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SOLITARY PULMONARY NODULE UNDER THE ANONYMITY OF COVID-19 INFECTION

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Abstract

We report the case of a 32-year-old male patient, a former smoker, with a known history of SARS - COV-2 infection, mild clinical form, condition that required follow-up evaluation. Despite being oligosymptomatic, the patient reports discreet respiratory symptoms, manifested by dry cough and a sensation of chest tightness. CT thoracic scan revealed a pseudo-nodular, diffusely contoured infiltrate of approximately 10 mm, in the apical left upper lobe segment (LUL), sequelae appearance, thought to represent SARS-COV-2 residual changes, with follow-up recommendation. Three months later, reassessment highlighted a slight progression of the lesion, with a spiculated appearance and umbilicated pleura, a context that mandated further respiratory-specific medical investigations, including bronchoscopic examination and positron emission tomography (PET CT). Given the diagnostic suspicion that included a pathology with neoplastic potential, the firm recommendation was to perform a nodular pulmonary biopsy through video-assisted thoracoscopy (VATS). Both the histopathological (HP) and immunohistochemical (IHC) examinations supported the diagnosis of primary pulmonary adenocarcinoma. The therapeutic course was completed by performing a left upper lobectomy with lymphadenectomy. The case is instructive, confirming that SARS-COV-2 infection is a perfect mimic (1), capable of imitating various other conditions.

In this context, the optimal scenario is distinguished, where monitoring after infection contributes to the early and incidental identification of neoplasia, thus suggesting that SARS-COV-2 infection may also offer certain benefits.

Keywords: *pulmonary nodules, lung biopsy, SARS-COV-2, adenocarcinoma.*

Rezumat

Vă prezentăm cazul unui pacient în vârstă de 32 de ani, fost fumător, cunoscut cu istoric de infecție SARS-COV-2, formă clinică ușoară, condiție ce a impus evaluarea post afecțiune. Deși oligosimptomatic, pacientul relatează simptome respiratorii discrete, manifestate prin tuse seacă și senzație de constricție toracică. Examenul CT toracic a evidențiat un infiltrat pseudo-nodular, cu contur difuz, de aproximativ 10 mm, în segmentul apical al lobului superior stâng, etichetat drept modificare reziduală post infecție SARS-COV-2, ce impune însă monitorizare periodică. Reevaluarea în dinamincă evidențiază discretă progresie lezională, cu aspect

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spiculat, ombilicat al pleurei, context ce a dictat efectuarea unor investigații medicale complementare de profil respirator, inclusiv examen bronhoscopic și tomografie cu emisie de pozitroni (PET CT).

Întrucât suspiciunea diagnostică viza inclusiv o patologie cu potențial neoplazic, recomandarea fermă a fost efectuarea biopsiei nodulare pulmonare prin toracoscopie video-asistată (VATS). Atât examenul histopatologic (HP), cât și cel imunohistochimic (IHC) au susținut diagnosticul de adenocarcinom pulmonar primitiv. Parcursul terapeutic a fost completat prin efectuarea lobectomiei superioare stângi cu limfadenectomie. Cazul este instructiv, confirmând faptul că infecția cu SARS-COV-2 este mimul perfect, putând imita diferite alte afecțiuni[1].

În acest context, se distinge scenariul optim, în care monitorizarea ulterioară infecției contribuie la identificarea timpurie și incidentală a neoplaziei, sugerând astfel că infecția cu SARS-COV-2 poate prezenta, de asemenea, anumite avantaje.

Cuvinte cheie: *nodul pulmonar, biopsie pulmonară, SARS-COV-2, adenocarcinom.*

Introduction

Solitary pulmonary nodule (SPN), frequently observed on chest radiographs and computed tomography (CT), is defined as a radiological entity characterized by a nodular opacity measuring less than 3 cm, surrounded by normal lung parenchyma and not associated with other thoracic anomalies. The absence of mediastinal or hilar adenopathies, as well as the absence of other radiological manifestations such as atelectasis or pleural effusion, is noted[2]. Currently, the management of lung nodules is supported by well-established guidelines with precise monitoring intervals. Surveillance scanning is conducted rigorously according to current recommendations, with size and growth rate serving as the primary indicators to determine the nature of a lung nodule[3]. Subsolid nodules (SSNs) are of concern due to their potential for proliferation, particularly because they may indicate underlying pulmonary conditions such as lung cancer. SSNs encompass both ground-glass nodules (GGNs) and part-solid nodules (PSNs), which are closely monitored for any changes in size or characteristics suggestive of malignancy[4,5]. Given the diverse imaging observations associated with COVID-19, the Radiological Society of North America issued

