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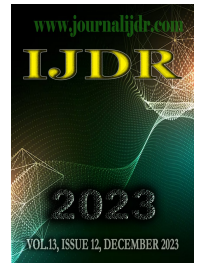
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RESEARCH ARTICLE

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PULMONARY ADENOCARCINOMA IN A NON-SMOKING YOUNG INDIVIDUAL: A DIAGNOSTIC CHALLENGE - CASE REPORT

SILVA, Jamyle Balla da*¹, FARIAS, Jessica Estorque¹, OLIVEIRA, Renata Cristina dos Santos¹, MIRANDA Paula Pires Teixeira de² and AZEVEDO Rômulo Simão Nina de³

¹Resident at Medical Clinic in Hospital Mater Dei Porto Dias, Av. Almirante Barroso; ²Infectious Diseases Doctor, Preceptor of the Medical Residency program at Mater Dei Porto Dias Hospital; ³Nephrologist Doctor, Coordinator of the Medical Residency at Mater Dei Porto Dias Hospital

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*Corresponding author:

SILVA, Jamyle Balla da

ABSTRACT

This is a case report highlighting the diagnostic complexity of pulmonary adenocarcinoma in a young, healthy, non-smoking patient. The study focuses on diagnostic hypotheses leading to the definitive diagnosis, addressing signs and symptoms, found in imaging exams such as chest radiography, computed tomography, and biopsy. The objective is to contribute to the medical literature by presenting relevant information on diagnostic hypotheses until reaching the definitive diagnosis of pulmonary adenocarcinoma, to stimulate future research and diagnostic reasoning, as well as raise awareness among healthcare professionals about early diagnosis to improve patient survival and enhance the quality of care.

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INTRODUCTION

Lung cancer is the most common of all malignant tumors, with an annual 2% increase in its worldwide incidence. Additionally, it ranks as the third most frequent cancer in Brazil for men and the fourth for women, constituting the leading cause of cancer-related death globally. Approximately 90% of these cases are associated with active or passive smoking, but other risk factors include exposure to asbestos, metals, and ionizing radiation, pulmonary fibrosis, HIV infection, and genetic predisposition (Barros, 2006). However, adenocarcinoma, a type of non-small cell carcinoma, originates in the periphery of the lung parenchyma and is more common in individuals who have never smoked. In this type of cancer, malignant cells exhibit distinct characteristics such as glandular, epithelial, or tubular morphology. In this context, several studies have demonstrated that young, non-smoking female patients with lung cancer are more likely to develop adenocarcinoma and to be diagnosed at a later stage. This is because this type of cancer is more common in women than in men and is more prevalent in young individuals than other types of lung cancer (Radzikowska, Gssaz & Roszkowski, 2002; American Cancer Society, 2023).

Furthermore, adenocarcinoma in non-smokers can be challenging to diagnose in its early stages because often there are no symptoms. However, some non-smokers with lung cancer may exhibit symptoms similar to those of smokers. These symptoms may include persistent or worsening cough, hemoptysis, ventilation-dependent chest pain, wheezing and stridor on pulmonary auscultation, anorexia, unexplained cachexia, fatigue, dysphagia, and edema in the face and/or neck. The diagnosis is commonly made through imaging tests such as Chest X-ray (CXR), High-Resolution Computed Tomography (HRCT), CT or combined PET-CT, cytological examination of pleural fluid or sputum, bronchoscopy-guided biopsy, and open lung biopsy or core biopsy (Keith, 2020). It is worth noting that bronchoscopy is often inconclusive, given the peripheral nature of the lesion, which complicates obtaining an adequate diagnostic lavage. In addition to the initial diagnosis, radiology plays a crucial role in monitoring treatment response. Follow-up examinations, such as computed tomography or magnetic resonance imaging, allow for the assessment of tumor size and characteristics after treatment, identifying changes that indicate treatment effectiveness (Karam et al., 2010). Continuous research and improvement of radiological techniques are essential for deepening understanding of this tumor

entity and further enhancing early diagnostic and therapeutic approaches. Therefore, this case report concerns a 29-year-old unmarried female patient from Marabá/PA, in good health and a non-smoker, diagnosed with stage IV lung adenocarcinoma after a seven-month investigation prompted by symptoms of cough, exertional dyspnea, and bilateral pleuritic chest pain. She had been under the care of a pulmonologist and infectious disease specialist previously. Given the observed diagnostic challenges, the conduct of this study is justified, aiming to broaden the diagnostic spectrum for healthy, non-smoking young individuals, with the goal of facilitating early diagnosis for timely therapeutic interventions.

