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How to Manage Solitary Pulmonary Nodule (SPN)

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INTRODUCTION

Solitary pulmonary nodule on chest x-ray often poses a practical management problem, especially in view of possibility of malignancy. Early diagnosis is important particularly in case of patients with small asymptomatic lesions since chances of long-term survival in those with malignant disease are increased. The prevalence of solitary pulmonary nodule is around 1-2/1000 chest x-ray. A solitary pulmonary nodule is a shadow within the lung parenchyma with well circumscribed, or without smooth borders. It may affect the pleura, mediastinum, or diaphragm and may contain calcium or cavitations. Multi-detector compound CT has increased the detection rate of SPN[1] in recent times. Management of SPN by four management algorithms by 2015 BTS guidelines has made it surprisingly easy and cost effective[2,3].

SPN

On a plain postero-anterior chest X-ray of an asymptomatic individual, a single, small, circular shadow may be noticed in the lung parenchyma. It is referred to as a Coin shadow or coin lesions. John Steel coined the term solitary pulmonary nodule (SPN), which has following features:

Solitary

Circumscribed margins

Round, ovoid or lobulated

Completely surrounded by normal lung

Smooth, speculated or notched border.

Minimal diameter i.e. double the cross-sectional diameter of blood vessel in its vicinity (1.5 cm). Homogeneous density without cavitation, or having a central calcified core.

Not associated with infiltration, volume loss, regional lymphadenopathy or satellite lesions.

Chest CT is useful from diagnosing missed lung lesions while HRCT can differentiate alveolar lesions from ILDS.

Table 1: Common causes of solitary pulmonary nodule (SPN)

Bronchial carcinoma
Benign lung tumor, hamartoma being the commonest
Infective granuloma, Tuberculoma, fungal granuloma.
Metastasis.
Lung abscess

ETIOLOGY

The possible causes include;

1. Bronchogenic carcinoma
2. Granulomatous lesions such as tuberculosis, Histoplasmosis, Wegener's granulomatosis
3. Benign tumors adenoma, hamartoma
4. Lung metastasis from a carcinoma in breast, thyroid, kidney, bone[4]
5. Hydatid cyst or bronchogenic cyst
6. Lung abscess
7. Slowly resolving pneumonia lipoid pneumonia, Paraffinoma
8. Pulmonary infract.
9. A.V. fistula
10. Lymphoma
11. Rheumatoid nodule, Amyloid nodule.
12. Mucoid impaction
13. Haematoma post trauma.
14. Benign pleural effusion
15. Infected fluid filled bulla.
16. Chest wall tumors, skin tumor, the nipple

Primary bronchial carcinoma accounts for thirty three to fifty percent of solitary pulmonary nodules in patients over the age of 50 years, but the risk falls almost to zero in patients under the age of 40 years. A variety of benign tumors along with localized infection and granulomas form the majority of non-malignant causes of solitary pulmonary nodules. The prevalence of fungal infection in North America accounts for fifty percent of granulomatous lesions. Tables I & 2 outlines some common causes of solitary pulmonary nodules.

MANAGEMENT

First step is to confirm that an opacity lies within the chest and that it is not caused by an overlying object such as nipple, hair plait, button, fibroma, lipoma or any soft tissue mass. Benign pleural thickening with unfolding of a lung segment may also mimic a tumor. A benign pleural plaque may be confused with a solitary pulmonary nodule but may be distinguished by tomography or fluoroscopy as

Table 2: Common causes of solitary pulmonary nodule (SPN)

More Common	Primary bronchial carcinoma	
	(PMEN)[2] Pulmonary Metastasis from	Breast Sarcoma Aminoma Hypernephroma
	Infection	Tuberculosis (Tuberculoma) Localized Pneumonia Abscess
Less common	Benign tumours	Hamartoma Bronchial Adenoma Chyloductoma Chondroma Fibroma Haemangioma Leiomyoma Myxoma Neurofibroma Papilloma Thymoma
	Other malignant tumours	Alveolar Cell Carcinoma Lymphoma Mesothelioma
	Chest wall lesions	Arteriovenolous malformation Lipoma Fibroma
	Cysts	Bronchiectatic Bronchogenic Hydatid Endometriosis Foreign Body Infection
	Mycosis and Parasitosis	Aspergillosis Coccidioidomycosis Histoplasmosis Nocardiosis Cryptoccosis
	Miscellaneous	Intrapulmonary Lymph Node Pulmonary Infract Pulmonary Sequestration Post- Traumatic Hematoma Rheumatoid Nodule/ Systemic Lupus Erythematosus Wegener's Granuloma

the pleural mass does not move relative to chest wall with respiration. General physical examination is important because the nodule may be a metastatic manifestation of the malignancy of breast, kidney, testes, or ovary.

