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Diagnostic Accuracy of Computerised Tomography in Differentiating Between Benign and Malignant Lung Masses and Need for Histopathological Studies for Final Diagnosis

KEYWORDS: CT, malignant, sensitivity, specificity

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ABSTRACT ***OBJECTIVE:*** *To analyse role of CT in differentiating benign from malignant lung mass and to establish the sensitivity, specificity, positive and negative predictive values of CT-thorax in diagnosing malignant masses.* ***METHOD:*** *Retrospective study in 100 patients who have undergone CT scan for lung mass. Based on CT features a provisional diagnosis was made, matched with pathology reports and results statistically analysed.* ***RESULTS:*** *The diagnostic accuracy of CT in diagnosing malignant lung lesions came out as 85%; 96% sensitive, 70% specific, 80% PPV and 93.5% NPV .* ***CONCLUSIONS:*** *CT is a highly sensitive but moderately specific diagnostic tool for evaluation of lung masses. High negative predictive value shows that benign lesions are diagnosed fairly accurately. So, ideally CT should be the first line diagnostic modality in differentiating benign from malignant conditions. Confirmatory histopathology can be used for appropriate therapy in malignancy and in indeterminate category lesions.*

INTRODUCTION:

Lung cancer is the most common cancer worldwide. The idea of radiological evaluation of suspected pulmonary lesions is to noninvasively differentiate between benign and malignant forms.

Computed Tomography (CT) is accepted as the state-of-the-art modality for detection of possible pulmonary nodules. . CT can identify specific features in lung nodules that are diagnostic of malignancy characteristics such as lesion size, location, contour and edge and density (including the presence or absence of calcifications or fat) which should be evaluated.

In order to confirm the CT diagnosis, a histopathologic follow-up is done for majority of the patients. But FNAC has its own set of complications. Hence if a lung mass can be diagnosed accurately just by imaging technique, complications associated with needle biopsy of lung can be avoided. This retrospective study conducted will show the diagnostic match rate between CT and histopathologic evaluation. This analysis will help to establish the sensitivity and specificity of CT scan as a diagnostic modality for detecting malignant lung masses.

Review of Literature:

A solitary pulmonary nodule is defined as a discrete, well-marginated, rounded opacity less than or equal to 3 cm in diameter that is completely surrounded by lung parenchyma. It does not touch the hilum or mediastinum, and is not associated with lymphadenopathy, atelectasis or pleural effusion.

Lesions larger than 3 cm are considered masses and are treated as malignancies until proven otherwise. The accurate characterization of a lung lesion as a benign or malignant form found on routine chest imaging is a diagnostic dilemma.

Standard radiologic evaluation of a suspected pulmonary lesion includes careful review of findings at chest radiography and when appropriate, comparison with findings of prior radiography, chest fluoroscopy, CT and correlation with clinical signs and symptoms.

In the study conducted at KMC Manipal, CT-scan is the imaging modality which has been used to evaluate pulmonary nodules.

CT is 10 to 20 times more sensitive than standard radiography and allows objective, quantitative assessment of calcification. Initial evaluation often results in nonspecific findings, in which case nodules are classified as indeterminate and require further evaluation to exclude malignancy.

Size of the lung lesion is an important factor for assessment, as majority of benign nodules are small in size. In a study conducted by Steele et al[1] 80% of solitary nodules larger than 3 cm in diameter are found to be malignant , compared to 20 % of nodules less than 2 cm in diameter, while studies done by Zerhouni et al demonstrated that more than 90 % of lesions larger than 3 cm are malignant.[2,3]

As per the study conducted by British Columbia Cancer Agency, the rate of malignancy is found to be highest-17% in lesions greater than 10mm size followed by lower rates - 1% and 0.2% in lesions of sizes 4-10mm and less than 4 mm respectively.[4]

According to Zwirewich CV et al, homogeneous attenuation is seen at thin-section CT in both benign (55%) and malignant (20%) nodules.[5]

As per studies done by Zwirewich,Weisbrod GL and Lee KS et al, pseudocavitation (small, focal, low-attenuation regions within or surrounding the periphery of a nodule) and air bronchograms within a nodule are suggestive of bronchioalveolar cell carcinoma and lymphoma respectively.[5,6,7]

Cavitations also occur in both benign and malignant nodules. Benign cavitating nodules generally have smooth, thin walls, whereas malignant nodules typically have thick, irregular walls.[8, 9]

Studies by Woodring JH et al states that most nodules with a wall thickness greater than 16 mm are malignant, whereas those with a wall thickness less than 4 mm are usually benign.[10, 11]

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However, there is significant overlap, and wall thickness alone cannot be used to confidently differentiate benign from malignant cavitary nodules .Other features like presence of intranodular fat indicates hamartoma.