an expert consensus document in March 2020. This document affirmed that COVID-19 pneumonia commonly presents with multifocal, rounded ground-glass opacities, sometimes accompanied by consolidation and thickening of the septa[6]. Studies have reported that in post-COVID-19 patients, common abnormalities on 1-year follow-up CT scans include ground-glass opacities (GGO), nodules, and subpleural lines, with a prevalence ranging from 16.2% to 55.7%[7,8,9,10].

In this presentation, we aim to elucidate the diagnostic process and the challenges encountered in the case of a young man incidentally diagnosed with a pulmonary nodule amidst a SARS-COV-2 infection context.

Case presentation

We present the clinical case of a young man, 32 years old, urban resident, a former smoker with a history of 15 pack-years who quit smoking one year ago, otherwise no notable exposure. He arrived at our clinic oligosymptomatic, but with a known history of SARS - COV-2 infection, mild clinical form, circumstances that required to perform a chest tomography to assess his COVID status. His past medical history was unremarkable, except for mitral valve prolapse, atopic conditions with documented allergies (dust, kitchen beetles), allergic rhinitis, nasal polyposis, and thyroiditis Hashimoto. Anamnestic, the patient reported discreet respiratory symptoms, manifested with dry cough, and anterior chest tightness. Given this clinical picture and the findings of the CT thoracic scan, he sought specialist consultation. Physical examination revealed abnormal lung sounds, and CT thoracic scan revealed a pseudo-nodular, diffusely contoured infiltrate of approximately 10 mm, located in the apical left upper lobe (LUL) segment (Figure 1a, 1b), believed to represent residual changes following SARS-COV-2 infection, sequelae appearance, with an indication for periodic monitoring. Thoracic CT reassessment in March 2021 revealed an apparently stationary pulmonary imaging aspect, but noted some inconsistencies such as a spiculated appearance and reticulated pleura, for the first-time raising doubts regarding the hypothesis of sequelae. Further investigations were deemed necessary, leading to a fiberoptic bronchoscopy examination with bronchoalveolar lavage (BAL). Utilizing the ultrathin bronchoscope (2.8 mm), visualization extended to the 3rd and 4th-order bronchial subdivisions in the LUL, including the left upper apico-posterior territory, without no-table modifications. No clear proliferative elements or active mucosa lesions in the reachable areas in both white light and autofluorescence (AF). BAL was performed in the LUL area, with 120 ml physiological serum with moderate recovery, further bronchial aspiration cytology, including cytoblock, and Ziehl-Neelsen staining. The bacteriological and cytological results were within normal parameters.

Given the variety of differential diagnoses assessing a lung nodule with prolonged evolution, suitable to any malignant or benign etiology, it was decided for a positron emission tomography (PET CT). A nodular lesion was identified in the apico-posterior segment of the LUL, exhibiting slightly increased metabolic activity, with recommendation for correlation with histopathological (HP) examination. Additionally, small areas of consolidation were observed in the LUL, displaying a ground glass appearance, increased metabolic

activity, and an uncertain substrate (Figure 2a, 2b).

The patient was referred to thoracic surgery and a left video-assisted thoracoscopy (VATS) was performed, with wedge resection of the pulmonary nodule located in the LUL, aiming to achieve a definitive diagnosis and subsequently to determine the appropriate therapeutic approach.

Macroscopically, intraoperatively, a 6.5/3.5/2 cm lung parenchyma fragment is described, completely covered by visceral pleura, with the parenchymal resection edge sutured with metal staples. Upon section, it was identified a well-delimited whitish nodule, measuring 1.9/0.9 cm, located 0.2 cm from the edge of the parenchymal resection, which slightly retracts the visceral pleura.

