

Ralph Llewel Sabang¹, Sevak Keshishyan², Christian Salib³, Qiqi Ye³, Liying Han³, Anna Rozenshtein⁴, Oleg Epelbaum²¹Department of Internal Medicine, Westchester Medical Center, Valhalla, New York, United States²Division of Pulmonary, Critical Care and Sleep Medicine, Westchester Medical Center, Valhalla, New York, United States³Department of Pathology, Westchester Medical Center, Valhalla, New York, United States⁴Department of Radiology, Westchester Medical Center, Valhalla, New York, United States

Double or nothing: old chest X-ray as a clue to lung mass

ABSTRACT

Mucoepidermoid carcinoma is a young person's lung cancer with no apparent causal connection to smoking. It exhibits slow growth, which can make it challenging to detect changes in size on serial chest imaging. Another way of describing its growth pattern is that mucoepidermoid carcinoma has an unusually long volume doubling time. We describe a case of an incidental lung nodule diagnosed as mucoepidermoid carcinoma in which a prior chest radiograph provided a clue to the indolent nature of the abnormality and therefore argued against typical lung cancer. In the same context, we underscore the value of volumetric analysis in improving the accuracy of nodule growth determinations, which further strengthens the argument that the importance of locating prior imaging has not diminished in contemporary pulmonary practice.

Key words: mucoepidermoid carcinoma, lung cancer, lung mass, volume doubling time, volumetric analysis

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Introduction

The incidental pulmonary nodule is a common reason for pulmonology consultation in the current era of abundant medical imaging. While in an active or former smoker conventional smoking-related lung cancer is the dominant clinical concern, diagnostic considerations are more diverse in the never-smoker. In the evaluation of such patients, especially as imaging has become increasingly sophisticated, the importance of comparison films — something basic and cost-free — is nowadays easily overlooked. We present a case of mucoepidermoid carcinoma of the lung in a young never-smoker, which illustrates that the value of prior images has not diminished even in today's pulmonary practice. Besides discussing this rare indolent lung malignancy, we also address the concept of volumetric analysis — a modern technique that has made comparison imaging all the more relevant.

Case report

A 49-year-old man presented to the emergency department (ED) of our trauma center after a motor vehicle collision in which he sustained a minor leg injury. On further questioning, he reported intermittent nonproductive cough and night sweats over the past 3 months as well as unintentional weight loss of approximately 7 kg during the same period. His medical history included hypertension and diabetes mellitus. He had no personal history of lung disease or malignancy, although approximately 11 months earlier he had been diagnosed with pneumonia at another hospital and treated with outpatient antibiotics. No post-treatment follow-up took place. He had never smoked but had experienced significant second-hand smoke exposure in his youth.

Upon examination in the ED, he was hemodynamically stable and afebrile. Cardiopulmonary auscultation was unremarkable. There were no palpable lymph nodes or masses. Routine laboratory evaluation was notable for normocytic anemia

Address for correspondence: Ralph Llewel Sabang, Department of Internal Medicine, Westchester Medical Center, Valhalla, United States; e-mail: ralph.sabang@wmchealth.org

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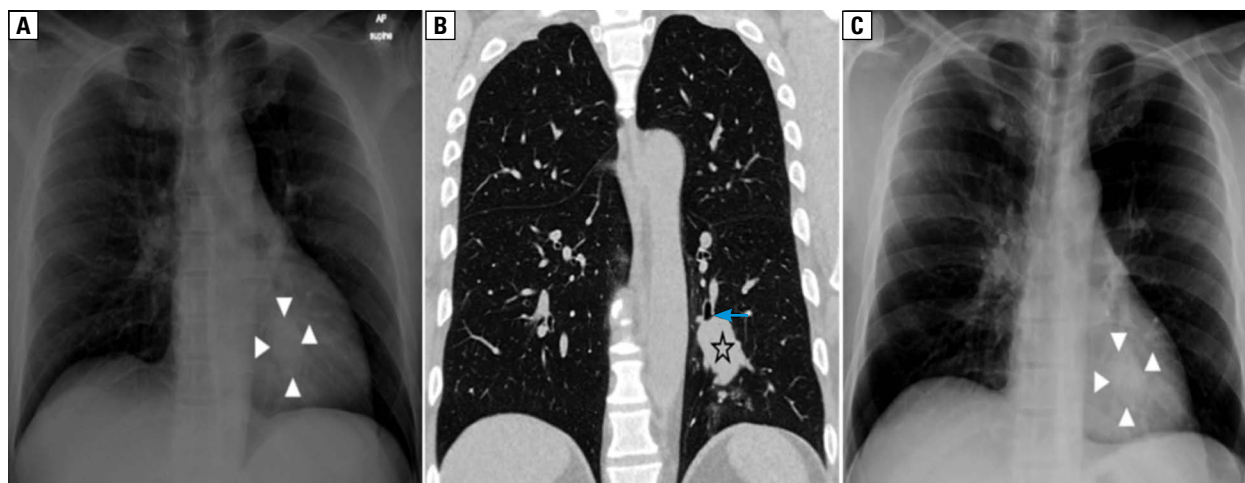


