A case report of suspicious lung cancer or atypical mycobacteria amidst the pandemic era

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ABSTRACT

Background: Starting 2020, the medical guidelines were shacked by COVID-19 pandemic. The threshold for hospital admission increased in order to limit Severe Acute Respiratory Syndrome coronavirus 2 spread. All this affected screening such as for lung cancer which remained largely undiagnosed. On the other hand, it became challenging to differentiate easily between COVID-19 and other diseases such as atypical infections and simple community acquired pneumonia. Moreover, immunocompromised patients are at higher risk of COVID-19 infection overshadowing any other infection such as tuberculosis and non-tuberculosis infections.

Case Presentation: We present the case of an 85-year-old female with a long history of scleroderma treated with methotrexate. Patient had a non-resolving pneumonia and after two negative RT-PCR, bronchoalveolar lavage showed positive Real Time Polymerase Chain Reaction. Imaging showed persistent 2.6 cm solid nodule in left upper lobe worrisome for an underlying neoplasm. However, culture of Bronchoalveolar lavage grew with few colonies of acid fast bacilli making the diagnosis atypical mycobacteria highly probable especially that patient is chronically immunosuppressed. Unfortunately, she refused further genotyping.

Conclusion: To authors' knowledge that are no, or few reported cases of associated COVID-19 with atypical mycobacterial infections and the treatment modalities are unclear. The diagnosis of mycobacterial infections is usually difficult and in the setting of COVID-19 this becomes more challenging. Hence, a more thorough clinical approach is needed for the future to help clinicians diagnose and treat complicated cases of COVID-19 and concomitant other infections such as TB or Nontuberculous Mycobacteria. Furthermore, amidst the pandemic screening of lung cancer should continue while maintaining safety precautions.

Keywords: Covid-19, screening lung cancer, atypical mycobacteria, NTM, pneumonia, methotrexate, scleroderma, case report, TB.

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Background

Starting 2020, the medical guidelines were disturbed due to by COVID-19 pandemic. People were avoiding hospital visits and all elective patients visits and medical exams were postponed. The threshold for hospital admission increased in order to limit SARS-Cov2 spread. Physicians chose to treat many patients at home losing the capacity of close monitoring. These changes affected screening campaigns and lung cancer remained largely under diagnosed. Healthcare professionals were reluctant about recommending the usual tests in the middle of the crisis despite numerous articles discussing this issue [1,2]. On the other hand, it became challenging to differentiate easily between COVID-19 infection and other diseases such as lung cancer, atypical infections and simple community acquired pneumonia. Indeed, the presence of ground glass infiltrates and consolidation in COVID-19 infection iconography can overshadow lung cancer and can be seen in other viral or atypical infections as well. Moreover, immunocompromised patients are also at higher risk of COVID-19 infection masking other infections such as tuberculosis and non-tuberculosis [3].

Case Presentation

We present the case of an 85-year-old female with a long history of scleroderma treated with methotrexate and folic acid for 10 years. Patient is a past smoker, stopped in the last decade. Two weeks before this presentation the patient had a cough, fever, and chest pain. She denies recent COVID-19 exposure, yet she is seeing her children frequently. An initial evaluation done as out revealed increased inflammatory markers [C- reactive protein (CRP) 3.87], abnormal transaminases, and suspicious infiltrates on simple chest X-ray. A RT-PCR COVID-19 was negative, and a chest scan showed the presence of

dense airspace opacities in the left upper lobe infectious in nature. There was also a 2.7 cm rounded density in the left upper lobe abutting the fissure with few foci of air that could be related to mucoid impaction due to current infection, yet a malignancy could not be ruled out (Figure 1).

