ATYPICAL RADIOLOGICAL MANIFESTATIONS OF ACTIVE PULMONARY TUBERCULOSIS IN SERIES OF PATIENTS FROM NORTH MACEDONIA ON COMPUTED TOMOGRAPHY

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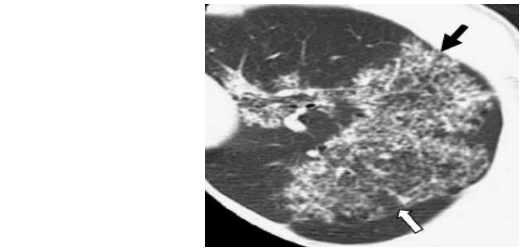
Abstract: Immunocompromised and patients with chronic diseases worldwide, as well as from North Macedonia, have a greater probability of acquiring tuberculosis (TB) in their lifetime, which is caused by the mycobacterial species and still represents one of the major burdens of the public health systems, as well as one of the most frequent causes of death. The disease itself can manifest in two forms, active and dormant. The active form of the disease manifests shortly after acquiring the infection, whilst the dormant one can occur after years of latency as a postprimary form. Negative microbiology results in tuberculous patients can delay and complicate the accurate diagnosis, so the diverse diagnostic imaging modules, especially the computed tomography (CT), have a supreme role in diagnosing, and following patients with pulmonary tuberculosis (PTB) after treatment.
Purpose: Our aim was to illustrate and analyze some atypical appearances of active pulmonary tuberculosis (PTB) in series of 30 patients from North Macedonia on computed tomography (CT).
Methodology: 30 consecutive chest CT scans of patients with microbiologically proven tuberculosis from North Macedonia were thoroughly analyzed. All patients underwent a non- contrast and then a contrast enhanced chest CT according to appropriate diagnostic protocol on a 64-slice Somatom Definition AS + computed tomograph (Siemens Healthineers, USA). We reviewed 30 CT scans and all the available information from the medical history of the patients, including their microbiology results.
Results: Some of the uncommon signs of PTB we observed on the CTs included: (1) various clusters of micronodules; (2) cystic patterns in PTB patients; (3) PTB with diffusely scattered non miliary nodules, (4) PTB in the setting of COVID 19 pneumonia, (5) organizing pneumonia.
Conclusion: Aside from the obvious decrease of the PTB incidence globally, there is an evident rise of atypical manifestations, clinically and on imaging. Mastering the knowledge of atypical CT imaging signs in active PTP will help in reaching diagnosis, following treatment response or residual activity of PTP in clinical practice. Diagnostic imaging also aids the detection of complications or sequels from the disease.
Keywords: tuberculosis (TB); computed tomography (CT); North Macedonia; clusters of micronodules; cystic patterns of PTB; non- military nodules;

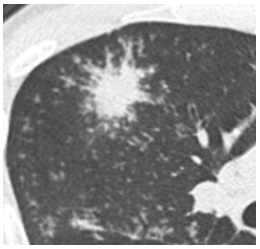
1. INTRODUCTION

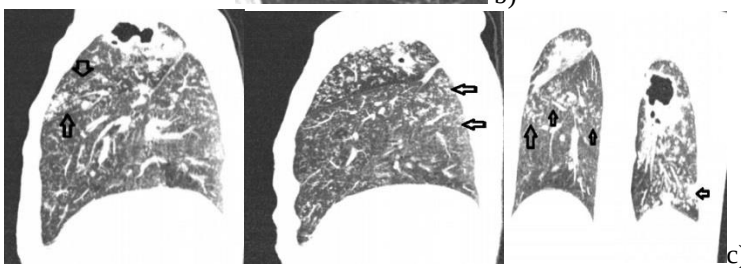
Immunocompromised and patients with chronic diseases worldwide, as well as from North Macedonia, have a greater probability of acquiring tuberculosis (TB) in their lifetime, which is caused by the mycobacterial species and still represents one of the major burdens of the public health systems, as well as one of the most frequent causes of death. There can be solely lung affection by the bacteria, as well as other extra pulmonary sites.
About a quarter of the world's population is infected with M. tuberculosis, equivalent to about 2 billion people. A relatively small proportion (5–10%) will develop TB during their lifetime. Until the coronavirus (COVID- 19) pandemic, TB was a leading cause of death from a single infectious agent, outranking human immunodeficiency virus (HIV). Best estimates for 2020 are 1.3 million TB deaths among HIV-negative people (up from 1.2 million in 2019) and an additional 214 000 among HIV-positive people (up from 209 000 in 2019), with the combined total back to the level of 2017(1, 2).
The disease itself can manifest in two forms, active and dormant. The active form of the disease manifests shortly after acquiring the infection, whilst the dormant one can occur after years of latency as a postprimary form. Most common CT findings in patients with pulmonary manifestation of tuberculosis include alveolar consolidation, ground glass opacities, cavities, tree-in-bud pattern, nodules, and they usually suggest endobronchial spread of tuberculosis. On the other hand, atypical manifestations of the disease only occur in certain stages and pose a debatable clinical and radiological diagnostic challenge(3, 4). Negative microbiology results in tuberculous patients can delay and complicate the accurate diagnosis, so the diverse diagnostic imaging modules, especially the computed tomography (CT), have a supreme role in diagnosing, and following patients with pulmonary tuberculosis (PTB) after treatment.
We aimed to illustrate some rare and atypical CT signs of PTB in 30 consecutive chest CT scans of patients with microbiologically proven tuberculosis from North Macedonia.