Nodule margins and contours can be classified as smooth, lobulated, irregular, or spiculated. According to Siegelman SS et al, although most nodules with smooth, well-defined margins are benign, these features are not diagnostic for a benign cause: 21% of malignant nodules have well-defined margins.[12] Rigler et al showed that a smooth border has a 20 % likelihood of malignancy. The likelihood increases to 60 % with a scalloped border, 90% with spiculations and 95% in the presence of corona radiatae.[13]

The presence and pattern of calcification can also help differentiate benign from malignant nodules. There are four benign patterns of calcification: central, diffuse solid, laminated, and "popcorn like." Lung cancers as well as typical and atypical primary pulmonary carcinoid tumours may calcify; calcification is detected at CT in up to one-third of carcinoid tumours. Thus, care must be taken to differentiate benign from malignant patterns of calcification. When present, these patterns of calcification are reliable indicators of a benign cause as suggested by Jeremy J Erasmus et al.[14]

Recent studies by Ann Leung and Robin Isthmus have shown that an air bronchogram is more commonly seen in malignant pulmonary nodules. It is most commonly seen in bronchi alveolar cell carcinoma and adenocarcinoma.[15]Associated features like lymph node metastases, bronchial cut-off and rib involvement have been considered as important contributory factors while evaluating the malignancy of the lesion.

Typical radiologic findings of a pulmonary metastasis include multiple peripherally located round variable-sized nodules (haematogenous metastasis) and diffuse thickening of the interstitium (lymphangitic carcinomatosis). [16,17] Among cases of multiple nodules detected with CT, 73% were reported to be pulmonary metastases by Gross BH et al. [18]

A few unusual radiologic features of metastases frequently encountered that make distinction from other non-malignant pulmonary diseases difficult include cavitation, calcification, haemorrhage around the metastatic nodules, pneumothorax, air-space pattern, tumor embolism, endobronchial metastasis, solitary mass, dilated vessels within a mass. Keeping these characteristics in mind the diagnostic criteria for the study was prepared.

The most common causes of benign solitary pulmonary nodule (SPN) are healed or non specific granulomas or active granulomatous infections of tuberculosis, aspergillosis and hamartomas. Less common miscellaneous causes of benign nodules are lung abscess, non specific fibrosis, round pneumonia, focal haemorrhage, and haemangioma etc.[19]

At histological analysis, most primary lung malignancies are adenocarcinoma, squamous cell carcinoma, large cell undifferentiated carcinoma or small cell carcinoma.

Hence depending upon clinical examination, CT findings and assessment of risk factors, a provisional diagnosis about the lesion is made whether it is benign, malignant or indeterminate. However, according to recent literature by Fletcher, CT has been shown to have poor specificity for characterization of the nodule and 70%-75% of the indeterminate nodules prove to be malignant.[20]

TNAB of lung is a well-established method in the cytological diagnosis of pulmonary nodules. Studies have shown that the diagnostic accuracy is greater than 80% for benign disease and greater than 90% for malignant disease .[21] CT guidance permits biopsy of nearly all lesions that are visible on CT scans, regardless of size or position. Needle placement in small pulmonary lesions or deep mediastinal nodes can be accurately determined with CT, and vascular and cardiac structures are well demonstrated and safely avoided .[21]

Studies by Goldsmith et al have shown that CT guided biopsy has sensitivity of 81% to 98% and specificity of 91% to 100% in diagnosing lung lesions. Hence, there is a need to follow up the report given by the CT scan by histopathologic studies like FNAC[22]. Complications are few and seldom serious.

Material and Method:

Study design : Retrospective

Duration : 12 June 2013 - 12 August 2013

Place of study : Kasturba Medical College, Manipal

Study population: 100 patients aged from 30 years to 75 years who have had chest symptoms and / or chest X-Ray positive for lung mass. Subsequent criteria for patient selection -CT with contrast and further referred for histopathologic (HP) examination like CT-guided FNAC and fluid cytology.

On consultation with a radiologist, the chest CT scans were observed and the size of the lesion, enhancement, and nature of its margins, internal attenuation, wall thickness, intranodular fat and calcium deposits were documented. Using these radiographic features, a provisional CT diagnosis of the lesions as benign or malignant was made followed by documentation of the CT-guided FNAC and/or fluid cytology results of the pulmonary nodules.

On the basis of these findings, a CT diagnosis of the nature of the lesion i.e. benign or malignant or indeterminate was made using the following set of criteria. [23, 24]

Not suspicious for malignancy- homogeneous, round, well defined margins, less than 3 cm

Low suspicion-non homogeneous, round, well defined margins, less than 3cm

Intermediate suspicion- non-homogeneous attenuation, well defined margins, more than 3 cm

Suspicious for malignancy - above features plus mediastinal lymph nodes or metastatic lung nodules, air bronchogram.