MATERIAL AND METHODS

This study is an observational research with a descriptive and qualitative data approach. A literature search was conducted in electronic databases: SciELO, Portal CAPES, (Lilacs), and Medline/PubMed, covering the period from 2002 to 2023, in both Portuguese and English languages, with the majority of selected articles being in English. By cross-referencing Health Sciences Descriptors (DeCS), the following were selected: Lung Adenocarcinoma, diagnostic examination, signs and symptoms, case report. The information in this work was obtained through a review of the medical record, photographic documentation of diagnostic methods to which the patient was subjected, and literature review. This article complies with Circular Letter 166/2018 from the National Commission of Ethics in Research (CONEP), directly linked to the National Health Council, approved under Opinion No. 6,465,841 of the Research Ethics Committee of Hospital Materdei Porto Dias in Belém do Pará.

CASE REPORT

This study involves a female patient, 29 years old, single, non-alcoholic, non-smoker, without systemic comorbidities, who was admitted with a history of cough, exertional dyspnea, and bilateral pleuritic chest pain lasting for seven months. Upon initial clinical examination, the patient was conscious and oriented, breathing comfortably in room air, normal colored, without edema in the upper and lower limbs, and with an oxygen saturation of 95%. Following a detailed medical history, it was found that the patient had already undergone bronchoscopy with inconclusive results, as well as sputum tests for TB, which were negative. A chest computed tomography (CT) scan performed on June 20, 2022, was evaluated, revealing a lobulated right-sided pleural effusion with fissural extension, multiple areas of confluent consolidation forming opacity, centrilobular ground-glass infiltrate diffusely bilateral, predominantly in the upper lobes, and a well-defined soft tissue density nodule in the middle lobe measuring 1.6 cm, typical findings of miliary-pattern mycobacteriosis (Figure 1). The diagnostic hypothesis includes interstitial pneumonitis, tuberculosis, or sarcoidosis. The medical management involved initiating treatment with Levofloxacin for seven days, followed by ciprofloxacin and clarithromycin without improvement in the clinical condition. Antibiotic therapy was then modified to ceftriaxone and clarithromycin. Laboratory tests, a new chest tomography, pulmonary biopsy, and evaluation by an infectious disease specialist were requested. The result of the new chest computed tomography performed on July 13, 2022, reveals apical right pleural effusion/thickening. Several reticulonodular parenchymal opacities, forming masses, accompanied by irregular nodular thickening of the interlobular connective septa. These lesions predominate in the upper middle third of the lungs, with some following the peribronchovascular axial interstitium. Larger nodules, the largest in the middle lobe measuring 1.6 cm, a small residual calcified nodule located in the posterosuperior segment of the left upper lobe. Osteolytic lesions in the vertebral bodies T6 and T12 (Figure 2). The surgical intervention procedure for biopsy involved segmentectomy of the right upper lobe of the right lung, segmentectomy of the right middle lobe, pleural biopsies, and right-sided thoracostomy with closed drainage. Finally, the specimen was

forwarded for histopathological evaluation. After the surgical procedure, on physical examination: the patient is conscious and oriented, tachycardic and tachypneic in room air, without the use of vasoactive drugs. Neurological examination assessed using the Glasgow Coma Scale with a result of 15, showing no deficits.

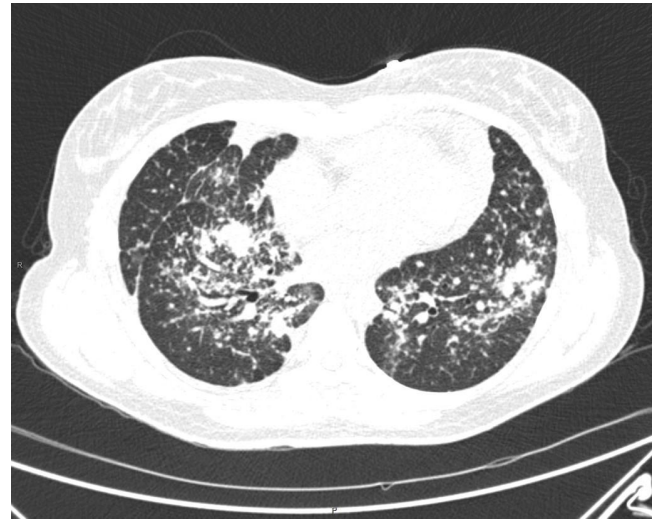


Figure 1. Tomographic aspects of the patient, showing pleural effusion, areas of consolidation, centrilobular ground-glass infiltrate diffusely bilateral

