



Case report

Late presentation of lung adenocarcinoma in a stable solitary pulmonary nodule: A case presentation and review of the literature

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ABSTRACT

A 67-year-old patient has been followed by our pulmonary clinic for Chronic obstructive pulmonary disease (COPD) and a stable pulmonary nodule. Solitary pulmonary nodule (SPN) was detected on the lung cancer screening by low dose computed tomography (CT) scan of the chest. It remained stable on repeat CT scan at 6, 12 and 24-months interval. Yearly lung cancer low dose CT scans of the chest showed stability of the SPN for 12 years. A mechanical fall necessitating trauma workup unveiled increase in size of the nodule from 4 mm to 11 mm within one year of the previous screening CT chest. Biopsy and Histopathology confirmed the diagnosis of lung adenocarcinoma. The patient then underwent right upper lobectomy followed by chemoradiation therapy. Current guidelines do not recommend follow up for a solitary pulmonary nodules less than 6 mm nodule if it remains stable for 12-24 months. Our case report of the late presentation of lung adenocarcinoma in a stable solitary pulmonary nodule suggests the need to exercise increased caution in the management of incidental pulmonary nodules.

1. Summary

A 67-year-old patient has been followed by our pulmonary clinic for Chronic obstructive pulmonary disease (COPD) and a stable pulmonary nodule. Solitary pulmonary nodule (SPN) was detected on the lung cancer screening by low dose computed tomography (CT) scan of the chest. It remained stable on repeat CT scan at 6, 12 and 24-months interval. Yearly lung cancer low dose CT scans of the chest showed stability of the SPN for 12 years. A mechanical fall necessitating trauma workup unveiled increase in size of the nodule from 4 mm to 11 mm within one year of the previous screening CT chest. Biopsy and Histopathology confirmed the diagnosis of lung adenocarcinoma. The patient then underwent right upper lobectomy followed by chemoradiation therapy.

2. Background

Current guidelines do not recommend follow up for a solitary pulmonary nodules less than 6 mm nodule if it remains stable for 12–24 months. The late presentation of lung adenocarcinoma in a stable solitary pulmonary nodule suggests the need to exercise increased caution in the management of incidental pulmonary nodules.

3. Case presentation

A 67-year-old former smoker has been followed by our pulmonary clinic for management of chronic obstructive pulmonary disease (COPD) and stable pulmonary nodule. History goes back twelve years ago when she had her first pulmonary clinic visit. She was diagnosed with Grade B GOLD stage 2 COPD, stable on long acting muscarinic antagonist (LAMA) therapy prescribed by her primary care doctor. She was sent for low dose computed tomography (CT) of chest as a part of screening for lung cancer. She was found to have a 4 mm solid right upper lobe nodule. She then underwent repeat CT scans of chest at 6, 12- and 24-month intervals, all of which revealed stability of the nodule. She was then followed by annual low dose CT scans as part of her screening regimen. The 4 mm solid nodule in right upper lobe remained stable for 12 years. Two months before a scheduled clinic visit, she had a mechanical fall from stairs necessitating a hospital stay. A trauma work-up done in the emergency department was negative for any bleed or fracture. However, CT chest showed increased size of right upper lobe nodule from 4 to 11 mm in size with speculations. Due to high probability of malignancy she was sent for positron emission tomography (PET) scan showing high fluorodeoxyglucose (FDG) avid right upper lobe lung nodule and a positive pre-carinal lymph node suggesting a

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radiological staging of IIIA. She then underwent endo-bronchial ultrasound guided mediastinal lymph node biopsy and staging. Aspiration of the pre-carinal lymph node was positive for adenocarcinoma. She was then referred to a tertiary center for lung cancer management where she underwent right upper lobe lobectomy followed by chemoradiation therapy.

4. Outcome and follow up

A year after the right upper lobe lobectomy and chemoradiotherapy, the patient returned to work as a grocery store manager. The patient had slight dyspnea on exertion and fatigue which negatively impacted quality of life. It was predicted after the course with chemoradiotherapy. The patient is scheduled to get pulmonary rehabilitation and a follow up whole body positron emission tomography (PET) scan.