Benign nodules are likely to be smaller than malignant lesions. An irregular lobulated or speculated contour is suggestive of malignancy, contrary to a smooth contour that suggests the nodule is benign, with exceptions. The two most useful radiological features to exclude

malignancy are no growth over two years and the presence of calcium. No growth almost completely rules out malignancy on comparison with old chest x-ray. The diagnostic value of calcium depends on the radiological distribution pattern; a dense central nidus or a laminated or diffuse pattern are reliable signs of healed granulomas; nevertheless malignancy may still develop in relation to the granulomas. Pepper pot calcification is associated with hamartomas. Calcification may sometimes be seen within a malignant lesion and hence diagnosed as benign, simply because of presence of calcification may not be true.

Computed tomography (CT) has been proposed as a reliable way of diagnosing benign disease. A history of previous malignancy should not prevent full investigations since resection of a solitary pulmonary metastasis may carry a good prognosis. Apart from routine haematology, specific precipitin (for example for aspergillus or histoplasmosis) or tuberculin testing may be indicated. If solitary pulmonary nodule is suspected to be extra thoracic metastasis; carcinoma of thyroid, breast, kidney or bone are common differential diagnosis.

In patients with cough or weight loss without fever diseases such as tuberculosis, histoplasmosis, blastomycosis, etc form the important differential diagnosis. Leukemic lung deposit can be excluded on clinical grounds or blood examination.

Two categories of further investigations are required to clinch in order to achieve specific diagnosis and also to assess the need for thoracotomy.

IMAGING MODALITIES

Plain Chest x-ray

Chest C-ray forms the cornerstone investigation[5]. The film in postero-anterior view is taken with the patient well positioned and in inspiration. Bronchial carcinomas may vary enormously in shape and radiographic density as well as in size and position. Notching in peripheral masses and speculation or corona maligna are said to be suggestive of malignancy. Nevertheless, such appearances are not pathoganomonic. Cavitation in a thick walled tumour and presence of atelectasis are features associated with a squamous cell carcinoma. The claim that a peripheral nodule is most likely to be due to an adenocarcinoma and that Iymphadenopathy is more often associated with small undifferentiated carcinoma, cannot he regarded as sufficiently specific to be conclusive.

Calcification within the solitary nodule is perhaps quite useful indicator of a benign lesion. Several different patterns of calcification are described, such as lamination, punctuate, central nidus, or popcorn; these may not always be discriminatory features. Calcification can also be seen in malignant tumours that engulf previously calcified lung tissue such as a Ghon's focus, and some metastasis (for example from an osteosarcoma).

Penetrated Film

In addition penetrated chest X-Ray can be informative. This is a film taken after exposing at a much higher kilo-voltage (and also using an anti-scatter device). The radiograph produced is usually darker than the standard film as it utilizes the x-ray absorption at higher energies to pass through the denser structure of the chest, thus revealing the anatomy of the tracheobronchial tree within the mediastinum. Such a film may show widening of the carina, bronchial occlusions, or intrabronchial masses within the mediastinum. Abnormal shadows otherwise concealed behind the cardiac silhouette may also become obvious. The penetrated film may also reveal either central necrosis or calcification within a dense intrapulmonary nodule, and it can be particularly useful in demonstrating an air bronchogram, i.e. air contained within the bronchi in a segment of abnormal lung; the presence of which offers a conclusive evidence that the lesion is a form of consolidation and it definitely lies within the lung.