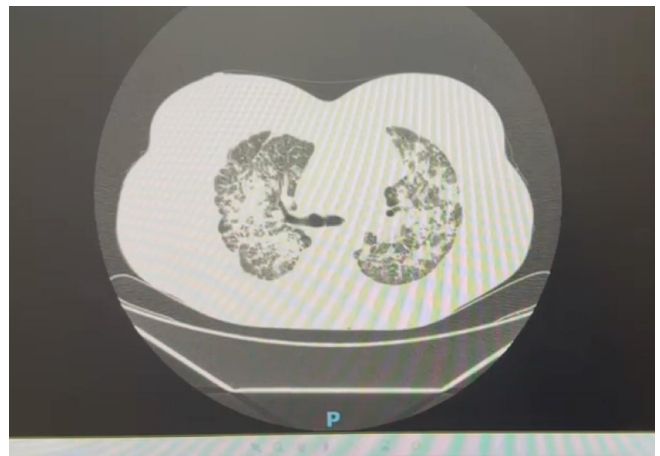


Figure 2. Tomographic aspects of the patient, displaying pleural effusion/thickening, parenchymal opacities, irregular nodular thickening of interlobular connective septa

Pulmonary Auscultation: bilateral vesicular breath sounds with crackles at the apex and middle third of the right upper lobe. Cardiac Auscultation: normophonic heart sounds in two phases, without murmurs. Abdominal examination shows present bowel sounds, no retractions or bulges, and no pain or visceromegaly on palpation. In the genitourinary examination, there is urinary output, and the patient is using a diaper. The musculoskeletal system shows no edema, TEC < 3 s. The diagnostic hypothesis is sarcoidosis or carcinomatosis. Admission tests were requested, O₂ catheter installation, and respiratory physiotherapy three times a day. Oral diet is allowed. The patient developed a clinical picture of desaturation, requiring the use of an O₂ catheter, tachypnea, leukocytosis, use of accessory muscles, and expectoration of thick pulmonary secretion in the form of a cork, which was sent for laboratory analysis (culture and PCR analysis for BK and Galactonona). The patient complained of chest pain. On physical examination, pulmonary auscultation revealed bilateral vesicular breath sounds with bilateral crepitations. A double-lumen catheter and chest tube were inserted. The medication protocol used included Ceftriaxone, clarithromycin 500mg, tazocin (initiated after 3 days of clarithromycin use), and enoxaparin 40mg.

On imaging examination, the X-ray shows expanded lungs with diffuse heterogeneous bilateral opacities. The removed specimen underwent histopathological evaluation for confirmation of the diagnosis, which resulted in stage IV adenocarcinoma with acinar and multifocal micropapillary patterns. After 6 days of hospitalization until the definitive diagnosis, corticosteroid therapy and emergency chemotherapy were initiated, and a molecular test was conducted to investigate driver mutations (EGFR, ALK, and ROS). After initiating corticosteroid therapy and chemotherapy, the patient showed partial improvement but remained tachycardic and tachypneic, requiring the use of a high-flow oxygen mask at 15 l/min, with a rising leukocytosis. After one day of treatment, the patient developed marked respiratory distress, leading to invasive mechanical ventilation, sedation, and attempted alveolar recruitment without success. The patient's clinical condition worsened, and after six days of treatment, she developed continuous fever, extremity cyanosis and distal livedo, bradycardia, and asystole, with no response to resuscitation maneuvers, eventually leading to death.

DISCUSSION

The diagnosis of lung cancer in young, healthy, non-smoking patients can be challenging as the symptoms resemble those of other diseases in their early stages (Gross, 2023)⁴. However, the likelihood of confirming cancer is much reduced compared to individuals with signs and symptoms suspicious of other diseases (American Cancer Society, 2023). Most of the time, lung cancer does not present symptoms in its early stages, or the symptoms can be confused with other conditions such as tuberculosis, sarcoidosis, and pneumonia, for example. Moreover, about 50-60% of lung cancers in non-smokers are adenocarcinomas, and approximately 10-20% are squamous cell carcinomas (American Cancer Society, 2023). In the analyzed case, as it involves a young, healthy, non-smoking patient without comorbidities, and due to symptoms of cough and exertional dyspnea, imaging tests were requested to assess potential pathology. Upon reviewing the results of the patient's computed tomography, the diagnostic possibilities included interstitial pneumonitis, sarcoidosis, tuberculosis, and pulmonary neoplasia. Interstitial pneumonitis is a heterogeneous group of diseases affecting the lung parenchyma, causing inflammation, and, in some cases, scarring. These conditions can exhibit structural changes, alveolitis, and alterations in the epithelium. Symptoms vary and may include exertional dyspnea, cough, fever, and weight loss. Imaging studies reveal changes in pulmonary structure, nodules, lines/reticulations, cystic lesions, ground-glass opacities, and consolidations (Lee, 2021).

