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Case report

Latent tuberculosis reactivation in the setting of SARS-Cov-2 infection: The analysis of the radiologic features that help the diagnosis ☆

Maria Iovino, MD[a], *Martina Caruso, MD*[b,*], *Antonio Corvino, MD, PhD*[c], *Nicola Vargas, MD*[d], *Federica Sandomenico, medical student*[e], *Andrea Cantelli, MD*[a], *Maurizio Rispo, MD*[a], *Vincenzo Pennacchio, MD*[a], *Giuseppa Fernandes, MD*[a]

[a] *Radiology Department, San Giuliano Hospital, Giugliano (NA), Italy*
[b] *Department of Advanced Biomedical Sciences, University of Naples Federico II, Naples, Italy*
[c] *Department of Motor Science and Wellness, University of Naples "Parthenope", Naples, Italy*
[d] *Medicine Department, San Giuliano Hospital, Giugliano (NA), Italy.*
[e] *University of Campania Luigi Vanvitelli, Naples, Italy*

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ABSTRACT

In Italy tuberculosis is a relatively rare disease and people coming from developing nations are usually affected. The radiological findings are variable and depend on the tuberculosis activity, if primary or post-primary. In literature, few data are reported about the co-existence of COVID-19 and lung tuberculosis. In this case report, authors describe the imaging features of latent lung tuberculosis in a patient with SARS-CoV-2 disease. The important role of CT imaging in identifying and diagnosing other infectious lung diseases presenting in the setting of the polymorphism and severity of SARS-CoV-2 disease is also discussed.

Introduction

Infection with a novel beta coronavirus, named SARS-CoV-2, was first identified as the cause of a cluster of pneumonia cases in Wuhan, China, in 2019. Since then, there has been a rapid spread of the virus, leading to a global pandemic of COVID-19 with about 271 million cases and approximately 5.3 million deaths worldwide according to the World Health Organization [1–3]. Tuberculosis is another infectious disease with a pandemic diffusion (about ten million cases in 2019) and a high mortality rate (about 1,2 million deaths per year), representing the tenth cause of death in the world [4]. However, the current COVID-19 pandemic has reduced vigilance over the spread of tuberculosis.

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* Corresponding author.
E-mail address: caruso.martina90@gmail.com (M. Caruso).

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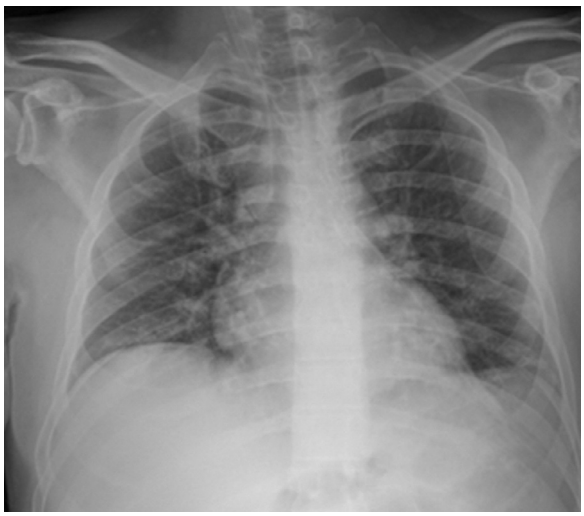

Fig. 1 – Chest x-ray performed at emergency department admission. Few and small airspace opacities are visible in the lower zones bilaterally associated with scissural thickening in the right lung.

In literature, few data are reported about the co-infection of COVID-19 and tuberculosis. Some evidence showed a deficit of T cell immunity caused by COVID-19, thus leading to the reactivation of latent tuberculosis [5]. Chest imaging, especially computed tomography (CT), plays a crucial role in the detection of pulmonary tuberculosis infection presenting in the setting of the polymorphism and severity of SARS-CoV-2 disease. The right diagnosis is fundamental to plan a correct therapy. Furthermore, identifying tuberculosis helps to trace contacts and limits its diffusion.