Figure 1. A. Frontal chest radiograph performed in the emergency department of our institution showed an ovoid, mass-like density in the retrocardiac region of the left hemithorax (arrowheads); B. Computed tomography of the chest (coronal reconstruction) performed without administration of intravenous contrast confirmed the presence of a lung mass in the posterior basal segment of the left lower lobe (star) with associated obstruction of the segmental bronchus (blue arrow); C. Comparison frontal chest radiograph performed at an outside institution approximately 11 months prior illustrated minimal interval growth of the lesion (arrowheads)

(hemoglobin 10.9 g/dL, normal range 14.0–18.0 g/dL). Blood interferon-gamma release assay testing was negative. Plain frontal chest radiograph (CXR) performed as part of the trauma protocol revealed an approximately 4 cm ovoid density in the retrocardiac region of the left hemithorax (Figure 1A). Subsequent computed tomography (CT) of the chest performed without intravenous contrast administration confirmed the presence of a lobular mass in the posterior basal segment of the left lower lobe (LLL) measuring approximately 3.8 cm in the greatest dimension (Figure 1B). Prior CXR taken 11 months earlier for the reported pneumonia demonstrated the same lesion (Figure 1C) with interval change in diameter of only 8 mm.

On bronchoscopy, an endobronchial mass occupying the posterior basal segment bronchus of the LLL (LB10) was noted. Biopsy revealed clusters of mucinous cells interspersed among intermediate and squamoid cells with conspicuous absence of cellular atypia and mitotic activity consistent with low-grade mucoepidermoid carcinoma (Figure 2).

Upon establishing the diagnosis of low-grade MEC, the patient was discharged from our hospital with instructions for evaluation by the thoracic oncology team of a cancer center located closer to his residence. He has not been seen in our institution since the time of discharge but reportedly has undergone resection of the MEC.

Discussion

In a relatively young never-smoker with an incidentally detected lung mass, cell types other

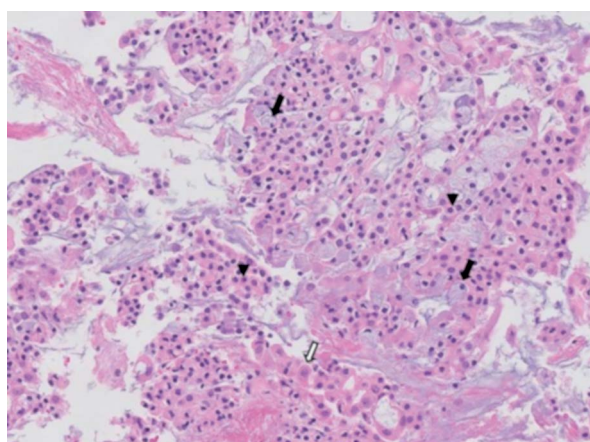


Figure 2. Microscopic section of the lung tumor showing mucinous cells (black arrows), intermediate cells (black arrowheads), and a rare squamoid cell (white arrow) (Hematoxylin & eosin, original magnification $\times 200$). Cellular atypia and mitotic figures are not observed (Ki67 index = 2%). These findings are consistent with low-grade mucoepidermoid carcinoma of the lung. Immunohistochemical stains were performed to exclude competing histologies and were confirmatory

than the most common smoking-related histologies, which are small-cell carcinoma, squamous cell carcinoma, and lung adenocarcinoma, should merit serious consideration. There is a category of indolent lung malignancies not directly linked to smoking that deserves attention in such a scenario (Table 1).

