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CME ARTICLE

The solitary pulmonary nodule

Jansen Meng Kwang Koh[1], MBBS, MRCP, *Gerald Jit Shen Tan*[2,3], MBBS, FRCR, *Choon How How*[4], MMed, FCFP

Mr TAB, a 69-year-old man presents to your clinic with a chest X-ray (CXR) that was done as part of a skeletal survey when he fell down a flight of steps during a holiday overseas. The CXR shows a 2-cm nodule. He has been on your follow-up for ten years for hypertension and is a heavy smoker. Physical examination was unremarkable. How should he be evaluated?

WHAT IS A SOLITARY PULMONARY NODULE?

The solitary pulmonary nodule (SPN) is a single, spherical, well-circumscribed radiographic opacity ≤ 3 cm in diameter. It is completely surrounded by aerated lung tissue. Importantly, it is not associated with atelectasis, hilar enlargement or pleural effusion.[1,2]

HOW RELEVANT IS THIS TO MY PRACTICE?

How common are lung nodules?

Lung nodules are common in clinical practice, with a frequency ranging from 0.2% in older studies involving CXRs to more than 50% in recent screening trials utilising low-dose computed tomography (LDCT).[1,3-8] This clinical problem is likely to increase given that primary care physicians frequently order a screening test for lung cancer. A recent survey of primary care doctors showed that 55% had ordered CXRs in the preceding 12 months, with an additional 22% having ordered a chest CT.[9] Although lung cancer screening by CXR has been shown to be ineffective,[10] lung cancer screening by LDCT may be implemented given the findings of the National Lung Screening Trial.[11] While some organisations have already advocated LDCT screening for high risk-individuals,[12,13] others have not. As lung cancer screening with LDCT gains more support on the ground, the frequency of detecting lung nodules is likely to increase dramatically.

Can I make a difference?

Detection and workup of SPNs is crucial as they may be malignant. The prevalence of malignancy in screening or incidentally detected pulmonary nodules is 33%–82%, with an increased risk for larger nodules.[14] While the five-year survival rate for advanced malignant disease remains dismal at below 5%, early lung cancer has a five-year survival rate of as high as 80%.[1] Accordingly, the only chance for cure of early lung cancer is prompt diagnosis and management. It is also important to review the CXR comprehensively as SPNs are frequently missed. It has been estimated that 19% of patients diagnosed with lung cancer have SPNs that are visible when previous CXRs are retrospectively reviewed.[15] Several concise reviews on CXR evaluation have been published, but this is beyond the scope of the article.[16,17]

You review the CXR and notice a right upper lobe, 2-cm solitary pulmonary nodule. Mr TAB mentions that the doctor overseas had recommended a specialist review. He is keen to know if this is warranted.

What should I do next?

There are several causes that can present as an SPN and these are listed in Box 1. The main issue now on everybody's mind is "Is this cancer"?

Box 1: Common causes of an SPN[18,19]

Malignant causes

1. Lung carcinoma
2. Solitary metastasis
3. Carcinoid

Benign causes

1. Granuloma (e.g. healed tuberculosis)
2. Benign tumours (e.g. hamartomas, chondroma)
3. Round pneumonia or lung abscess
4. Aspergilloma
5. Rheumatoid nodule
6. Arteriovenous malformation

Reviewing old CXRs

Whenever possible, it is crucial to review old CXRs. If the nodule has remained stable for two years or more, this suggests a benign aetiology, as most malignant lesions are expected to

[1]Department of Respiratory & Critical Care Medicine, Changi General Hospital, [2]Department of Radiology, Tan Tock Seng Hospital, [3]Lee Kong Chian School of Medicine, [4]Singhealth Polyclinics – Sengkang, Singapore

Correspondence: Dr How Choon How, Deputy Director, Singhealth Polyclinics – Sengkang, 2 Sengkang Square, Sengkang Community Hub, Singapore 545025. How.Choon.How@singhealth.com.sg

double in volume every 20–300 days.[20-24] A two-year interval radiographic stability is currently an acceptable way of excluding malignancy.[1,2] However, there are exceptions, as certain slow-growing tumours, such as bronchioloalveolar carcinoma (now termed as adenocarcinoma *in situ*), have exceptionally long doubling times of up to 1,486 days.[21,24]

Determining the appropriate management strategy

At this juncture, there are a few options available to you. You could: reassure the patient that there is no cause for concern and discharge him; advice him to return for a CXR and clinical review in 3–6 months' time; or refer him to a respiratory physician. In order to come to a decision, it is important to be aware of the various management options available to your patient. There are three possible management options and they include careful observation, further diagnostic testing and surgery.[25] Determining which option is appropriate for your patient in turn depends on consideration of the following three factors: cancer risk assessment; surgical risk assessment; and a patient's preferences on treatment.

