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Case reports

Solitary lung nodule with possible occupational origin in a patient admitted for musculoskeletal complaints - case presentation and review of literature concerning exposure in rubber industry

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Abstract

This case report illustrates the critical necessity of detailed occupational history no matter the chief symptom for the hospital admittance. If any exposure to carcinogens has been noticed, the target organ of the identified hazard(s) should be screened for cancer.

We present a case of a 51-year-old male admitted for musculoskeletal complaints in which the occupational history revealed exposure to carcinogens and the chest X-ray showed a solitary pulmonary nodule (SPN). The patient, a current smoker with a 22.5 pack-year index, had a significant past occupational exposure, having worked in a rubber manufacturing company as a vulcanizer/wringer for approximately ten years (1991–2002). Given the patient's smoking history and exposure to chemical carcinogens in the rubber industry – classified as a Group 1 carcinogen by IARC – lung cancer screening was initiated. A chest X-ray and subsequent CT scan confirmed an 11mm solitary nodule in the left upper lobe. Based on standard clinical risk models, the nodule's malignancy probability was estimated between 7.42% and 13.5%, classifying the case as intermediate risk (Lung-RADS Category 4B). Further diagnostic efforts, including bronchoscopy and bronchoalveolar lavage, yielded only a benign cytology with an acute nonspecific inflammatory appearance. Given the intermediate risk profile and occupational background, the patient will be followed according to the Fleischner Society 2017 guidelines, starting with a repeated CT scan in 3 months.

The case underscores that an occupational etiology for lung cancer is highly probable, even in a smoking patient, and emphasizes that occupational factors must be considered significant in etiology, even long after exposure has ceased.

Keywords: *solitary lung nodule, rubber industry, occupational carcinogens, smoking*

Introduction

Cancer represents a major public health issue, with significant impact on life expectancy. In men, lung cancer has the highest mortality rate in Romania [1]. Smoking still represents the most frequent cause of lung cancer, although smoking rates dropped across decades. Due to this decline in smoking habit, the proportion in pulmonary cancers in non-smokers is expected to rise. Even in 2023, in non-smokers, lung cancer is the fifth most frequent cause of mortality due to cancer worldwide, notably in women and in the Asian population [2].

Known risk factors for pulmonary cancer in non-smokers include passive smoking, indoor air pollution, occupational exposure to certain chemical substances and the genetic susceptibility [3].

Occupational cancer refers to cancer that occurs after exposure at work to carcinogen(s). There is a long latency from the initial occupational exposure to the first detection of the tumour and workers who have been exposed should be monitored during their lifetime, even if exposure has been stopped.

The International Agency for Research on Cancer (IARC), classifies rubber manufacturing industry in the group 1 carcinogen due to the substances used (benzene - group 1, 1,3-butadiene - group 1, 2-naphtylamine - group 1). Other carcinogenic agents such as carbon black, styrene and talc are listed as group 2B. This type of pure elemental carbon, found as colloid particles, is used widely as an intensifier for tires and other products, but also as a pigment for typographical ink and plastic materials [3-6].

In this article we ilustrate the necessity of lifetime surveillance, by presenting a case who was admitted for musculoskeletal symptoms related to his current work activity and to whom, the occupational anamnesis revealed a past exposure associated to carcinogens in a rubber manufacturing company and the chest X-ray confirmed a solitary lung nodule.

Case presentation

A 51 year old male was admitted in september of 2025 to the Occupational Medicine Clinic for lumbar pain irradiating along the right sciatic nerve towards the plantae, right knee pain, cervical pain irradiating in both arms towards the elbows and digital paraesthesia in both hands. The musculoskeletal complaints have a history of approximately 5 years, with progressive aggravation.

Personal medical history of the patient consists of Basedow's disease diagnosed in 2020, treated with thiamasole 10mg/day and levothyroxine 25mcg/day ('block and replace' management) and propranolol 10mg/day.

The patient was a current smoker. He started smoking 30 years before, having an index of pack years of 22.5 and a moderate nicotine dependence of 6 points (Fagerstrom test).

Regarding his occupational history, the patient has been working as a professional driver for 17 years within multiple companies. He experienced occupational postural stress, including low intensity vibrations, muscle strain, prolonged vicious positions. These conditions led to the patient's algic current symptomatology.

