# Morphological features of secondary lung tuberculosis in HIV-patients

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**ABSTRACT:**

In modern conditions, socially dangerous diseases (tuberculosis, HIV infection) are characterized not only by a high level of epidemiological indicators, but also by profound changes in the pathogens themselves (multiple drug resistance, etc.), changes in the course of diseases, its' complications, causes of death, clinical and morphological manifestations, the appearance of co-infections, which is regarded as a negative phase of pathomorphosis or as reversion. At the same time, the pathomorphosis of diseases significantly complicates their diagnosis. There are objective reasons that do not allow to verify certain nosological units. Under conditions of nosomorphosis due to changes in the biological properties of the pathogen and reactive properties of the organism, in clinical practice and in the study of sectional, surgical and biopsy materials often have difficulties in diagnosis of various forms of tuberculosis and HIV, patho-, morpho- and thanatogenesis. Untimely diagnosis often leads to disability and mortality of patients. Therefore, in clinical practice, undiagnosed forms of socially dangerous diseases are more common.

In 2018 251,000 people who had both TB and HIV are estimated to have died [1]. This is in addition to the 1.2 million people who

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died from TB alone. A total of 477,461 TB cases among HIV positive people were reported in 2018 (56% of the estimated incidence of 862,000 cases) [2]. Of these 86% were on antiretroviral therapy. In comparison, in Ukraine in 2019 5943 HIV deaths were reported, 1448 among them had TB and HIV coinfection (24.36%) and 811 of them were on antiretroviral therapy (56%).

Due to all these statistics we can make a conclusion that TB in HIV patients is one the main causes of death in HIV-patients. Furthermore, due to the statistics even antiretroviral therapy does not have great affection on the TB and HIV coinfection course. TB/HIV coinfection is a global substantial problem and it means that all international guidelines have to be better implemented.

Keywords: HIV, TB, antiretroviral therapy, coinfection.

## INTRODUCTION

TB and AIDS coinfection is one of the most dangerous states among all of the infection diseases. Furthermore, this coinfection creates a lot of difficult diagnostic and therapeutic challenges and this creates an increased pressure on health care systems. TB is top 1 cause of death in patients with AIDS (26% of AIDS-related deaths) [2]. TB and HIV have huge effects on the host's immune system alone, however while there is a coinfection it changes the course of TB as well as AIDS because both diseases potentiate each other, that is why diagnostics as well as treatment become a very difficult task. It is known that almost the one-third of the planet population is latently infected with M. tuberculosis, and HIV is one of the most common causes of the M. tuberculosis reactivation.

It is generally known that approximately one third of the whole population are latently infected with the M. tuberculosis. Although, the rate of activation of the latent TB vary differently. However, most of the cases show that approximately 10% of latently TB-infected patients will have the disease development. Nonetheless, immunocompromised patients (HIV-positive) are 10–15% more likely to develop the disease if the they were latently infected previously [3].

During the latent phase of the TB the bacteria is not fully eradicated so as soon as host's immune system become compromised (with HIV for example) it leads to the TB reactivation. Surely, reactivated Tb in patient with compromised immune system will lead to the changings in clinical manifestation.

In 90% of cases TB affects lungs with formation of granulomas which are organized cellular structures which contains Mycobacteria. CD4+ T cells and TNF took an important role in granuloma organization. Thus, this explains why granuloma formation usually fails in patients with TB and AIDS coinfection. However, Tb and AIDS coinfection lesions are much more diffuse. For example, instead of granuloma formation in the lungs, patients with TB and AIDS coinfection usually have granulocytic infiltrate with necrosis which is much more diffuse lesion in comparison with well-defined granulomas. Moreover, up to 80% patients with TB and AIDS coinfection have extra pulmonary forms of TB or even could course in a form of systemic disease. Another one phenomenon to develop is IRIS (immune reconstitution inflammatory syndrome). It could develop in patients who receive both antiretroviral and anti-Tb treatment. This is still debated, however some patients have developed some of IRIS predictors including low CD4+ levels and high viral load prior to antiretroviral therapy and an increase of CD4+ counts after the beginning of the antiretroviral therapy. Possible mechanisms responsible for IRIS may be a sustained Th1-response against mycobacterial antigens, which is followed by dysregulation of cytokine secretion and T cell migration to the inflammatory site. Two types of IRIS presentation could be described: unmasking of undiagnosed tuberculosis and a paradoxical deterioration of existing tuberculosis lesions or appearance of new lesions after initial improvement [4].