Moderately high suspicion- non-homogeneous attenuation, irregular margins, more than 3 cm and associated features

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High suspicion-non-homogeneous attenuation, lobulated and spiculated margins, more than 3 cm and associated features

Lesions in category a, b, c were considered benign and those in d, e and f were considered malignant and interpreted. In some cases wherein some overlapping features were observed, CT diagnosis was given as indeterminate. The biopsy/cytology report gave the final diagnosis as benign/infective or malignant.

Cases were classified as true positive, true negative, false positive or false negative depending on the provisional diagnosis by CT and the final histopathology (HP) diagnosis. Cases which turned out to be -

Malignant both by CT and HP were true positive (TP)

Malignant by CT but benign by HP were false positive (FP)

CT negative for malignancy but HP positive are false negative(FN)

Benign proved by both CT and HP were classified as true negative cases (TN)

This data was analyzed to give the final result. Statistical parameters like sensitivity, specificity, PPV and NPV were calculated.

Results:
A total of 100 patients having pulmonary lesions on CT scan were randomly selected who were subsequently biopsied under CT guidance or underwent the required conformational examination according to criteria. 2 of these biopsy specimens were diagnostically inadequate for opinion and a repeat biopsy could not be performed due to various reasons. So, they were excluded from the study.

Number of cases:
TP-48
FP-12
TN-29
FN-2

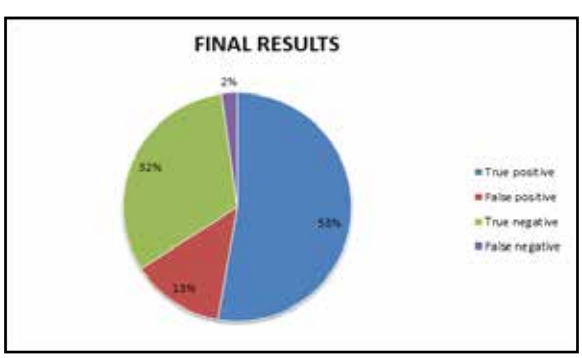

FIG 1: The above pie-chart shows the percentage of cases in each category**.**

The true negative cases turned out to be absolutely benign lesions like that of pulmonary tuberculosis. The histologically malignant cases included squamous cell carcinoma (n=16), adenocarcinoma (n=10), small cell carcinoma (n=7), rest metastatic nodules.

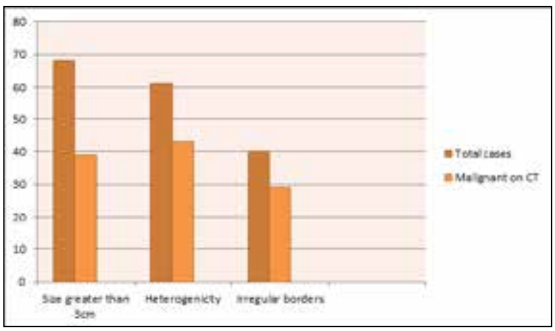

FIG 2: shows the number of malignant cases based on each diagnostic criteria

Using statistical parameters

Sensitivity = 96%, Specificity = 70%,

Positive predictive value (PPV) = 80%

Negative predictive value (NPV) = 93.5%

Thus, the overall diagnostic accuracy of CT in detecting lung malignancy comes out to be 85%.

DISCUSSION

CT features suggestive of lung malignancy with high sensitivity are large size, heterogeneous attenuation, irregular/spiculated margins with associated features like metastasis, rib destruction. Definitive benign features include smooth round mass of small size or thin-walled cavities with soft tissue density, air bronchogram.

Sensitivity of 96% concludes that CT scan is a very effective evaluation tool for screening malignant lung masses. However, diagnosis of malignancy with only one modality is not suggested since 'malignant case' comes with a lot of therapeutic implications; needs to be confirmed by histopathology, as treatment option depends on histological typing.

Specificity of 70% suggests that benign lesions are also diagnosed fairly well on CT but not suitable as a confirmatory test unless the radiologist strongly feels that there is minimal chance of the lung mass being malignant.

The 80% PPV indicates that if a lung mass is diagnosed as malignant on CT; there is 80 % chance that the confirmatory test will agree with the CT diagnosis. Similarly the 93.5% NPV indicates the CT is good in deciding mass to be non-malignant. Thus it can be concluded that for benign masses, CT is good enough and invasive confirmatory tests can be avoided.

The overall diagnostic accuracy of CT is 85% indicating that it is an excellent screening technique for suspected lung lesions. It can be used as a localising tool prior to CT guided percutaneous biopsy which is highly specific and sensitive.

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