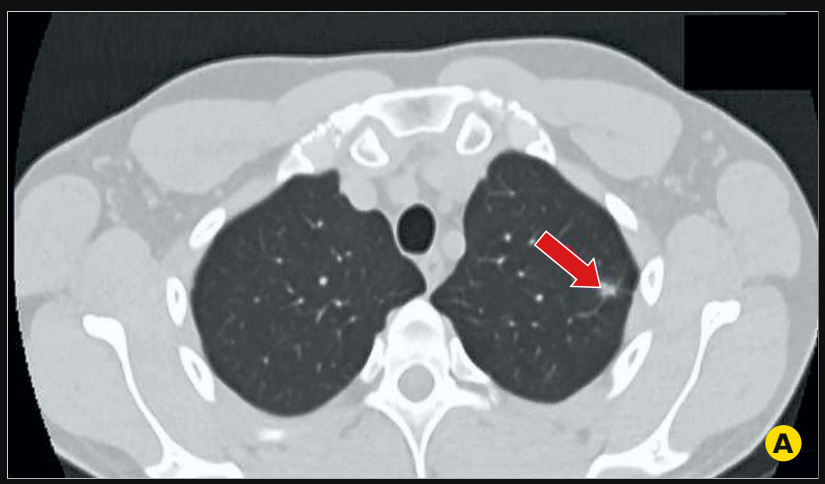
The histopathological examination revealed a lung parenchyma fragment describing a well-defined nodule with a fibrous stroma centrally, ribbed in patches by smooth muscle fibers and slightly inflamed blood vessels, along with moderate inflammatory lymph-plasma cell infiltrate, associated with rare eosinophils and neutrophils, disposed diffuse or in small lymphoid aggregates with germinal centers and anthracosis pigment. Towards the periphery of the fibrous area were detected alveolar spaces with bronchiolization phenomena (spaces containing alveolar macrophages and siderophages, lined by a pseudostratified cylindrical ciliated epithelium without atypia, slightly reactive, with 1 typical mitosis/10 HPF, bordered or occasionally separated by smooth muscle fibers). Others were slightly dilated, extending towards the visceral pleura, with alveolar spaces lined with larger, reactive pneumocytes, achieving aspects of adenomatoid hyperplasia, but without obvious atypia.

The nodule gently retracted the visceral pleura without invading it. Additionally, no images of stromal invasion or desmoplastic stroma were detected in the examined sections.

Subsequently, immunohistochemistry tests were conducted, which did not support malignant tumor proliferation. The markers (Cytokeratin 7) CK7 and thyroid transcription factor 1 (TTF1) were positive, and along with antigen Ki-67 staining showed a low proliferation rate (less than 1%) in the described nodule.

Given the absence of desmoplastic stroma (Figure 3a), clear histological signs of stromal invasion, atypia (Figure 3b), and atypical mitotic figures, as well as the extremely low Ki-67 proliferation index (Figure 3c), the diagnosis of a pulmonary fibro-inflammatory nodule with associated adenomatoid changes, most likely induced by SARS-CoV-2 infection, was favored.

Since the histopathological examination yielded equivocal results and there were



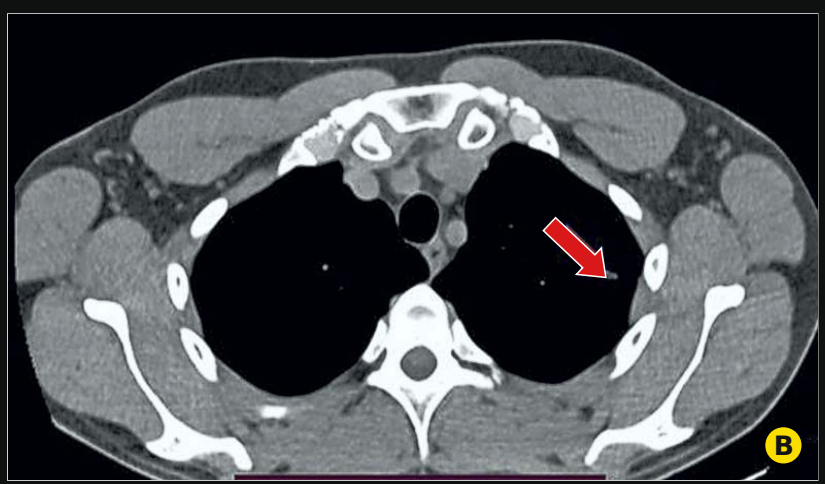


Figure 1. *CT Scan – Axial aspects describing a pseudo-nodular, diffusely contoured, infiltrate of approximately 10 mm, located in the apical left upper lobe (LUL), interpreted as a possible sequelae*