## DIAGNOSIS

The most common test for the TB – Sputum smear microscopy is usually not representative in patients with Tb and AIDS coinfection because the rate of the smear-negative Tb represents up to 60% of all TB cases in HIV patients [5]. This is the main reason why the methodology of TB diagnosis in patients with

compromised immune system have to be revised. With advancing immunosuppression, extra pulmonary involvement, intra-thoracic/ mediastinal lymphadenopathy, lower lobe infiltrate and miliary TB become more common. That was the reason why WHO provided the guideline with the recommendation for the diagnostics of the TB in HIV-positive patients which helped to reduce the diagnostic delay and therefore decrease morbidity and mortality of TB in HIV-positive patients [6].

## SMEAR-POSITIVE PULMONARY TUBERCULOSIS

- One sputum smear examination positive for acid-fast bacilli (AFB) and
- Laboratory confirmation of HIV infection or
- Strong clinical evidence of HIV infection. Smear-negative pulmonary tuberculosis
- At least two sputum specimens negative for AFB and
- Radiographical abnormalities consistent with active tuberculosis and
- Laboratory confirmation of HIV infection or
- Strong clinical evidence of HIV infection1 and
- Decision by a clinician to treat with a full course of antituberculosis chemotherapy OR
- A patient with AFB smear-negative sputum which is culture-positive for Mycobacterium tuberculosis. Extrapulmonary tuberculosis
- One specimen from an extrapulmonary site culture-positive for Mycobacterium tuberculosis or smear-positive for AFB OR
- Histological or strong clinical evidence consistent with active extrapulmonary tuberculosis and
- Laboratory confirmation of HIV infection or
- Strong clinical evidence of HIV infection1 and
- A decision by a clinician to treat with a full course of antituberculosis chemotherapy. [7]

Pathomorphological examination of HIV / TB co-infection usually reveals multiple areactive caseous-necrotic and caseous-purulent foci (Figure 1) without the typical granulomatous inflammation characteristic of tuberculosis (Figure 3 and Figure 4), which often complicates the morphological verification of the tuberculosis process (Figure 1). In the study of micropreparations stained by the method of Ziel-Nielsen, in caseous-necrotic and caseous-purulent masses can be found a large number of acid-fast mycobacteria (Figure 2).

## TREATMENT

The TB and HIV coinfection treatment is still a very discussable problem. Multiple studies were launched, however there are still no clear evidences for some special treatment for such type of patients, so they should receive the

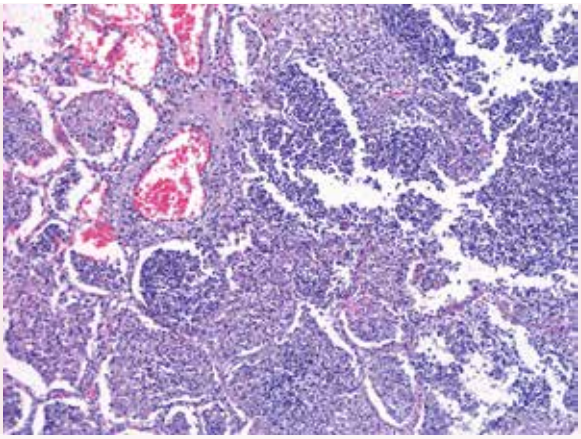

**Figure 1.** Caseous pneumonia in HIV infection. Staining with hematoxylin and eosin, x100

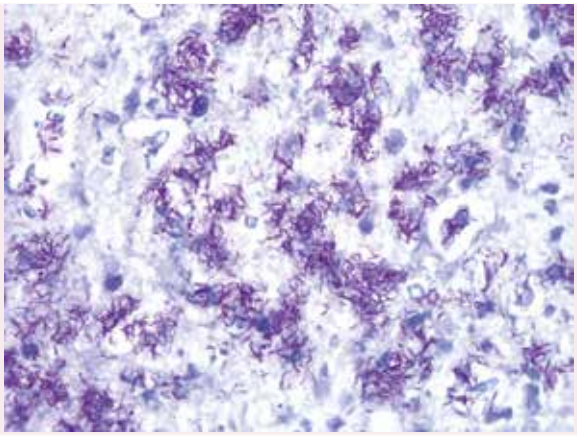

**Figure 2.** Acid-resistant mycobacteria of tuberculosis in the foci of caseous pneumonia in HIV infection. Stained with Ziehl-Neelsen stain, x1000.