Prior to his professional driver activity, during 1991-1994 and 1995-2002, he worked in a rubber company as a vulcanizer/wringer, contributing to the preparation of the rubber (cutting the natural rubber, treating it with carbon black or chalk powder). This company is still active, manufacturing rubber compounds (styrene-butadiene rubber – SBR, nitril-butadiene rubber – NBR, ethylene propylene diene monomer – EP(D)M, neopren, natural rubber), rubber foam, boots, soles, sheets, rubber molded products, rolls and wheels. No detailed data of exposure from the period he has been employed were available.

The clinical examination revealed bilateral contracture of trapezius muscle, lumbar contracture of paravertebral muscles, thoracic scoliosis, pain inflicted by spinous lumbar apophyses percussion, and enlargement of the thyroid gland, without obstructing the deglutition process. The lungs were clear at auscultation. No reno-urinary symptoms such as dysuria, pollakiuria, nocturia or weak urinary stream were present.

The investigation plan included the general lab exams (total blood count, urinary examination, common inflammatory biomarkers, such as erytrocyte sedimentation rate, fibrinogen, C-reactive protein) and the abdominal ultrasound which was unremakable. The others, targeted to support a diagnosis, are briefly presented bellow.

1. For the lumbar and cervical pain: The MRI of the vertebral column described a multilevel degenerative disc disease of L2-L3, L3-L4, L4-L5, L5-S1 and C3-C4, C4-C5, C5-C6, C6-C7.

2. The cardiometabolic status, including the assessment of the thyroid function: The ECG revealed a right bundle branch block, with nonspecific repolarization modifications. TSH, T3, T3 were in

normal range. The lipid profile was abnormal: HDL-cholesterol = 27.6 mg/dL, LDL-cholesterol = 182 mg/dL, total cholesterol = 245 mg/dL. On ultrasund, the thyroid echostructure was diffusely nonhomogenous, with no cystic or nodular formations; there was a slight enlargement of gland (left lobe =17.3/16.5/17.8mm and the right lobe = 20.2/22.5/20.5mm and istm 18/2.8mm) [7].

3. Screening for prostate cancer, considering his age and the highest incidence in men's cancers in Romania [1]: PSA= 3.97ng/dL (upper limit for age = 3.1ng/dL), free PSA 0.42ng/dL, and the fPSA:PSA = 0.10579. The ultrasound examination of the prostate showed a homogenous echostructure, measuring 29/33mm in size. The fPSA:PSA ratio for the age was low in our patient and supported the need for urologic assesement because a low ratio increases the chance to diagnose a malignant prostatic tumour upon biopsy [8].

4. Screening for lung cancer was considered appropriate despite any respiratory symptoms, based on his exposure to various chemical substances used in the rubber industry and his personal history of active tobacco smoking (22.5 pack years); initially a chest X-ray and a spirometry were recommended. The X-Ray showed a solitary nodule with a diameter of 1 cm, well-defined, located at the third rib level, in the left upper lobe (Figure 1).

Due to the hyperthyroidism and the „block and replace" medication of the patient, the administration of the iodinated contrast agent was questioned, as in older protocols, the iodine adminstration was not allowed. With the written agreement of the attending endocrinology physician, in accordance to the updated endocrinological guidelines stating that „Patients on thyroid hormone replacement are not at risk for ICM-induced TD (n.b. iodine based contrast induced thyroid disfunction) and do not require specific management" [9], the patient underwent a thoracic CT with contrast. The CT showed a solitary nodule of 11mm in the left upper lobe, nonspecific and discreet centrilobular emphysema located bilaterally in the apical regions and discreet nonspecific peribronchial densifications (Figure 2 and Figure 3). According to Solitary Pulmonary Nodule (SPN) Malignancy Risk Score (Mayo Clinic Model), upon entering the patient data, there is a 13.5% probability of malignancy [10]. According to Solitary Pulmonary Nodule Malignancy Risk Calculator in adults (Brock University cancer prediction equation), the probability of cancer is 7.42% [11]. According to Lung Imaging Reporting and Data System (Lung-RADS) this SPN would fit in the Category 4B (suspicious) [12].