Figure 2. *PET CT Scan - nodular lesion in the apico-posterior segment of the LUL, exhibiting slightly increased metabolic activity, small areas of consolidation, ground glass appearance and an uncertain substrate.*

inconsistencies between the histopathological findings and the imaging suspicion, a second medical opinion was requested for the histopathological examination. Surprisingly, or not, the second opinion revealed an aspect of pulmonary parenchyma with subpleural tumor proliferation, with lepidic pattern and acinar contingent (<5 mm in size on the examined fragment).

Also associating desmoplasia, consisting of cylindrical-cubic epithelial cell elements, non-mucinous, atypical, with rugged nuclei, nucleolated, large; no mitoses were identified; the adjacent pleura was not tumor infiltrated, without carcinomatous microembolisms, on the examined fragment.

Both the histopathological aspects and immunohistochemistry (IHC) tests supported the diagnosis of a primitive lung adenocarcinoma, minimally invasive, with a lepidic pattern - G1, based on the examined fragment.

Furthermore, despite the patient's request for a third opinion, the diagnosis remained consistent with pulmonary adenocarcinoma, minimally invasive, with molecular markers showing positive results for the anaplastic lymphoma kinase (ALK) mutation and negative results for epidermal growth factor receptor (EGFR) and programmed cell death ligand (PDL-1). The next step to complete was the surgery with left upper lung lobectomy, with lymphadenectomy, and complete resection with no residual tumor (Figure 4a, 4b, 4c). The patient's postoperative evolution was favorable, with no signs of tumor recurrence noted approximately 4 years after the initial diagnosis.

Solitary pulmonary nodule (SPN), frequently observed on chest radiographs and computed tomography (CT), is defined as a radiological entity characterized by a nodular opacity measuring less than 3 cm, surrounded by normal lung parenchyma and not associated with other thoracic anomalies. The absence of mediastinal or hilar adenopathies, as well as the absence of other radiological manifestations such as atelectasis or pleural effusion, is noted[2]. Currently, the management of lung nodules is supported by well-established guidelines with precise monitoring intervals.

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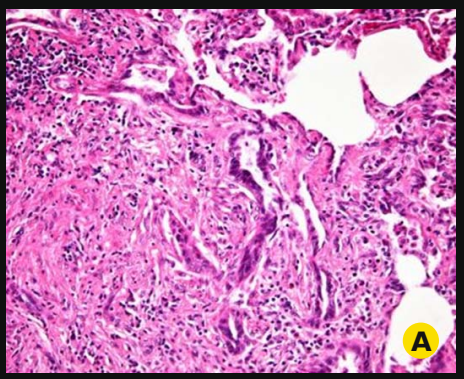
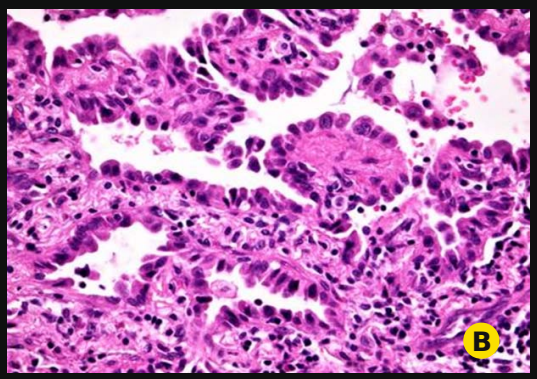