Case report

A 45-year-old man presented to our attention for the onset of dyspnea and fever. The nasopharyngeal swab for SARS-CoV-2 resulted positive for variant beta and the chest X-ray showed few and small airspace opacities in the lower zones bilaterally; scissural thickening in the right lung was also noted (Fig. 1). To better evaluate the extension of lung disease, a CT scan was performed, which showed several ground glass opacities in all lobes associated with small air space consolidation in the median lobe (Fig. 2). Thus, the patient was admitted to the COVID Unit. After 15 days of therapy, two subsequent negative nasal swabs and symptoms remission, he was discharged. However, chest CT at discharge showed only a slight improvement of interstitial pneumonia. Three months later, the patient presented again for the onset of productive cough, hemoptysis and myalgia. In the suspicious of post-COVID hemorrhagic vasculitis, a chest CT with intravenous injection of contrast medium was performed, which revealed partially excavated consolidation areas in the lower right lobe and in the median lobe. Some small excavated nodular areas were also seen in other lobes. In addition, multiple well-defined centrilobular nodules (2-4 mm in size) and branching linear structures resembling tree-in-bud appearance were identified bilaterally (Fig. 3). These findings were suspicious for an opportunistic infection, such as Aspergillus or Mycobacterium tuberculosis, or for septic embolism. For these reasons, galactomannan antigen test and beta-d-glucan test, specific for Aspergillus, were performed in the broncho-alveolar lavage fluid and resulted negative, while sputum sample and Ziehl-Neelsen stain for acid-fast bacilli were positive, thus confirming the radiological suspicious of tuberculosis. Patient had no history of tuberculosis, and no contact with suspected cases was reported. He was isolated and specific anti-tuberculosis therapy began. The following CT scans performed during therapy showed initially a paradoxical worsening, while then they revealed a slow improvement, although sputum smears were negative. The patient was discharged when clinical symptoms improved, haemophtoe disappeared and three consecutive sputum smears were negative, although CT findings were not completely resolved. Furthermore, all components of his family were screened and three of five resulted positive to Mantoux test showing a latent disease.

Discussion

Tuberculosis encompasses an enormously wide disease spectrum affecting multiple organs and body systems predominantly caused by Mycobacterium tuberculosis, only a small proportion can be caused by Mycobacterium bovis [6]. The prevalence and incidence vary from different countries, in particular tuberculosis continue to be very common in developing nations, while in Western industrialized countries it has become uncommon, but is increasing in prevalence among immunocompromised patients, mainly those with HIV/AIDS [7].

Tuberculosis is usually confined clinically to the respiratory system. Historically, pulmonary tuberculosis has been divided into primary and post-primary tuberculosis. Both of these two forms have characteristic radiological findings [8]. Specifically, primary tuberculosis shows four characteristic findings: 1) lung parenchymal disease with consolidations; 2) ipsilateral hilar and mediastinal lymphadenopathies; 3) pleural effusion; 4) miliary tuberculosis [8,9]. These radiological patterns may be isolated or associated. Consolidations can be located anywhere within the lung in children, whereas there is a predilection for the upper or lower zones in adults. This appearance ranges from too small to be detectable to patchy areas of consolidation or even lobar consolidation. In 2/3 of cases, the infection becomes localized and tends to resolve without sequelae. In the 9% of patients, a calcific mass named tuberculoma forms representing a granulomatous lesion, which may show a central area of caseous necrosis and peripheral rim enhancement after injection of medium contrast, often misdiagnosed with neoplastic disease. The miliary disease, seen both in primary and post-primary tuberculosis, represents hematogenous dissemination of uncontrolled tuberculous infection and is characterized by 1-3 mm diameter nodules uniformly distributed in more than 2/3 of the lungs as snowstorm pattern [10]. Post-primary pulmonary tuberculosis, also known as reactivation tuberculosis or secondary tu-

Fig. 2 – Chest CT scans. Images are reported in axial views (A and B) and in coronal view obtained with multiplanar reformation (C). Several ground glass opacities are present bilaterally associated with small air space consolidation in the median lobe (B and C).