Clustered micronodules (CMN sign) depicts a conglomerate of multiple, dense micronodules in the range of 1 to 3mm, who are mainly distributed around small airways at subsegmental level (Figure 1a-c). There is usually a centrally located, dilated bronchus with thickened wall but patent lumen. If there is coalescence of the nodules, obstruction of the bronchial lumen can occur or larger nodules and consolidation may be a common progression. When small nodules congregate and form a larger nodule, some distribute at the periphery, thus resembling the Milky way galaxy and the finding is named galaxy sign (5, 6). These atypical manifestations of the disease are common in younger patients, have a predilection for the proximal and mid lung parenchyma zones, usually foretell a well confined disease, and resolve after appropriate tuberculosis treatment.

Figure 1(a- c).


a)

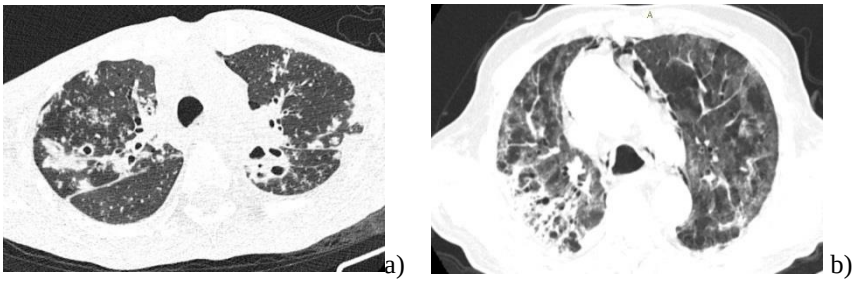

b)


c)

a) clusters of micronodules (CMN's) with spare spaces between them and some reticular interstitial markings in the upper left lobe in a patient with TB b) galaxy sign phenomena when multiple small nodules arranged around a larger conglomerate of nodules c) clusters of small nodules coalescing and forming larger nodules and some areas of subsegmental consolidation.

Tuberculous cystic patterns are an occasional finding in the course of infections or trauma, and seldom manifest as thin wall cavities filled with air. In the setting of pulmonary tuberculosis, they are extremely rare. The cystic changes form when the affected and consolidated lung tissue necrotizes and drains, thus obstructing the drainage bronchioles, who exhibit inflamed and thickened walls and narrowed lumens(7). The cystic pattern can involve one or multiple lung lobes and their diagnosis on computed tomography doesn't represent a diagnostic problem.(Figure 2 a, b)

Figure 2 (a, b)

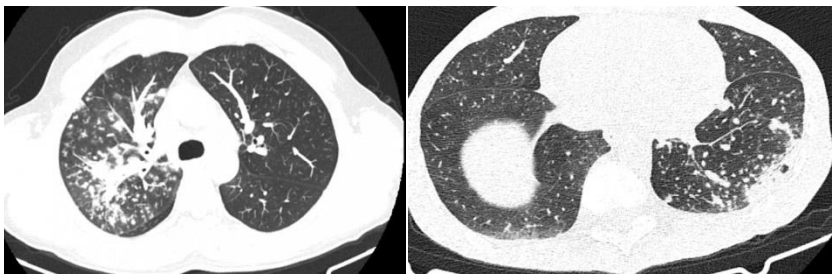


a) b)

Figure 2 a) There are some cystic lung patterns in both upper zones, combined with small nodules of various sizes, some with a tree in bud distribution; b) Cystic lung findings in the mid to lower parts of the right lung, subpleuraly, together with some mosaic attenuation, ground glass opacities and interstitial reticular patterns.