With these results, a probable diagnosis of community acquired pneumonia was established while taking into consideration a larger differential diagnosis including infections such as tuberculosis especially in an immunocompromised state. Oral antibiotics -ceftriaxone was started for a total of 7 days and on day 10 the patient was advised to repeat imaging and labs. Meanwhile, she was feeling slightly better and denies fatigue, nausea, and fever resolved but she has a persistent nonproductive cough. A repeat chest scan failed to show improvement in airspace consolidation in the left upper lobe and there were new rounded peripheral ground glass opacities in the right upper lobe consistent with multilobar pneumonia. The 2.6 cm solid nodule in the left upper lobe was still present: worrisome for an underlying neoplasm (Figure 2). A repeat PCR COVID-19 testing was negative again. Decision to admit the patient to hospital for better evaluation and management was taken.

Subsequently, we ordered *Mycoplasma*, *Legionella* testing, and respiratory bacterial panel on the patient's sputum samples all of which were negative. Inflammatory markers increased further, and liver tests were still disturbed. Patient had a high suspicion of COVID-19 infection even with two negative PCR tests. Despite the high risk of contamination, a bronchoscopy - with personal and environmental protection precautions for COVID-19 - was done and bronchoalveolar lavage sent for studies. The bronchoscopy was indicated in the setting of a persistent suspicious nodule to rule out an endobronchial tumor but also to acquire acceptable samples for a thorough infectious workup. The procedure was well tolerated, and no endobronchial mass was visualized, airways were normal without inflammation or secretions. Once again on the BAL the respiratory bacterial panel by PCR was all negative and there were no atypical cancerous cells on cytology. Ziehl-Nelson coloration was negative as well as PCR Tuberculosis. Specimens were sent to culture for tuberculosis and atypical mycobacteria. The diagnosis was a COVID-19 pneumonia since PCR COVID-19 on BAL turned positive.

Based on these results, methotrexate was stopped because of the disturbed liver enzymes and the patient was treated with systemic steroids at a dose of 0.5 mg/kg for 10 days followed by gradual tapering. At the end of the treatment, she was completely asymptomatic and her chest X-ray as well as the Computed tomography (CT) scan revealed a complete resolution of Ground glass opacities (GGO) and alveolar opacities, but a remaining nodular opacity had increased in volume a month later in the left upper lobe (Figure 3).

Upon follow up, 8 weeks later, the culture of the BAL grew a few colonies of acid-fast bacilli. The presence of the nodule along with the positive acid fast was highly indicative of a mycobacterial infection confirming the presence of either TB or NTM. Since PCR Mycobacteria tuberculous (MTB) and Ziehl were negative, the most probable diagnosis is a NTM. Genotyping was not possible for further identification.

A decision to treat with both anti-tuberculosis and levofloxacine was taken since further aggressive investigations were refused by the patient as well as the physician was reluctant to redo a bronchoscopy or a transthoracic biopsy due to her age and because of her COVID-19 fragile lungs.

Discussion

This case is challenging since initially two negative RT-PCR failed to identify the causative agent of the pneumonia. Initially, our patient might have been COVID-19 free and since she is on chronic methotrexate, she had a