If your patient has a high risk for lung cancer coupled with a low risk for surgical intervention, surgery (i.e. lobectomy) should be recommended, taking into consideration the patient's preference. Similarly, in a patient with a low risk for lung cancer but a high risk for surgery, careful observation and monitoring can be adopted, especially for patients who are not keen on further invasive investigation or management. Patients with an intermediate risk for lung cancer or who are unsure about undertaking the risk of surgery can undergo further diagnostic testing before a definitive management plan is made.

Cancer risk assessment

The first step in deciding which management option to take is to perform an estimation of the probability of cancer. This estimation is made using both clinical factors as well as the radiological characteristics of the SPN on CT. These risk factors are presented in Box 2. Although CT characterisation is important in predicting the risk of cancer, factors such as age, smoking history and size of the nodule may be sufficient to determine the risk of cancer. In this case, Mr TAB would be deemed as having a high risk for lung cancer given his age, heavy smoking history and the size of the nodule on CXR.

Internet-based and mobile device applications are now available to facilitate cancer risk assessment for patients with SPN. One such example can be found on this website: http://www.chestx-ray.com/spn/spnprob.html. These risk prediction calculators are based on models using logistic regression that have been validated. Interestingly, it has been shown that there is no significant difference between the results from logistic models and the predictions of physicians,[27] thus emphasising the point that physicians should always estimate the pre-test probability of cancer by evaluating the risk factors and using clinical judgement.

Box 2: Risk factors for lung cancer in patients with SPNs[25,26]

Clinical factors

1. Increasing age
2. Prior cancer history
3. Smoking history
4. Chronic obstructive lung disease
5. Haemoptysis

Radiological factors

1. Nodule size
2. Nodule characteristics (i.e. smooth vs. spiculated edges)
3. Contrast enhancement on CT

Surgical risk assessment

Assessing the potential risk and benefits of surgery is critical. A patient who has severe comorbidities such as severe chronic obstructive pulmonary disease poses a high surgical risk. Factors such as low exercise tolerance, poor performance status or lung function could exclude lobectomy as a viable management strategy.

Patient's preference

A patient's preference for a treatment option is often formed from prior experiences and personal beliefs and knowledge, which may be biased and skewed. It is important that we provide them with accurate information on the available management options so that our patients can make an informed decision. A patient who has made an informed refusal on further diagnostic tests not only obviates the risk of these diagnostics tests, but also saves money for the patient and time for everyone. In practice, many patients require some confirmation of lung cancer (e.g. t issue diagnosis) from these tests before reaching a decision threshold for surgery.

Unfortunately, you do not have any previous CXR to compare. You make an assessment that Mr TAB is at high risk for lung cancer and probably a good surgical candidate. You promptly recommend that he be referred to a respiratory specialist and he agrees. Mr TAB returns to your clinic in four months for review of his hypertension. He informs you that further testing has led to the diagnosis of early lung cancer and that he had undergone a right lobectomy. He was glad that the CXR done for his fall had led to the discovery of his lung cancer at an early stage. He asks if a screening CXR could be done for his wife, who is also a heavy smoker but asymptomatic.

LUNG CANCER SCREENING

Clinical practice guidelines issued in 2010 by the Ministry of Health (MOH) recommend against routine screening for lung cancer.[28,29] Since then, a number of large randomised trials have been published, of which two are notable. The first involved 150,000 patients followed over a period of 13 years, of which

