiography, HRCT, magnetic resonance imaging (MRI), and scintigraphic imaging have been discussed in the literature. There have been improvements in HRCT imaging quality and scan time, as well as advances in the field of nuclear medicine and MRI. There have been more studies on the use of PET-CT in the evaluation of patients with metastatic pulmonary disease.[13] In comparison with plain X-ray of chest, HRCT is more sensitive for detecting pulmonary nodules, due to its lack of superimposition and its high-contrast resolution.[12,13] In patients who are diagnosed with malignant disease, HRCT scan is recommended if the initial chest radiograph reveals an apparent solitary pulmonary nodule or an equivocal finding. If the chest radiograph is negative, HRCT is recommended if the underlying primary malignant disease is highly known for dissemination to the lungs, such as breast, renal cell, colon, and bladder carcinoma. Even if there are multiple nodes in the lungs on plain X-ray, HRCT of the chest is indicated if FNAC/biopsy or definitive treatment by metastasectomy or systemic therapy is planned.[14] HRCT scanning is more sensitive than conventional CT, allowing the detection of a significantly larger number of nodules and also a larger number of small nodules. In this study, a 16 slice spiral CT scan was used to evaluate pulmonary metastases. Review of literature shows a few studies that have correlated HRCT findings with surgical or pathologic findings, and they offer encouraging results. McCormack *et al.*[15] found that CT underestimated the surgical pathologic findings in 25% of cases. More thorough detection of metastatic nodules is possible at thoracotomy by means of manual palpation of the entire collapsed lung.[16,17] In the present study, 46 patients with nodular

Table 3: The CT scan features of patients with primary malignancy presenting with pulmonary metastases (*n*-39)

Primary diagnosis	Size		Round	Oval	Polygonal	complex	Solid	Mixed	Ground glass	Smooth margin	Irregular margin
	5 mm	6–10 mm									
Lymphomas - 9	1	4	0	1	6	2	5	2	1	5	4
Renal - 3	1	2	1	1	1	0	2	0	1	2	1
Hepatic - 2	1	1	0	0	1	1	1	0	1	1	1
Bone - 6	4	2	2	2	1	1	3	1	2	4	2
Gonads - 4	3	1	1	1	1	1	2	1	1	2	1
Trophoblastic - 3	3	0	0	1	1	1	2	0	1	2	1
Head and neck – 6	1	5	0	0	2	4	3	1	1	4	2
Oral cavity - 3	0	3	0	0	1	2	1	1	1	2	1
Soft tissue sarcomas - 3	0	3	0	0	0	3	2	0	1	2	1

CT: Computer tomography

Table 4: The sensitivity and specificity of CT scan reports in the diagnosis of pulmonary metastases (*n*-27)

Observation	True positive	False positive	True negative	False negative
Cytology and histopathological reports	19	1	4	02
Specificity	80%	-	-	-
Sensitivity	90.47%	-	-	-

CT: Computer tomography

features on plain X-ray of the chest were included. They were grouped as those with primary malignant disease and those without. Overall 94 metastatic lesions in the lung were investigated in this study. It is now recognized that even small pulmonary nodules may represent malignant lesions. In a study of a series of patients undergoing video-assisted thoracoscopy resection of small (≤1 cm) pulmonary nodules, 28 malignant lesions were diagnosed in 27 patients with a history of previous malignancy; 23 lesions (84%) were malignant, including 15 metastases (54%) and eight new lung carcinomas (29%), and five nodules (18%) were benign.[18] In this study, HRCT scan types were compared with results obtained from the FNAC and histopathological examinations. FNAC was done in 21/46 (45.65%) of the patients, and biopsy (by thoracotomy) followed by histopathological examinations of the tissues was done in 12/46 (26.08%) patients in this study. Only 6/12 (50%) patients who underwent thoracotomy and biopsy had undergone FNAC also. Overall 27/46 (58.69%) patients were classified according to the cytology/pathology reports (in other words 27 nodules). Among these 27 nodules, 13/27 (48.14%) were each <5 mm in diameter and identified on HRCT scans, were studied separately. The specificity of CT in any given series depends on several variables: (1) The behavior of the underlying primary malignant disease to disseminate to the lungs, (2) the stage of the primary disease, (3) selection factors for the study population, and (4) patient age, smoking history, history of prior treatment for the primary malignant disease, and likelihood of prior granulomatous disease.[16] In one study, 22% (9/41) more malignant nodules were found intraoperatively than were detected by helical CT.[20] In a study by Stefano *et al.*,[21] the sensitivity of CT scan was 82%. They concluded that the CT scan sensitivity decreased according to the size of metastases: No false negatives for lesions ≫10 mm, 11/34 (32%) for lesions ≪10 mm and ≫6 mm, and 20/52 (38.5%) for lesions ≫6 mm were observed. The sensitivity of CT scan for lesions ≫6 mm was 91% (11/121 false-negatives). Similar conclusions were proposed by Diederich et al.[22] in their CT surgical correlation on 43 histologically proven metastases, and the sensitivity of CT scan for lesions ≫6 mm was 95% but decreased to 69% for lesions <6 mm. In this study, there was a correlation between CT scan reports and cytology/histopathological studies in 19/27 of the patients (70.37%) (true positive). There were 01/27 (07.40%) false positive pathology reports, 04/27 (18.51%) true negative reports, and 02/27 were false negative reports. The specificity and sensitivity of CT scan findings in the diagnosis of secondaries in the lungs were calculated and found that the sensitivity was 90.47% and specificity was 80%.

CONCLUSIONS

CT scan of chest plays a vital role in the diagnosis of pulmonary metastases either primarily or secondarily. CT scan remains the preferred imaging modality for pulmonary metastases. The technique has some limitations in the detection of pulmonary metastases, especially for nodules <5–6 mm. The specificity of CT scan was 80% and the sensitivity was 90.47% in the present study.

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