Support for the presence of one of these low-grade tumors would be provided by demonstrating that the so-called “volume doubling time” of the mass in question is very long. The volume doubling time (VDT) of a spherical tumor is a lo-

Table 1. List of examples of slow-growing malignant primary lung tumor histologies

Histological cell type	Remarks
Carcinoid	Spherical, vascularized, usually endobronchial
Mucoepidermoid carcinoma	Current case
Adenoid cystic carcinoma	Like MEC arises from submucosal salivary glands
Granular cell tumor	Extremely rare
BALT lymphoma	Indolent lymphoproliferative disorder

BALT — bronchus-associated lymphoid tissue; MEC — mucoepidermoid carcinoma

garithmic function that can be solved — assuming a constant growth rate — by measuring its diameter on two different CXRs separated by a known period of time. According to the theory of exponential tumor growth, the more rapidly dividing the neoplasm, the shorter will be its VDT in an exponential manner [1]. For example, using diameter measurements on CXR, it has been determined that lung adenocarcinoma has a mean VDT of about 220 days, whereas the much more active small cell carcinoma has a VDT of about 86 days, with squamous cell carcinoma falling in between at about 115 days [2]. Limitations of the planar approach (CXR or CT) for extrapolating change in volume based on change in diameter include the assumption that the lesion is perfectly spherical, that it grows symmetrically, and that its diameter can be reliably determined — something that is subject to significant interobserver variability [3]. Additionally, because the volume of a sphere is related to the cube of its diameter, a simple comparison of diameters underestimates the degree of volume change. For example, a 10-fold increase in diameter from 1 mm to 1 cm (10 mm) corresponds to a 1000-fold (10^3) increase in volume. In the modern era of CT scanning, it has become possible to generate spatial reconstructions of lung nodules for volumetric analysis, which overcomes the deficiencies of two-dimensional methods and allows for direct volume calculations and comparisons (Figure 3). The expectation is that volumetry therefore results in more accurate determinations of VDT [4].

With the above principles in mind, it was felt that the most important initial diagnostic maneuver would be something fundamental and cost-free: obtaining the outside CXR performed 11 months earlier for pneumonia, which indeed demonstrated the same lesion (Figure 1C) with interval change in diameter of only 8 mm, corresponding to a doubling time of 359 days. Although compatible with some estimates for more indolent lung adenocarcinomas and even

squamous cell carcinomas, such slow growth prompted consideration of unusual cell types such as MEC: the eventual diagnosis.

MEC is a malignant salivary gland neoplasm that can rarely arise from the minor salivary glands of the bronchial submucosa. It accounts for < 1% of all lung cancers and is often diagnosed at an unusually young age: nearly a third of patients are under 40 [5]. There is no definitive etiological link to cigarette smoking, which likely accounts for its early presentation [6]. The usual gross appearance is that of a polypoid mass confined to the airway lumen and frequently associated with post-obstructive infection or mucus plugging [7]. MEC can be classified as low-grade or high-grade based on the degree of cellular atypia. With rare exceptions, low-grade tumors remain localized and therefore manifest 5-year survival rates exceeding 90% [5]. High-grade MEC, on the other hand, is an aggressive malignancy with a propensity for local invasion and distant spread; its survival figures are far inferior to those of low-grade MEC [5]. Surgical resection is considered the primary management strategy for this uncommon lung cancer and is feasible in the vast majority of cases.

This case illustrates how something as basic as a comparison with a prior CXR can help assess the growth pattern of a lung mass and thereby categorize its aggressiveness. Strikingly indolent behavior increases clinical suspicion of unusual lung malignancies, among them MEC. In hindsight, it is apparent that what was diagnosed as pneumonia 11 months prior to our encounter with this patient was actually lung cancer in a young never-smoker, which highlights another important use of comparison chest imaging: documentation of pneumonia resolution following treatment.

Conflict of interest

None declared.