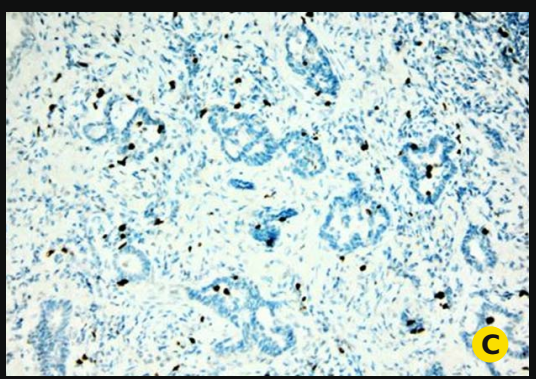
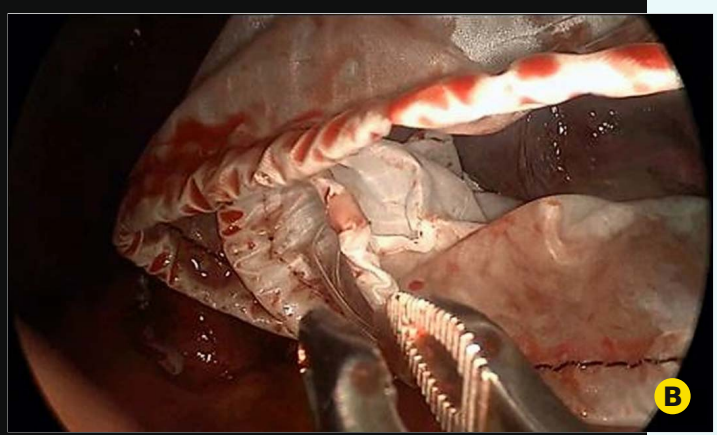


Figure 3. *Histopathologic examination. (Figure 3a) absence of desmoplastic stroma; (Figure 3b) clear histological signs of stromal invasion, atypia, and atypical mitotic figures; (Figure 3c) low Ki-67 proliferation index*



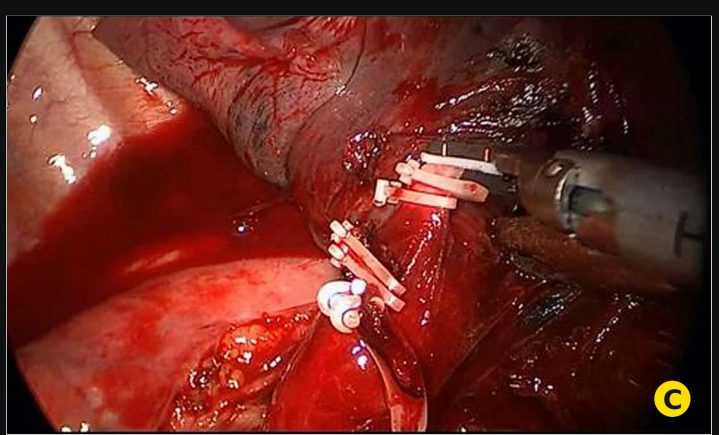


Figure 4. *Intraoperator images during left upper lobectomy revealing anthracotic deposits on the pleural surface.*

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Discussions

The case highlights the challenge posed by the discrepancy between the imaging findings and the absence of a clinical picture with systemic impregnation, which could potentially delay the diagnosis of lipid ADK in a young patient with un-characteristic symptoms, while making it difficult to assess the onset of the disease.

A literature review documented an occurrence rate of irregularly shaped nodules in post-COVID-19 patients, ranging from 3% to 13%[11-13], a fact that may pose serious challenges to practitioners. It underscores the importance of lung biopsy and the necessity of immunohistochemistry testing for personalized cancer treatments. Emphasizing a comprehensive approach to the differential diagnosis is crucial, incorporating ongoing evaluations based on clinical and paraclinical data.

The multidisciplinary team plays a pivotal role in ensuring diagnostic and therapeutic precision. Moreover, recognizing and addressing individual limitations is paramount, with the overarching goal of achieving a balance between curative and palliative treatments, ultimately aiming to enhance the quality of life for each remaining day. In this case, we notice a “positive” effect of COVID-19, the post-infection evaluation helping to reveal the neoplastic nodule, but this could have been considered as a solitary lung nodule with irregular edges, characteristic of COVID-19 infection.

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