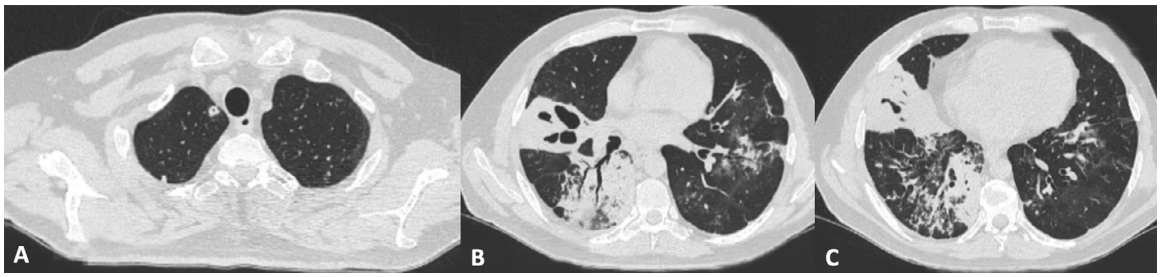

Fig 3 – Axial chest CT scans. Some small excavated pseudo-nodular areas (A), partially excavated consolidations in the right lower lobe and in the median lobe (B and C), multiple micronodules and branching lesions resembling tree in bud appearance (B).

berculosis, occurs years later, often in the setting of an immunodeficiency. In the majority of cases, posterior segments of the upper lobes or superior segments of the lower lobes are involved, and the typical appearance is represented by patchy consolidations [9]. Post-primary infections are far more likely to cavitate than primary infections and are seen in 20%-45% of cases, usually in the posterior segments of the upper lobes (85%). If excavated, these nodules are pathognomonic for the diagnosis of primary and post-primary tuberculosis. Only in 10% of cases, an air-fluid level is present, and it implies communication with the airway, thus with the possibility of contagion. Endobronchial spread along nearby airways is a relatively common finding, resulting in well-defined centrilobular nodules and branching linear structures (tree-in-bud sign), which are better visualized on high-resolution CT [11–13].

One-third of the world population is affected by latent tuberculosis and most of these patients develop a protective T cell immunity that lasts a long time, T CD4+ cells play a crucial role [14,15]. Hence, their dysfunction in patients with HIV leads to tuberculosis reactivation [16]. The same mechanism likely occurs in patients with SARS-CoV-2 infection and may explain the tuberculosis reactivation. Indeed, Diao et al. [17] reported a significant reduction of T cell counts and a functional exhaustion of T cells in patients with COVID-19. During COVID-19 pandemic a rapid increase of tuberculosis cases has been registered. Moreover, a correlation between the Calmette-Guarine Bacillus vaccination and the prevalence and mortality of COVID 19 is reported, but still under investigation [18,19].

In cases of co-infection, imaging plays a fundamental role in raising the suspicion of tuberculosis, especially in patients who do not report previous pulmonary infection or show atypical radiological patterns [20]. In our patient, indeed, CT findings at re-admission were heterogeneous. According to other studies conducted in patients with co-infection of SARS-Cov-2 and tuberculosis, our patient showed atypical CT findings including bilateral cavitary lesions and micronodules associated with branching linear structures in a tree-in-bud appearance, both of them suggestive for an opportunistic infection in active phase. Based on these CT findings, microbiological tests were performed and the correct diagnosis of latent tuberculosis was made.

Conclusions

One-third of the world population is affected by latent tuberculosis, which may be re-activated in case of SARS-CoV-2 infection due to the disfunction of T cells. In this setting, an early diagnosis is mandatory and CT imaging plays a crucial role in raising the diagnostic suspicion, as in our case.

Patient consent

All performed procedures were part of the routine care and the collected data were anonymized. The Patient gave his written informed consent.

Author contributions

Maria Iovino: Conceptualization, Data curation, Formal analysis, Writing - original draft, Martina Caruso, Writing - original draft; Antonio Corvino: Data curation, Formal analysis, Writing - original draft, Writing - review & editing; Nicola Vargas: Formal analysis, Writing - original draft, Writing - review & editing; Andrea Cantelli: Conceptualization; Maurizio Rispo: Conceptualization; Vincenzo Pennacchio: Data curation; Giuseppa Fernandes: Writing - review & editing.

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