Other plain Film Views

Sometimes a useful information can be obtained from the posteroanterior view taken in expiration, which effectively alters the mediastinal shape, the filling or the pulmonary vasculature, and the relation of the lung parenchyma to the adjacent chest wall structure. (this effect can also be obtained with an anteroposterior view). Rarely an intrabronchial mass can lead to a ball valve effect with air trapping beyond an intermittent obstruction that occurs particularly in expiration. Decubitus films can be useful on confirming the presence of a liquid pleural reaction; so called horizontal beam film can be taken with the patient lung on the affected side, when free fluid drains from the top of the diaphragm along the chest wall; even small quantities may become obvious.

Fluoroscopy

It helps in locating abnormal shadows in the anteroposterior plane and also to detect the relationship of the suspected lesion to the thoracic cage and the intrathoracic mediastinal structure. For example, pulsation may occasionally be seen or alteration may be noted in the size or shape of the lesion with the changes in the respiratory phase, suggesting a vascular rather than a solid lesion.

Tomography[6]

Tomography apparently increases detail by its ability to blur out all planes except the plane of interest. Therefore, the lesion at the apex of the lung are usually obscured by upper ribs on the standard chest film may be well seen by apical tomography and the anatomy of the carina and bronchi within the mediastinum may be better appreciated when the neighboring structures have blurred out of focus. Also flecks of calcium can be better revealed by tomography.

Tomography may also reveal a rather prominent but otherwise unremarkable pulmonary artery. Whole lung tomography may be used to exclude multiple lesions particularly while considering resection of an apparently solitary pulmonary nodule.

Table 3: Role of CT in solitary pulmonary nodule

1. To diagnose the nature of the nodule and to detect calcification in a nodule than conventional trims.
2. To demonstrate the spread of disease.
3. To localize accurately the nodule prior to bronchoscope or percutaneous needle biopsy.

CT

CT has clear advantages over standard radiographic technique. Third and fourth generation CT scanners allow increased spatial resolution (better with improved contrast resolving relative to conventional radiography) with which lesion of 3 mm or more can be demonstrated. It is claimed that measurement of the tissue attenuation can indicate the likelihood of malignancy. Metastasis is more commonly found in the lung periphery and, like small pleural effusion, small peripheral metastases are more radically seen by using CT. CT also usefully distinguishes vascular masses such as aneurysms from solid tumors. It differentiates pleural disease from intrapulmonary disease and effectively supports the need for diagnostic artificial pneumoperitonium or pneumothorax. CT can reveal a mass that is otherwise lost within distal consolidation in conventional radiography. For a bronchial neoplasm CT scanning alone cannot be used to assess operability; Nevertheless, CT examination of other parts of the body such as the liver may demonstrate metastasis. Utility of CT in SPN are listed in Table 3.

Ultrasound

Following radiologically demonstrated mass such as cyst, abscess or tumor which a bud the chest wall, ultrasound is used. Ideally this should be described under non-radiological investigation. Since only air tree structures can be visualized, ultrasound has a limited use in the assessment of chest pathology. It is better than chest radiography sand superior to physical examination and can obviate the need for CT thorax in certain situations. Radial EBUS in SPN has been found quite useful. Lung ultrasound quickly rules out consolidation, atelectasis and pleural effusion, however it has limited role in obesity, chest wall oedema, chest wall dressing, subcutaneous air and heavy musculature[7,8].

Radioisotope Studies

Radioisotopes allow the assessment of function rather than anatomy. As such, these techniques are useful in the search for bone, liver, and cerebral metastasis. Positron emission computer assisted tomography has increased the accuracy of evaluating utility in SPNF[5]. PET digital detector technology provides higher spatial resolution, thus improving image quality and making the evaluation of smaller nodules more reliable and with acceptable accuracy[9].

Tumor - seeking agents such as gallium may sometimes be useful, particularly in the evaluation of lymphoma. However, the technique is expensive and time consuming and lacks specificity as the isotope is also taken up in abscesses and pulmonary inflammation, especially sarcoid[10]. Usually malignant thyroid tissue appears cold on scanning but this technique can be useful in demonstrating metastasis after the normal thyroid has been ablated. The uptake in metastases is relative to the differentiation of the thyroid tumor cells.