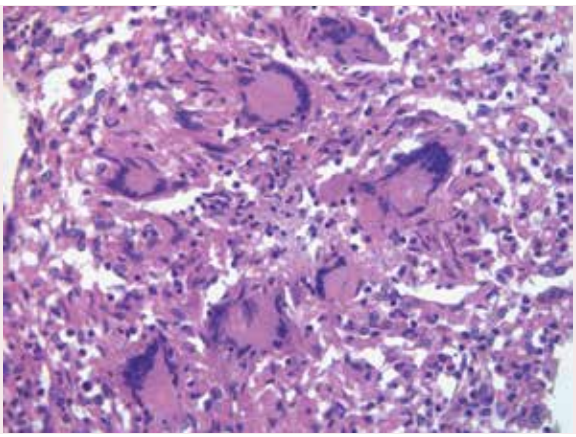

**Figure 3**. Non-necrotizing giant cell granulomas in lymph node tuberculosis without HIV infection. Staining with hematoxylin and eosin, x400

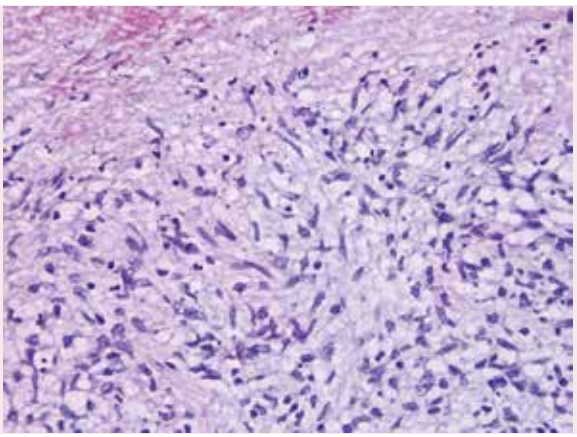

**Figure 4.** Epithelioid granulomas in lymph node tuberculosis without HIV infection. Staining with hematoxylin and eosin, x400

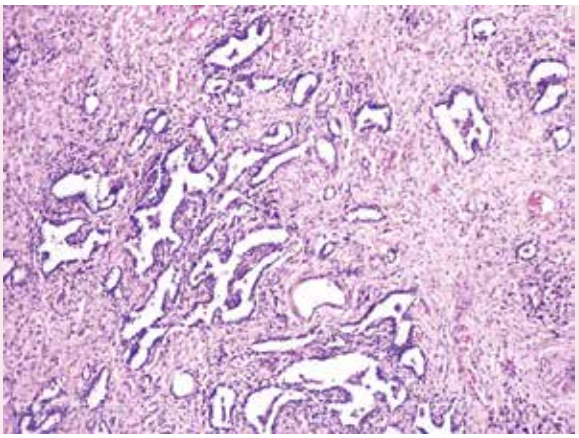

**Figure 5**. Remodeling of the lung parenchyma in the healing of tuberculous inflammation. Staining with hematoxylin and eosin, x100.

treatment for both HIV and Tb respectively [8, 9]. One of the main tactics is to begin ART within the first few weeks as soon as TB treatment is tolerated and the patient is stable, after treatment of active opportunistic infections, especially for patients with profound immunosuppression [4]. However, the timing of the beginning of ART therapy is still a very discussable question.

## CONCLUSION:

TB and HIV coinfection remains a huge problem for a global healthcare system. Despite all the huge improvements in diagnosis and treatment of the TB and AIDS coinfection the numbers of patients with this coinfection still relatively huge, thus global healthcare systems have to conduct new researches in this field to lower the morbidity and mortality rates.

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