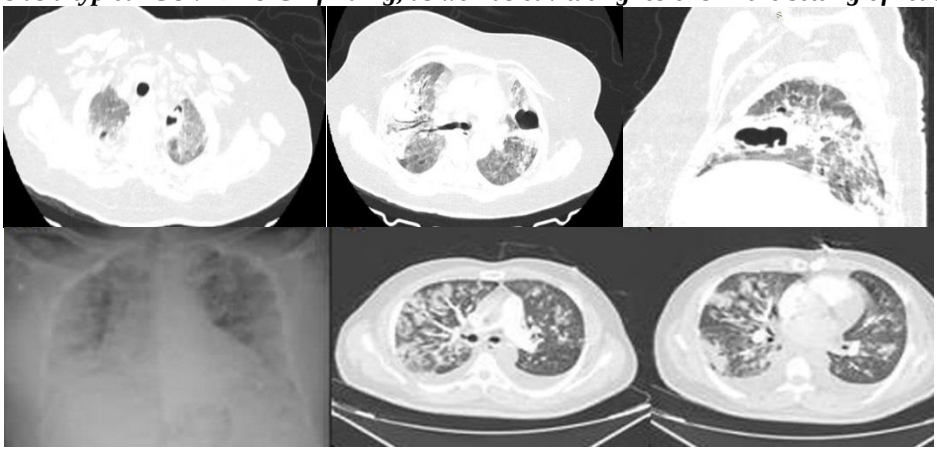
The CT findings of PTB with diffusely scattered non miliary nodules show randomly disseminated nodules that have various sizes but similar attenuation, they are non- segmental and predominantly occupy the subpleural spaces or they relocate along the bronchovascular bundles. They usually appear in a subacute or chronic stage of the disease, can misguide the diagnostician and be inaccurately diagnosed as secondary infiltrative changes, emboli or some other granulomatous diseases(Figure3)(8, 9).

Figure 3 (8, 9). Multiple diffusely scattered non military nodules with similar attenuation but various sizes.



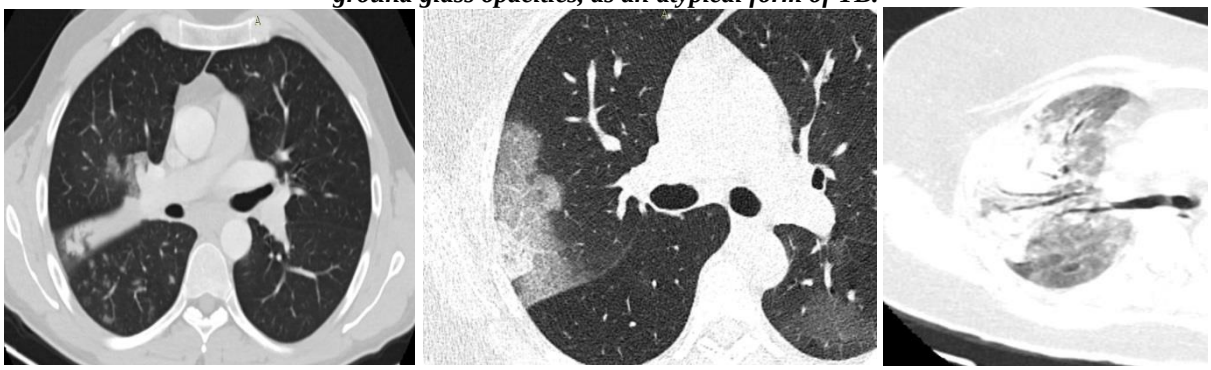
PTB on the background of COVID-19 pneumonia. During the assessment of the series of 30 patients with microbiologically proven PTB, we came across several cases of co- existing COVID 19 pneumonia and reactivated post primary PTB with cavitation and signs of endobronchial spread, probably due to the suppression of the immune system response (Figure 4).

Figure 4 Diffuse ground glass opacities and more intensive peripheral zones of consolidation with positive air bronchograms as a typical COVID 19 CT finding, as well as cavitating lesions in the setting of reactivated PTB.



Organizing pneumonia in the setting of PTB is an inflammation that penetrates the air spaces distal to the terminal bronchioles, and it packs the respiratory bronchioles and alveoli with caseous granulation tissue. Typically, the organizing pneumonia is provoked by infective agents, some chronic systemic connective tissue disorders, drugs, radiotherapy and organ transplantation. Mycobacterium tuberculosis rarely induces the occurrence of organizing pneumonia(10- 15). The CT findings in such cases are infrequently typical and we usually encounter areas of organized alveolar consolidation and ground glass opacities. (Figure 5).

Figure 5 Patients with microbiologically proven PTB, showing areas of organized alveolar consolidation and ground glass opacities, as an atypical form of TB.



2. CONCLUSION

Pulmonary tuberculosis can exhibit a wide range of atypical forms on computed tomography that itself presents huge diagnostic challenge. Considering the fact that the atypical manifestations of PTB are on global rise, mastering the knowledge of atypical CT imaging signs in active PTP will help to reach a solid diagnosis, to follow response after treatment or residual activity of PTP in clinical practice. Diagnostic imaging also assists the detection of eventual disease complications or sequels.

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