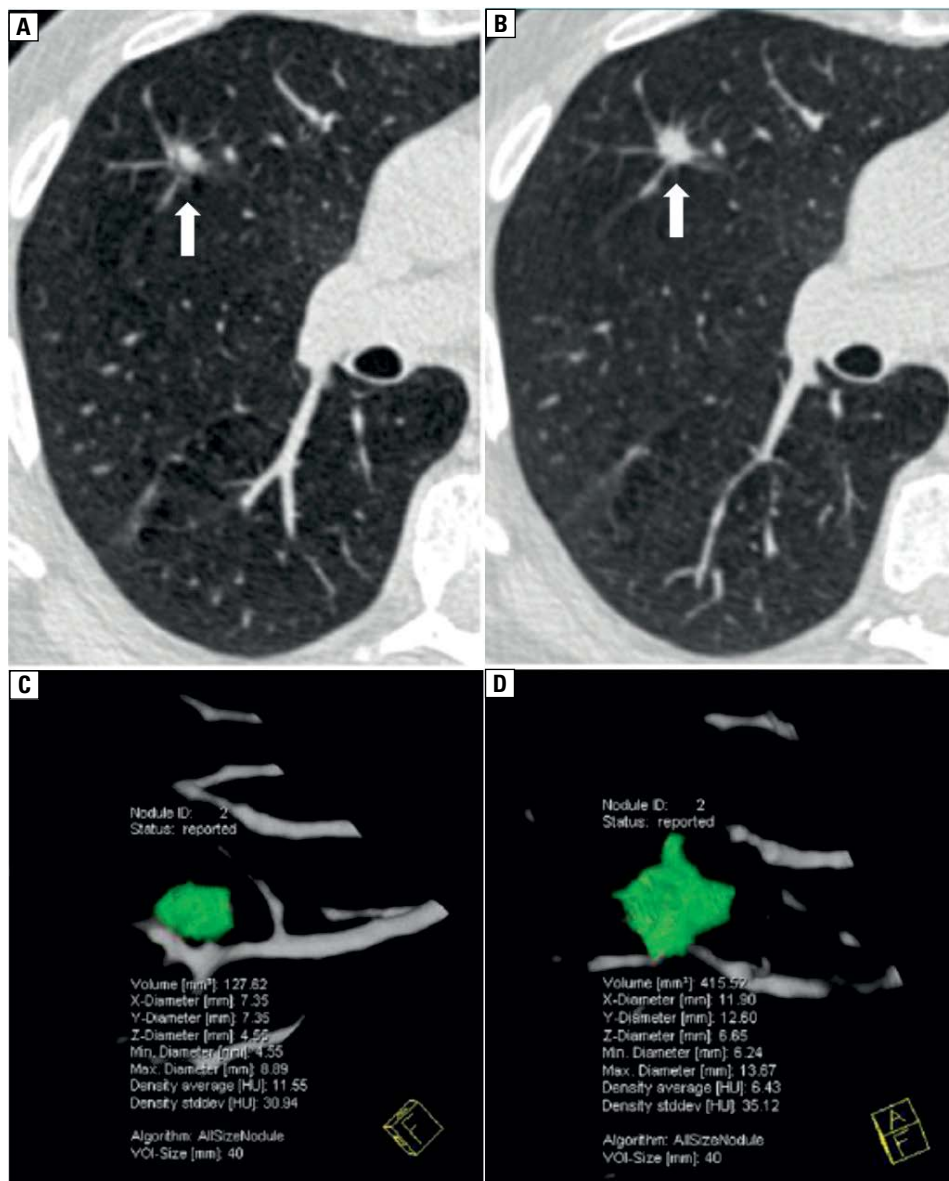


Figure 3. Example of volumetric analysis applied to a solitary pulmonary nodule (white arrow) detected on an initial (A.) and 12-month follow-up (B.) chest computed tomography. The corresponding spatial reconstructions used for volumetric calculations are shaded in green in panels C. and D. The interval increase in nodule diameter of 13 mm amounted to a 15% change, whereas the corresponding increase in volume of 288 mm³ amounted to a 325% change. The volume doubling time (VDT) extrapolated from the change in diameter was 580 days, an excessively long duration for usual lung cancer histologies. The VDT derived from volume measurements was 214 days, entirely consistent with typical lung cancer [4]. This patient turned out to have adenocarcinoma of the lung (Image reused, with permission, from Radiology 2017 ©RSNA [4])

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