Furthermore, sarcoidosis is common in individuals aged 20 to 40 years, with a higher prevalence in women. It is a systemic inflammatory disease characterized by the formation of non-caseating granulomas. Symptoms are diverse, including cough, dyspnea, fever, night sweats, fatigue, and chest pain. Computed tomography changes include heterogeneous lesions, lymphadenopathy, peribronchovascular thickening of interlobular septa, micronodules, and scar tissue formation (Sah, 2023). Additionally, tuberculosis affects the lungs and can disseminate to other organs. Symptoms include persistent cough, pain while breathing or coughing, a sensation of breathlessness, fatigue, low-grade fever, and weight loss. The initial parenchymal lesion or a new infection leads to central necrosis, liquefaction, and elimination of material through a draining bronchus. Computed tomography reveals diffuse micronodules, cystic lesions, ground-glass opacities, consolidations, budding tree-in-bud appearance, and pleural effusion (Dias & Storrer, 2022). However, lung adenocarcinoma is a common type of lung cancer that can be challenging to diagnose in regions endemic for tuberculosis, where there are enlarged mediastinal lymph nodes on tomography. In these cases, surgical procedures are necessary for confirmation. In rare instances, lung adenocarcinoma can develop in individuals whose lungs have scarring caused by other lung diseases, such as tuberculosis (Keith, 2023). Initially, upon evaluating the computed tomography of the reported case, it was observed that the findings were suggestive of tuberculosis. When imaging studies strongly

suggest disease activity, they become useful in establishing the clinical picture in patients with negative bacilloscopy and/or indeterminate radiographs (Gross, 2023). In this context, there was consideration to initiate empirical tuberculosis (TB) treatment due to the clinical presentation and suggestive tomography. However, the designated tuberculosis treatment center in the city denied the provision of medications based on the negative result of bronchoscopy. Nevertheless, the literature stipulates that institutions should provide appropriate treatment in cases where high-resolution chest computed tomography, coupled with a presumptive clinical picture, suggests disease activity even with negative bacilloscopy and indeterminate radiography (Gross, 2023).

It is understood that other measures to elucidate the clinical case should be taken. The patient under study underwent a new tomography, blood tests, and a surgical procedure for histopathological analysis. However, the confirmation of lung adenocarcinoma was only possible after the biopsy result, characterized as stage VI. As described by the American Cancer Society (2023), the diagnosis of lung cancer is made through a combination of tests such as chest X-rays, computed tomography, magnetic resonance imaging, positron emission tomography (PET), and bone scintigraphy. The definitive diagnosis is made by observing a sample of lung cells in the laboratory (American Cancer Society, 2023). Given the result and established diagnosis, it was possible to outline the appropriate treatment for the patient, using a combination of two chemotherapeutic agents, namely Pemetrexed and Cisplatin. Since the disease was in stage IV, the goal was to prolong survival and palliate symptoms. However, the average survival is only 9 months, with less than 25% of patients surviving for 1 year. Palliative surgical procedures may be necessary, including thoracentesis and pleurodesis, the installation of catheters for delayed pleural drainage, the placement of stents to prevent airway occlusion, and in some cases, stabilization of the spinal cord to prevent impending spinal cord compression (Keith, 2023). Although diagnosing lung cancer in young patients is challenging, the performance of imaging exams and regular monitoring is crucial to increase the chances of treatment success and cure of the disease. The significance of early diagnosis lies in the increased chances of cure, as when the disease is identified in the initial stage, patients can receive more effective treatment (Brazil, 2021; American Cancer Society, 2023). Thus, encouraging clinical reasoning to consider lung cancer even in unusual scenarios, as in the reported case, is essential to provide greater diagnostic capacity and support early therapy, thereby avoiding the prolongation of misdiagnoses and the inability to provide accurate patient care.

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