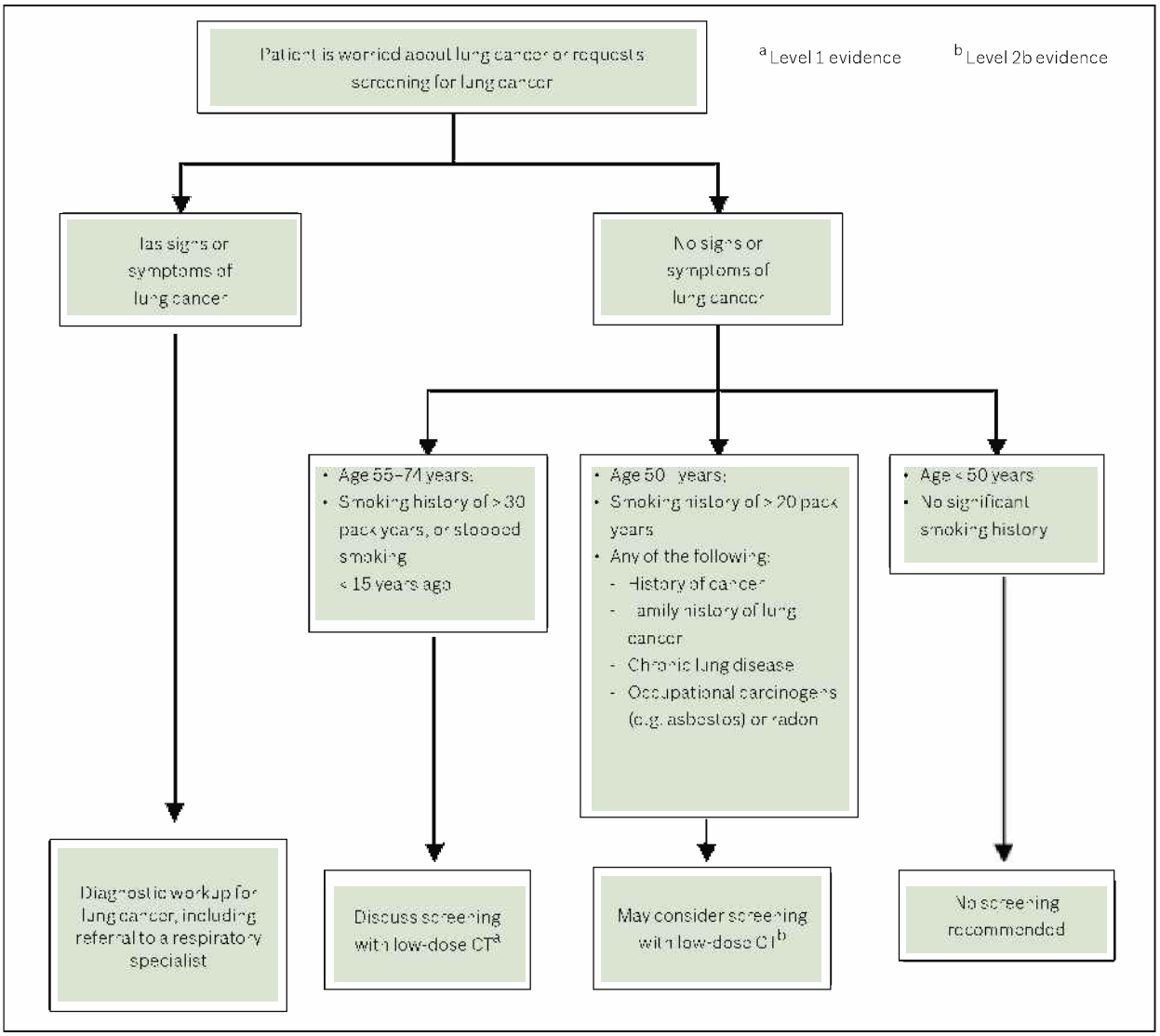

Fig. 1 Suggested algorithm for patients requesting lung cancer screening. Based on NCCN Guidelines® January 2002.[12] In all cases, patients should be counselled to stop smoking.

half underwent annual CXR screening. The results confirmed earlier studies showing that CXR screening did not result in a significant reduction in lung cancer mortality.[10] The second study, the National Lung Screening Trial, randomised 53,000 high-risk patients to two groups. This trial showed that the group undergoing annual screening with LDCT had a significant reduction in lung cancer mortality as compared to the group undergoing annual CXR screening.[11]

As a result, the American Lung Association and National Comprehensive Cancer Network Guidelines® now recommend that high-risk patients consider annual screening for lung cancer with LDCT, while at the same time reaffirming that low- and moderate-risk patients should not have routine lung cancer screening (be it by LDCT, CXR, sputum cytology or other methods).[12,13] However, other bodies such as the American Cancer Society do not endorse screening due to concerns over the implementation details, cost-effectiveness and consequences of increased false positives with LDCT screening.

Until these issues are resolved, it is our opinion that LDCT screening be performed opportunistically in a selected group of high-risk individuals, following an informed discussion between the respiratory specialist and the patient. A possible approach is shown in Fig. 1. Note that this screening algorithm applies to asymptomatic individuals – patients presenting with signs or symptoms suspicious for lung cancer should be evaluated appropriately. In all cases, smokers should be counselled to quit smoking, as smoking cessation, more than any form of screening, is the single most important factor that can bring about a decrease in the incidence of lung cancer.