5. Discussion

Lung cancer is one of the most fatal malignancies worldwide. It leads to 1.3 million estimated deaths annually [3]. It makes up almost 25% of all cancer-related deaths. Risk factors associated with lung cancer are smoking, age, race, occupational exposure, environmental toxins, pulmonary fibrosis, alcohol and dietary factors and prior pulmonary nodules. Lung cancers are classified as either small-cell carcinoma, non-small cell carcinoma or mesothelioma. The main subtypes of non-small cell carcinoma lung are adenocarcinoma and squamous cell carcinoma.

United States guidelines regarding lung cancer screening are summarized in Table 1.

The main challenge in lung cancer screening with low dose CT scan is the high prevalence of pulmonary nodules and low malignancy incidence. The incidence of SPNs in the general population is 23–70%. It is 8–51% in patients with high risk for lung malignancy [4]. More than one million nodules are detected each year on pulmonary imaging. The risk of malignancy in screening detected nodules is 2–13%.

Evaluation of SPNs is often complex as benign and malignant features may overlap. Initial assessment involves clinical inspection, radiological features, risk factor survey, demographic information and use of lung cancer predictive models. Clinical factors increasing the risk of malignancy in a nodule include age more than 35 years, smoking or occupational exposure, and prior personal or family history of lung cancer or comorbid lung conditions. Radiological risk factors include nodule growth rate, nodule size, attenuation of nodule on CT scan, nodule margins, pattern of calcification, lobar location.

Doubling time (DT) is an essential parameter to monitor [5]. DT is calculated by measuring the diameter of a nodule on two different imaging tests separated by a known time period. The time span a nodule takes to double in size varies between 20 and 400 days [6]. Nodules with faster or slower DTs usually follow a malignant course. Stability of nodule size over two years typically indicate a benign nature [7].

Once identified, an SPN must be evaluated to determine likelihood of malignancy. CT scan of the chest without contrast using low dose radiation technique remains the preferred method to evaluate the pulmonary nodule for the risk of malignancy. Coronal and sagittal plane images are sometimes taken to localize the nodules [8].

Follow up of pulmonary nodules includes either no further management, CT or PET scan surveillance, tissue biopsy or combination of these. The various management recommendations, reported in published guidelines, are summarized in Table 2.

These recommendations are based on nodule size and attenuation. The Fleischer Society recommend no further workup for 6 mm or smaller solid nodules in high risk individuals if the nodule remained stable at 12-months follow up examination. The risk of malignant conversion in these nodules is less than 1%.

The case we report is unique as, to the best of our knowledge, it is the first example of an SPN with benign nature and stability over twelve

Table 1

United States guidelines regarding lung cancer screening.

Organization	Recommendation
American Association of Thoracic Surgery	Recommends annual low-dose CT scan screening for high-risk individuals (ages 55–79 years with ≥ 30 pack-year history of smoking and current smoker or quit within past 15 years); age 50 to 79 with ≥ 20 pack-year history and cumulative risk $\geq 5\%$ over next 5 years; or are lung cancer survivors with no incidence of disease for 24 years.
American Cancer Society	Recommends annual low-dose CT scan screening for high-risk individuals (ages 55–74 years with ≥ 30 pack-year history of smoking and current smoker or quit within past 15 years).
American College of Chest Physicians	Recommends annual low-dose CT scan screening for high-risk Individuals (ages 55–77 years with ≥ 30 pack-year history of smoking and current smoker or quit within past 15 years).
American Society of Clinical Oncology	Recommends annual low-dose a CT scan screening for high-risk individuals (ages 55–74 years with ≥ 30 pack-year history of smoking and current smoker or quit within past 15 years).
Canadian Task Force on the Periodic Health Examination	Recommends screening asymptomatic adults aged 55–74 years with at least a 30 pack-year smoking history who smoke or quit smoking <15 years ago with low-dose CT every year for 3 consecutive years.
National Comprehensive Cancer Network	Recommends annual low-dose CT scan screening for high-risk individuals (ages 55–74 years with ≥ 30 pack-year history of smoking or if no longer smoking, smoking cessation within 15 years, or age ≥ 50 years with a ≥ 20 pack-year history of smoking with one additional risk factor).
US Preventive Services Task Force	Recommends annual low-dose CT scan screening for high-risk individuals (ages 55–80 years with a 30 pack-year history of smoking and current smoker or quit within past 15 years). Discontinue when person has not smoked for 15 years or if limited life expectancy.
Centers for Medicare and Medicaid Services	Recommends annual low-dose CT scan screening for high-risk Individuals (ages 55–77 years) with ≥ 30 pack-year history of smoking and current smoker or quit within the past 15 years.
American Academy of Family Physicians	Concludes that evidence is insufficient to recommend for or against low-dose CT scan screening in persons at high risk for lung cancer based on age and smoking history.