Figure 1. Posteroanterior chest X-ray revealing a solitary nodule

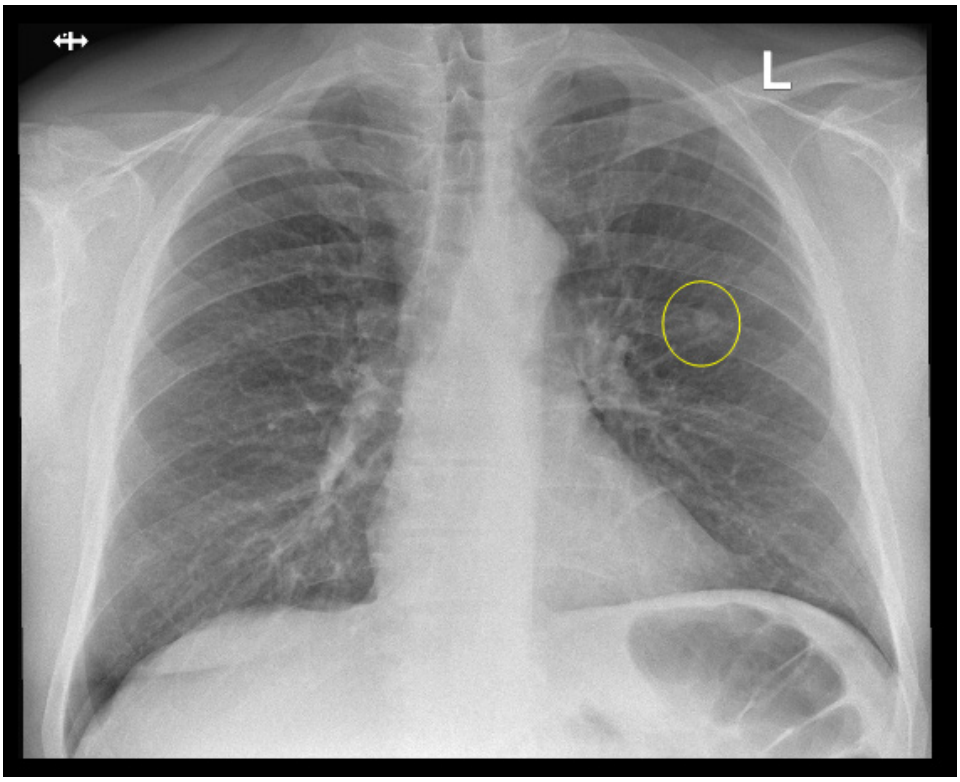
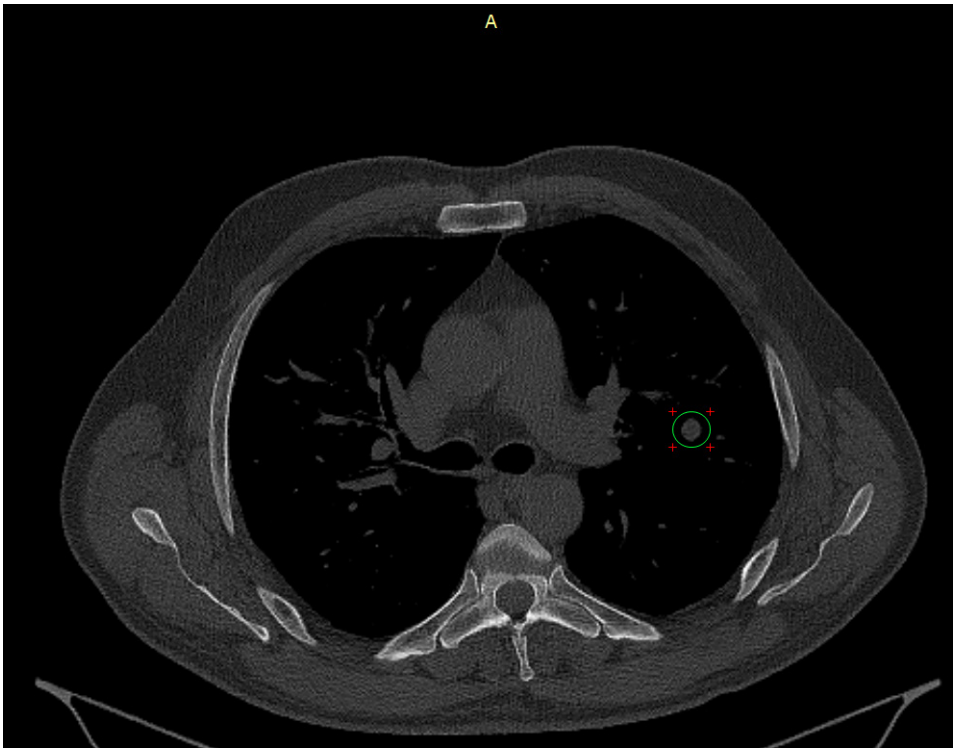
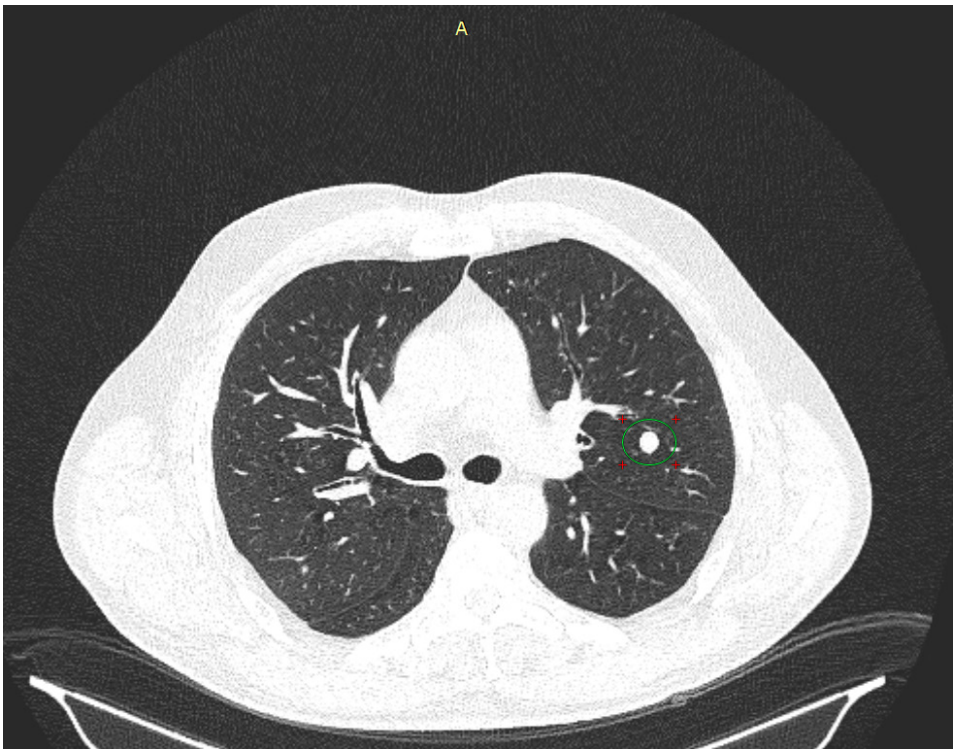