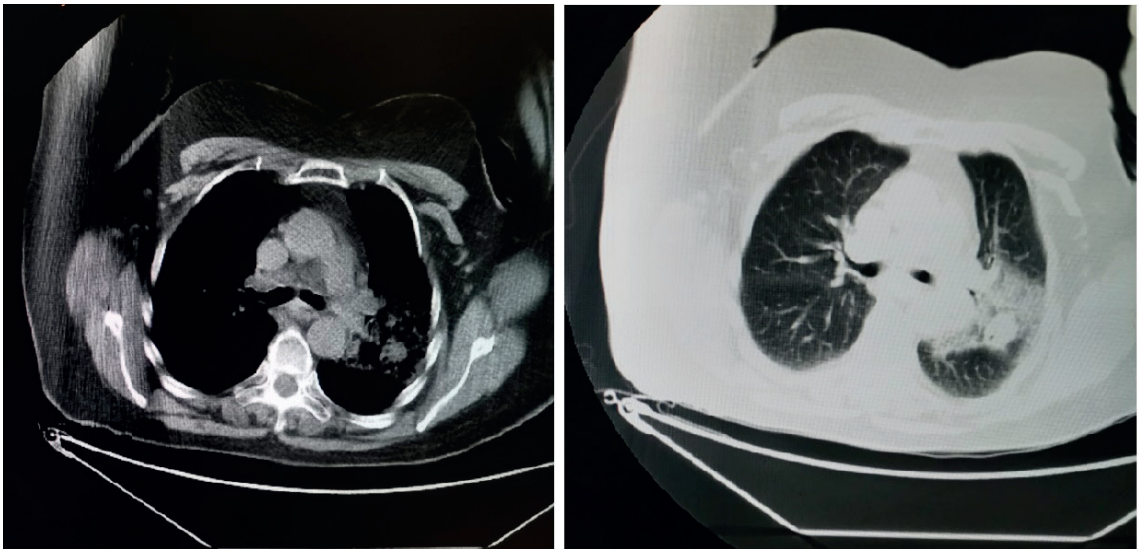

Figure 1. *Initial chest CT scan showing dense airspace opacities in the left upper lobe with a 2.7 cm rounded density in left upper lobe.*

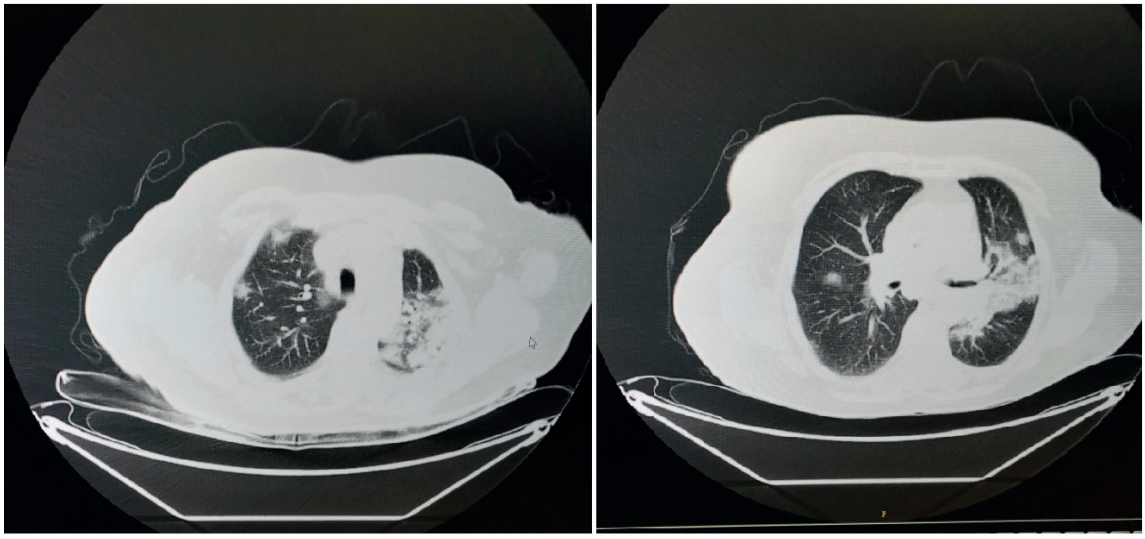

Figure 2. *Repeat scan stable airspace consolidation on the left and the 2.6 cm nodule in left currently showing new right GGO.*

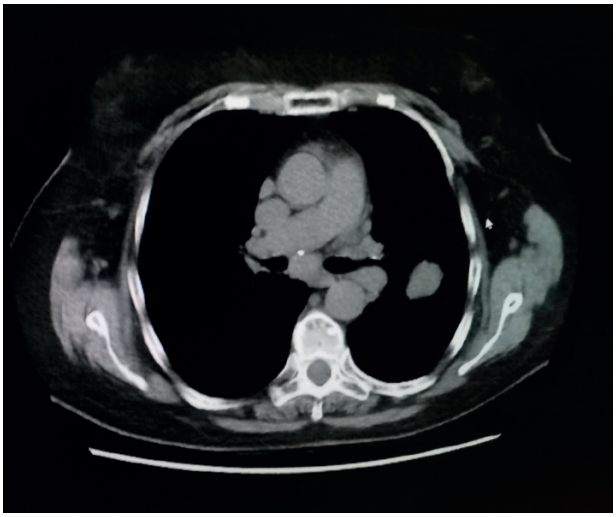

Figure 3. *One month later CT scan showing a complete resolution of GGO and alveolar opacities with remaining nodular opacity increased in volume in the left upper lobe.*

latent atypical mycobacterial infection that was initially silent [4]. On top of her immunocompromised state and the underlying opportunistic infection (tuberculosis or non-tuberculosis mycobacteria), she had COVID-19 pneumonia. These events highlight the emergence of atypical and mycobacterial infections that may now occur in combination of COVID-19 infections [5,6].