years and a later doubling time of less than 300 days with conversion to adenocarcinoma. It demonstrates the importance of remaining alert when managing pulmonary nodules encountered during lung cancer screening.

In conclusion, several associations have recommended low dose CT scan as the lung cancer screening modality in high risk patients. Pulmonary nodules are one of the common incidental findings observed in lung cancer screening. Management recommendations of pulmonary nodules in this population subgroup are based on nodule characteristics but should be individualized. Increased vigilance and careful follow up is required in patients with pulmonary nodules even years into the clinical course to ameliorate mortality and morbidity.

6. Learning points

- Risk for progression to malignancy is still possible even after a period of stability in a low risk SPN.

Table 2
SPN follow up and management.

A: Solid Nodules*					
Nodule Type		Nodules <6 mm (<100 mm ³)	Nodules 6–8 mm (100–250 mm ³)	Nodules >8 mm (>250 mm ³)	Comments
Single	Low risk	No routine follow-up	CT at 6–12 mo, then consider CT at 18–24 mo	Consider CT at 3 mo, PET/CT, or tissue sampling	Nodules <6 mm do not require routine follow-up in low-risk patients
Single	High risk	Optional CT at 12 mo	CT at 6–12 mo, then at 18–24 mo	Consider CT at 3 mo, PET/CT, or tissue sampling	Certain patients at high risk with suspicious nodule morphology, upper lobe location, or both may warrant 12-mo follow-up
Multiple	Low risk	No routine follow-up	CT at 3–6 mo, then consider CT at 18–24 mo	CT at 3–6 mo, then consider CT at 18–24 mo	Use most suspicious nodule as guide to management; follow-up intervals may vary according to size and risk
Multiple	High risk	Optional CT at 12 mo	CT at 3–6 mo, then at 18–24 Mo	CT at 3–6 mo, then at 18–24 Mo	Use most suspicious nodule as guide to management; follow-up intervals may vary according to size and risk
B: Subsolid Nodules*					
Nodule Type		Nodules <6 mm (<100 mm ³)	Nodules ≥ 6mm (≥100 mm ³)	Comments	
Single	Ground glass	No routine follow-up	CT at 6–12 mo to confirm persistence, then CT every 2 y until 5 y	For certain suspicious nodules <6 mm, consider follow-up at 2 y and 4 y; if solid component(s) develops or growth occurs, consider resection	
Single	Partly solid	No routine follow-up	CT at 3–6 mo to confirm persistence; if lesion is unchanged and solid component remains <6 mm, annual CT should be performed for 5 y	In practice, partly solid nodules cannot be defined as such until they are ≥ 6 mm, and nodules <6 mm usually do not require follow-up; persistent partly solid nodules with a solid component ≥ 6 mm should be considered highly suspicious	
Multiple		CT at 3–6 mo; if lesion is stable, consider CT at 2 y and 4 y	CT at 3–6 mo; subsequent management based on the most suspicious nodule(s)	Multiple <6-mm pure GGNs' usually are benign, but consider follow-up at 2 y and 4 y in select patients at high risk	

- Physicians should be vigilant in the management of SPNs despite current guidelines not recommending any follow up for small SPNs stable for 12–24 months.
- Management of SPNs should not only be based on nodule characteristics but also should be individualized.

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