Lung perfusion scans are useful in diagnosing of pulmonary emboli when combined with ventilation studies. Nevertheless they may also be used in the preoperative assessment of patients with bronchial tumors; a lung cancer may markedly decrease pulmonary vascularity and this may be particularly so when the tumor abuts or lies at the hilum. Isotope angiography is less invasive than conventional arteriographic studies but may lack sufficient anatomical precision. However it helps to differentiate mediastinal structures from the aorta and major vessels; it allows confirmation of a suspected aortic aneurysm and readily demonstrate superior vena caval obstruction.

Nuclear Magnetic Resonance (NMR), like ultrasound, is non invasive and involves non ionizing radiation. While its clinical application is still in its infancy, in NMR allows the production of two - dimensional cross-sectional images derived from the suffering proton density of different tissue. As such, its theoretical value in the detection of cancer is obvious since changes occur early at the molecular level and become evident long before the neoplasm shows itself by virtue of the more gross anatomical distortion revealed by conventional radiography. However, the study of intrapulmonary masses surrounded by air filled long tissue is less encouraging.

Angiographic Techniques

CT has reduced the application of angiography. Nevertheless, when there is an abnormal intrathoracic mass lesion either within or juxtaposed to the mediastinum, aortography is useful in excluding an aneurysm and thus may help in avoiding an unwise biopsy. Furthermore, when an intrapulmonary mass lesion is in fact due to a sequestrated lung segment (it is usually in the left base posteriorly) aortography can demonstrate the feeding arteries that arise from the descending thoracic aorta.

Pulmonary angiography is useful in diagnosing a pulmonary artery aneurysm. Various vascular techniques such as subclavian, thyroid, and internal mammary arteriography have been used on occasion to demonstrate masses of thymic, thyroid or parathyroid origin rarely, other techniques such as azygos and thymic venography may be of value in specific cases. Computerized digital vascular techniquehas a considerable potential for the use of digital image subtraction at different energies in chest radiography in particular, since the detection rate of low contrast intrapulmonary nodules is increased by the suppression of overlying rib detail.

NON RADIOLOGICAL DIAGNOSIS:

These investigations are very important in reaching the conclusive diagnosis[11].

Sputum Examination

The presence of pus cells or bacteria may suggest that lesion is inflammatory. Malignant cells should always be sought in at least three early morning Sputum specimens. Sputum induction can be utilized to improve the sample if sputum sample is not enough[12].

Bronchoscopy[13,14]

When the suspicion of malignancy remains high, Bronchoscopy is usually considered to be the next step. Unless the lesion is clearly inoperable on clinical or radiographic grounds. Bronchoscopy is also indicated to asses' operability even if sputum cytology reveals malignant cells. BAL analysis provides additional diagnostic information in concluding the aetiology of SPN[15].

Fibroptic transbronchial lung biopsy under local anesthesia has become increasingly useful[16,17]. The size of each biopsy is smaller but the range of vision, particularly of the upper lobes, is superior. With fluoroscopic guidance, the field is further improved[18]. The incidence of side effects is low. Pneumothorax occurs in 1-5 percent of cases. This rarely requires intercostals drainage.

Mediastinoscopy and Thoracoscopy

Medioastinoscopy through a small incision in the suprasternal notch is useful for the examination and biopsy of mediastinal glands. Mediastinal lymph nodes are involved in fifty percent of all patients with primary lung cancer[19].

The presence of a pneumothorax allows the introduction of a thorascope into the pleural space, to investigate cases of pleural effusion and tumours.

Percutaneous needle biopsy[20]

This commonly used technique involves the insertion (under local anaesthesia) of a fine 23- gauge aspiration needle and alternatively of a small 20 guage screw-tipped needle and cannula. While the patient holds his breath, the needle is inserted through the chest wall, avoiding the intercostal bundle. Using fluoroscope guidance, the needle tip is positioned within the lesion and saline aspiration can be repeated several times. This method gives a better diagnostic yield than the transbronchial approach, with positive result in 80-90 percent of cases. However, the diagnostic accuracy of cell type may be less. The risk of both haemorrhage and pneumothorax is increased. Spread of infection and seedlings of tumour cells along the needle track are insignificant risks. Both transbronchial and percutaneous lung biopsy are contraindicated in the presence of pneumothorax and bleeding diathesis. Peripheral lesions over 2 cm in diameter are most suitable for this technique. The direct aspiration of intrathoracic lesions enables the diagnosis of primary carcinoma of the lung. Solitary pulmonary nodule in a renal transplant recipient may make difficulty in diagnosis because of immunosupression[21].