Figure 2 and Figure 3. Chest CT scans indicating the solitary nodule





On spirometry, the forced vital capacity was 89% of predicted, the forced expiratory volume in the first second was 83% of predicted and a maximal expiratory flow at 50% (MEF50) of 62% of predicted, compatible with a slight distal obstruction.

The patient was referred for bronchoscopy in the Pulmonology Department in the attempt to reach a final diagnosis. Unfortunately, due to the localisation, the tumour could not be reached via bronchoscopy. As a result, bronchoalveolar lavage was performed and a sample of 47ml of cloudy, whitish liquid with multiple whitish flakes was collected. After being centrifuged for 5 min at 1250 rpm, smears from the sediment were analyzed, with the following cytological description: the lavage had elevated cell numbers, consisting of respiratory-type ciliated cylindrical epithelial cells, isolated or in small cell groups, some with reactive changes; type 2 pneumocytes isolated/in groups; frequent medium/large macrophages, uni/multinucleated, some loaded with intracellular hemosiderin pigment; multiple squamous cells; relatively frequent lymphocytes and neutrophils; frequent red blood cells; numerous bacterial colonies identified. The conclusion was of benign cytology, acute nonspecific inflammatory appearance. The bacteriological examination was negative for Enterobateriaceae, Staphylococcus Aureus, Streptococcus Spp., Pseudomonas Spp. The mycological examination: negative for Candida Spp. Stain of the smear for acid-alcohol resistant bacilli was negative. Gram stain of the smear showed relatively frequent epithelial cells, relatively frequent polymorphonuclear cells, rare Gram + cocci located outside the leucocytes.