Usually RT-PCR is enough to diagnose COVID-19 but opportunistic pathogens are difficult to grow on sputum culture and might necessitate BAL samples to obtain a diagnosis. The limitation is that bronchoscopy with bronchoalveolar lavage is not always possible because of the high risk of contamination but also if patients are hypoxemic due to COVID-19. In general, the management of SARS-Cov2 infected patients is difficult because of high transmission rates; investigations are usually restricted to rigorous necessity in order to limit the personnel in contact with the patient (e.g., radiology technicians, endoscopy nurses…) [7]. Moreover, these patients are at high risk of superimposed bacterial infections and sepsis at any time and because of their high underlying inflammatory reaction further transportation and investigations should be ordered wisely. In our case and with the clinical and radiological deterioration, bronchoscopy was an essential key to rule out cancer or atypical infections that are difficult to grow on sputum culture. Luckily our patient was a fit candidate and tolerated the procedure well.

The second step was to decide upon treatment modalities. COVID-19 pneumonia drastically improved with steroids but since the patient is on chronic immunosuppressive therapy and with the persistent lung nodule, we decided to treat the mycobacteria with empirical therapy. The hypothesis that the corticosteroids used for a limited period (10 days) could have contributed to an activation of a latent tuberculosis infection is less likely to be accepted since lavage samples were taken prior to steroids and lung nodule was present on initial chest scans. She was advised to pursue in the future follow up chest scans to document resolution of the lung nodule with correct treatment for atypical mycobacteria or in case of failure of therapy, to undergo a biopsy to rule out cancer.

Conclusion

A more thorough clinical approach is needed for the future to help clinicians diagnose and treat complicated cases of COVID-19 and concomitant other infections such as TB or NTM or even fungal infections. Nevertheless, amidst the pandemic and the measures taken to limit the spread of infection, lung cancer screening should still be a priority because of its high incidence and high mortality rates. Hence, while maintaining safety precautions, pulmonologists should still encourage smokers to do their annual

chest scans and to order necessary tests for COVID-19 infected patients when an atypical, superimposed infection is suspected.

What is new?

Immunocompromised patients are at higher risk of atypical infections but in the middle of COVID-19 pandemic they are usually misdiagnosed. There are no or few reported cases with COVID-19 and atypical mycobacteria infections. Moreover, screening of lung cancer was delayed because of the pandemic and should be a priority again while respecting measures.

List of abbreviations

BAL	Bronchoalveolar lavage
CRP	C- reactive protein
CT	Computed tomography
GGO	Ground glass opacities
MTB	Mycobacteria tuberculous
NTM	Nontuberculous Mycobacteria
RT-PCR	Real Time Polymerase Chain Reaction
SARS-Cov2	Severe Acute Respiratory Syndrome coronavirus 2

Conflict of interest

The authors declare that there is no conflict of interests regarding the publication of this case report.

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None.

Consent for publication

Written informed consent was taken from the patient.

Ethical approval

Ethical approval is not required at our institution for publishing an anonymous case report.

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Summary of the case

1	**Patient (gender, age)**	Female, 85 year old
2	**Final diagnosis**	COVID-19 with atypical mycobacteria, possible underlying lung cancer
3	**Symptoms**	Fever, cough and dyspnea
4	**Medications**	Steroids, levofloxacin, anti tuberculous
5	**Clinical procedure**	Bronchos copy with bronchoalveloar lavage
6	**Specialty**	Respiratory, infectious disease, oncology