- Immuno-compromised hosts have interference with inflammatory responses.
- Clinical, pathological and radiological responses are often blunted.
- Serologic tests are useful only in pre-transplant setting.
- Transplant patients are vulnerable to drug resistance.
- Antimicrobials are often inadequately effective in the presence of undrained fluid collection.
- Within 30 days of transplant, risk of microbial and drug resistance organism infection is higher.
- In one to six months risk of developing opportunistic infections such as P. jirovevecci cryptocollosis, histoplasmosis, TB, cytomegalo, herpes, verisella zoster is ruled, Cryptosporidiosis, toxoplasmosis, strongiloidosis, listeriosis and nocardiosis is higher.
- After six months (80%) community acquired viral pneumonia (influenza, para-influenza, respiratory syncytial virus and human metapneumo virus), bacterial infections (streptococcus pneumonia, haemophylus influenzae) and cryptococal infections are common. 15% chronic viral infections (adenovirus, polioma virus BK, hepatitis C and human papilloma virus) are common.
- 5% have cryptococcal neoformans cytomegalo virus, nocardia, Rhodococcus, and aspergilosis.
- Smear of excised tissue may show the organism after diligent search or delayed / scanty growth may be obtained after prolonged incubation of culture.

COMMENTS

Applied strategies of management include careful observation, use of CT, FNAC, PET and bronchoscopy and surgery[22] with accuracy and cost effectiveness[23]. A doctor has three possible options in managing a solitary pulmonary nodule: to do nothing, to undertake invasive investigations or to perform a thoracotomy. As an operation offers the only chance of curing local malignant disease, the initial approach is determined by the probability of malignancy and the possibility of surgery. Primary bronchial malignancy is rare in non-smokers and patients under 35, but the possibility of a solitary secondary tumour from a breast or testicular primary tumour or a lymphoma must not be ignored. Geographical and ethnic factors may point towards granulomatous or hydatid disease. Endobronchial ultrasonography can be a useful tool to diagnose TB, sacoidosis and malignancy[24,25] Controversy exists whether biopsy should be performed before a surgical operation. A negative result seldom excludes malignancy and a positive result in a fit patient leads to a thoracotomy. Therefore if a lesion seems to be operable and the patient could tolerate a thoracotomy, perform a compound tomography of the abdomen and thorax. If no mediastinal metastasis are found then thoracotomy is recommended for a cure or definitive diagnosis.

If surgery is contraindicated because of poor lung function, age, co-existent cardiovascular disease, or by the results of compound tomography, further management is influenced by symptoms and the probability of malignant disease. In an older patient with no symptoms, it is always better to watch and wait. In younger patient or a patient with symptoms, further management will be influenced by whether malignancy is positively diagnosed. Bronchoscopy is well tolerated. Biopsy or needle aspiration through the bronchoscope with fluoroscope improves the chance of a positive diagnosis. A diagnosis may be made by transbronchial lung biopsy in a quarter of cases in which the nodules are smaller than 2 cm and in about two third of cases in which these are larger. CT scan is informative and CT guided fine needle aspiration biopsy is diagnostic, particularly for malignant lesions. Percutaneous needle biopsy is simpler but is contraindicated in case the patient has a bleeding diathesis, severely compromised lung function, pulmonary hypertension, or suspicious of a hydatid cyst or arteriovenous malformation from sequestrated lung segment. In malignant lesions, the diagnostic yields from needle biopsy increases with increasing size, reaching 80-90 percent for single sample from tumours larger than 3 cm and further potentiated to 95 per cent for two or three sample.

An attempt has been made to evaluate the effect of these three management strategies (an operation, biopsy, or observation) on life expectancy by using decision analysis. The results vary with the management strategies. However the difference between the strategies happens to be surprisingly small. Hence patient's choice for opting a treatment modality should be given a preference. At the same time, excessive interventions in a high percentage of patients with SPN have lead to excessive radiation exposure and thus requires professional cautionary attention as well[26].

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