The patient will be followed according to Fleischner Society 2017 guidelines, namely a CT scan every 3 months or, if available, by performing PET/CT [13-15]. A definite diagnosis is bioptic. Considering the patient in the moderate smoking category and the occcupational exposure, the first step chosen together with the pulmonologists team was to repeat the CT after 3 months.

Discussion

We report a case of occupational disease due to the current exposure to musculoskeletal strains, in which a detailed anamnesis revealed a possible other occupational disease: an occupational lung cancer. Therefore, we underline that recording a very detailed occupational history is mandatory in all workers, even if the exposure has stopped long ago. To illustrate this statement, in the following lines we will discuss firstly the medical surveillance of a solid pulmonary nodule (SPN) and secondly, the possible occupational etiology of this nodule.

Concerning the medical surveillance, in 2013, the American College of Chest Physicians (ACCP) developed guidelines for SPNs. In brief, for any SPN on X-Ray, the CT imaging is mandatory. If there is any previous radiological image available, comparison with this image should be done to evaluate any change. Solid nodules between 8mm and 30mm are divided into low, moderate, and high pretest probability groups [16] (Table 2). According to this guideline, patients with a low clinical probability of cancer should have low-dose CT scans at 3 to 6 months, 9 to 12 months, and 18 to 24 months, with a moderate clinical probability of cancer should have PET or serial CT scans, or with a high clinical probability of cancer should go straight to surgical diagnosis with either biopsy or surgical excision [12].

Table 1. Criteria for inclusion in a risk category [17]

Low risk <5%*	Intermediate risk = 5%-65%	High risk >65%
- young age - less smoking - smaller nodule size - regular margins - location in an area other than the upper lobe	- both low and high risk characteristics	- older age - heavy smoking - larger nodule size - irregular or spiculated margins - upper lobe location

*estimated risk of cancer

Based on the above criteria, our patient is included in the intermediate risk and the decission of 3 months follow up is the most suitable.

In terms of the occupational etiology for lung cancer, according to IARC, rubber manufacturing industry is listed in the category for which there is sufficient evidence in humans for stomach, lung, urinary bladder.

A) Carcinogens related to lung cancer

In terms of chemical carcinogens, dusts and fumes and a mixture from rubber-manufacturing industry include class 1 and 2 carcinogens such as N-nitrosamines, polycyclic aromatic hydrocarbons, solvents and phthalates [18]. A study from 2019 of male rubber factory workers showed statistically significant higher rates of pulmonary cancer from cumulative exposure to rubber dust and rubber fumes and from cumulative exposure to nitrosamines (sum of NDMA – N-nitrosodimethylamine, Nmor – N-nitrosomorpholine, NDBA – N-nitrosodibutylamine, NDEA – N-nitrosodiethylamine and NPIP – N-nitrosopiperidine) [19].

Hazards such as N-nitrosamines and carbon black are also used in the rubber industry. Carbon black is a part of group 2B of carcinogens, whereas nitrosamines are mostly part of group 2B, with the exception of N-nitrosodimethylamine which is 2A [5]. The reason why it is still not included in the group 1 results from the conflicting epidemiological studies on the incidence and long term effect of cessation of exposure: a study from 2007 reported an overall elevated standardized mortality ratio (1.46) for lung cancer in a carbon black workers cohort although with significant differences between the 3 different plants which have been considered in the analysis [20]. In a US cohort, this relation was not confirmed [21], while a German analysis of people exposed to carbon black showed that the risk did not decline following the cessation of exposure [22], supporting the need for the long term follow up.

Although there is not enough direct epidemiological evidence of the relationship between CB (Carbon Black) and lung cancer like DEP (Diesel Exhaust Particles), there is a great deal of literature that long-term exposure to CB can increase cancer risk in many ways. These results showed that the plasma of the workers' exposure to the CB could activate pathways similar to direct and indirect exposure to DEP and might promote lung cancer by activating TNF-α signaling. Carbon black could make a notable damage in a patient's body: it could activate biological processes related to the cell cycle and inflammation, increase the eosinophils in peripheral blood (which might increase the risk of cancers), increase genomic instability in peripheral lymphocytes (which is a proven biomarker predicting tumorigenesis). Chronic inflammation has been a well-recognized cause of tumour occurrence and development. The genes of CB exposed workers are highly associated with the presence of IL-6 in the serum. This study further indicates that the inflammatory character of the internal systemic environment caused by CB exposure might increase the genome instability of bronchial epithelial cells, eventually enhancing the risk of lung cancers. Furthermore, the association between nanoparticles exposure and lung cancers was verified through survival analysis which indicates the genes changed by nanoparticles exposure could affect the prognostic of cancers. This suggests that substances produced by inhaled particles that lead to increased genetic instability may cause further damage to lung tissue through the circulatory system, eventually increasing the risk of cancer [4].