TAKE HOME MESSAGES

1. SPNs are common clinical problems and are likely to be increasingly encountered.
2. An SPN raises the issue of possible cancer and should receive prompt evaluation.
3. Reviewing old CXRs are important in a patient with an SPN.
4. The probability of malignancy should always be assessed based on clinical and radiographic factors.
5. CXR should not be used for lung cancer screening.

ABSTRACT The solitary pulmonary nodule on chest X-ray (CXR) is a common problem in pulmonary medicine. Its presence raises the question of lung cancer. As five-year survival after resection of a solitary bronchogenic carcinoma can be as high as 80%, prompt evaluation is crucial. This should begin with a cancer risk assessment based on clinical and radiographic factors. The risk and benefits of surgery should next be assessed, and together with the patient's preferences, a management plan can be decided upon. Surgery is recommended for patients at high risk of malignancy with a low surgical risk, while careful observation is adopted for patients at low risk of malignancy coupled with a high surgical risk. Further diagnostic tests may be warranted to aid in this decision process. Although CXR is not useful for lung cancer screening, low-dose computed tomography imaging is increasingly recommended for individuals at high risk for lung cancer.

Keywords: lung cancer, lung cancer screening, lung nodule, solitary pulmonary nodule

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SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME

(Code SMJ 201206B)

	True	False
1. A solitary pulmonary nodule (SPN) is a spherical, well-circumscribed radiographic opacity ≥ 3 cm in diameter.	☐	☐
2. SPNs usually occur with pleural effusion or atelectasis.	☐	☐
3. CXRs are ineffective for lung cancer screening.	☐	☐
4. The size of a nodule has no relevance to the likelihood of malignancy.	☐	☐
5. Early lung cancer can have a five-year survival rate up to 80%.	☐	☐
6. Patients can be reassured that they do not have a malignancy if the size of their lung nodule remains stable for more than one year.	☐	☐
7. All SPNs require lung lobectomies.	☐	☐
8. SPNs < 1 cm are not malignant and can be observed at two-yearly intervals with CXR.	☐	☐
9. Patients assessed as high risk for lung cancer with low surgical risk should be offered lung lobectomy as one of the management options.	☐	☐
10. Male gender, smoking and chronic obstructive pulmonary disease increase the probability of malignancy in a patient with an SPN.	☐	☐
11. Patients may refuse lung operation due to unfounded fear or over-estimation of the risk of complications.	☐	☐
12. Patients who have made an informed refusal for definitive management such as lung operation should not be offered further invasive investigations.	☐	☐
13. High-risk individuals who are keen for screening can be referred for low-dose CT imaging of the chest to screen for lung cancer.	☐	☐
14. Smokers with SPNs will no longer have health benefits from smoking cessation.	☐	☐
15. Smoking cessation is the single most important modifiable factor to decrease the incidence of lung cancer.	☐	☐
16. If the patient's old CXR done five years ago was reviewed and noted to show the same nodule, the nodule is unlikely malignant, but he is still at high risk for lung malignancy.	☐	☐
17. The patient's neighbour, a 48-year-old non-smoker, requested for lung cancer screening. In view of her low risk, a CXR will be appropriate here.	☐	☐
18. The patient's colleague, a 32-year-old man with five years of smoking but otherwise asymptomatic, should not be referred for CT imaging for lung cancer.	☐	☐
19. Current MOH guidelines recommend an annual lung cancer screening with CXR or sputum cytology for heavy smokers above 55 years of age.	☐	☐
20. A patient presenting with weight loss and haemoptysis but having no other risk factors for lung cancer does not require further investigation.	☐	☐

Doctor's particulars:

Name in full : _____

MCR number : _____ Specialty: _____

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SUBMISSION INSTRUCTIONS:

(1) Log on at the SMJ website: http://www.sma.org.sg/cme/smj and select the appropriate set of questions. (2) Select your answers and provide your name, email address and MCR number. Click on "Submit answers" to submit.

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(1) Answers will be published in the SMJ August 2012 issue. (2) The MCR numbers of successful candidates will be posted online at www.sma.org.sg/cme/smj by 16 July 2012. (3) All online submissions will receive an automatic email acknowledgement. (4) Passing mark is 60%. No mark will be deducted for incorrect answers. (5) The SMJ editorial office will submit the list of successful candidates to the Singapore Medical Council. (6) One CME point is awarded for successful candidates.

Deadline for submission: (June 2012 SMJ 3B CME programme): 12 noon, 9 July 2012.