In our case, if the SPN develops a lung cancer, the occupational etiology is highly probable, but should be taken together with the influence of smoking. Several studies evaluated the exposure in rubber industry, smoking and the risk of lung cancer. For example, a study on lung cancer mortality of workers exposed during 1973–1997 in a rubber manufacturing plant in Shanghai, China, the association with lung cancer was related to the lenght of exposure and this association remained significant even after adjustment for smoking or economic status [23], confirming that the occupational factor should be considered as significant in the etiology of lung cancer.

B) Carcinogens related to other forms of cancer

Additionally, if 1,3-butadiene is present, there is also enough evidence for causing leukaemia and lymphoma. For lung, oesophageal, pancreatic and kidney cancers, for butadiene and styrene exposure, there was no evidence of positive exposure response [24]. For oesophagus, larynx and prostate cancer, the evidence is limited in humans.

Several hazards present in rubber industry are considered as carcinogens. In synthetic rubber production, styrene has limited evidence in humans for leukaemia, lymphoma and multiple mieloma [25]. As a recent meta-analysis showed, the risk of lung cancer was mainly for those exposed in earlier times [26].

Another line of discussion is the possible association with the prostate cancer and rubber manufacturing

activity.

Considering the substances used in the rubber industry and mentioned in this paper, as well as the patient's abnormal serological findings (fPSA:PSA ratio at the limit between 0.10 and 0.11, which means a higher chance of finding a malignant tumour upon prostatic biopsy), it is important to also note the prostate cancer risk these substances possess. Rubber dust, rubber fumes and NSS (N-nitrosamines sum score = a sum of NDMA, NMor, NDBA, NDEA and NPIP) are considered to be a carcinogen for the prostate according to this study [19].

C) Nonmalignant respiratory diseases in rubber industry

Beside cancer, there is also a high risk for Non-Malignant Respiratory Diseases (NMRDs),

such as COPD and pneumonia [24]. This interferes with smoking: the frequency of respiratory complaints was significantly higher in the smoking group than the non-smoking group. The concurrent effects of cigarette smoking and occupational exposures might have a synergic impact on lung function, as exposure to both occupational hazards from rubber industry and smoking increase 12 times the risk of lung function impairment compared to non-smokers not exposed to occupational carcinogens. Compared to same non-exposed, non-smokers individuals, the occupational exposure without smoking led to an 3.45-fold higher risk and smoking without occupational exposure to a had a 3.48-fold higher risk of abnormal spirometric findings [27]. In another study, focused on talc exposure in rubber industry, the group of exposed smokers, compared to smoker controls, had higher rates of cough (smokers, 42.4% vs control, 13.5%) and productive cough lasting 3 weeks or more each year (smokers, 27.3% vs control, 5.4%) [28]. In this study, there was also a significant decline in lung function parameters among smokers compared to non-smokers. Increased odds of chronic cough (OR= 2.8) and productive cough (OR 2.1) were also observed among the smoking workers compared to non-smokers from a plant in India [29]. Overall, there is relatively good consensus about a higher risk of respiratory symptoms in smokers from rubber industry.

Conclusion

It is of utmost importance to acknowledge all the former occupations of our patients and identify the substances they were exposed to. Even without respiratory symptoms, a tumour formation can still develop and maybe make itself present when it is too late. When facing a pulmonary tumour in a smoking patient, it is necessary to outrule any other possibility such as former exposure to carcinogens in the occupational field and not disregard the diagnosis as being subsequent to tobacco use - it most definitely 'helped' by slowing down the action of the ciliary processes of clearance, but it was not the primary cause. For this patient, further follow up is neccesary to asses the evolution of the pulmonary nodule and to adjust the diagnostic procedures and treatment, accordingly.

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