

TUBERCULOSIS OF AXILLARY LYMPH NODES AS A MEANS FOR THE DIAGNOSIS OF HIV INFECTION: A CASE REPORT

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Abstract: With the onset of the HIV epidemic, there was an alarming increase of cases with pulmonary (3%) and extra-pulmonary tuberculosis (TB) as a result of the lymphohematogenous dissemination of the primary pulmonary infection. In the initial stages of HIV infection, the localized pulmonary TB is the most frequent, that is attributed to a reactivation of an infection with *Mycobacterium tuberculosis*. In the advanced stages of the immunosuppression, the TB infection is a primary one, which is produced mainly by atypical mycobacteria. About 120 species of non-tuberculous mycobacteria are known to be able to cause infections with lung, lymph node, bone, soft tissue, skin localization and central nervous system impairment. In TB endemic countries (with over 50 cases/100.000 persons) the risk of extra-pulmonary TB infection is significantly associated with the multidrug resistance of the mycobacteria. We present the case of an HIV positive patient detected from a particular lymph node TB in terms of evolution and site.

INTRODUCTION

With the onset of the HIV epidemic, there was an alarming increase in cases of tuberculosis (TB), not the localized ones (3%) but especially the extra-pulmonary ones (20%) (1), atypical radiologically and paucibacillary TB forms and also causing death in 1 out of 3 HIV cases.(2) Global statistics in 2013 recorded 9 million cases of tuberculosis from which 1.1 million were associated with HIV infection, accounting for 14.8% of the patients infected with HIV; in Sub-Saharan Africa HIV-TB co-infection was estimated to be at 50-80% of cases.(3) On the other hand, it is well known that HIV-infected patients are prone to infection and reinfection with TB, the acquisition of multidrug resistance bacteria and the resistance to rifampin secondary to the gastrointestinal malabsorption to specific medication.(4) In countries where in the last 10 years, TB cases decline has been recorded, for example in the USA, in 2008 there were 12.904 cases of TB, of which 1.103 (8.5%) were extra-pulmonary localized TB as an lymphadenitis (5), more common in women compared to male gender (composite ratio 1.4: 1) with a peak incidence in the age group of 30-40 years. In fact in the USA, as in other non- endemic countries for TB (with under 40 cases/100,000 persons), the TB cases belong mainly to the immigrants from endemic countries. US officials recount the susceptibility to TB lymphangitis in people from Southeast Asia, India and Africa.(6-10) Extra-pulmonary tuberculosis is the result of the lymphohematogenous dissemination of the primary pulmonary infection, favoured besides HIV infection by other disorders responsible for decreased immunity: diabetes, renal failure, alcoholism, blood dyscrasia, Castleman's disease, drug reaction, hematological malignancies or prolonged corticosteroid therapy etc.(11,12) TB lymphadenitis is found isolated at the level of one lymph node groups, most often the cervical one, with progressive and slow growth in 1-2 months, with variations from 3 weeks to 8 months (13,14), accompanied by higher overall events particularly in the combination with HIV infection; like fatigue, weight loss, poor appetite or fever.(15)

We present the case of a patient with fistulous and abscessed tuberculous lymphadenitis in the thoracic wall as a way for the diagnosis of HIV infection.

CASE REPORT

We report the case of a 29-year-old Caucasian man who was admitted to the Surgery Department for chills, fever 40°C, about 10kg weight loss with an onset 2 months ago, diarrhea for about a month, symptoms accompanied by the appearance of swelling in the right axilla, with a tendency to local extension and abscessing to the thoracic wall with limited upper limb mobility. The patient reports no family or personal history for the presence of pathological diseases, except for the presence of an extended thoracic herpes zoster which involved more dermatomes a years ago; he is chef in a remote touristic area. On admission, at the clinical examination, the patient presented fever 40.2°C, malaise, pale skin, dry lips, oropharyngeal candidiasis, about 1cm lateral cervical lymph nodes, right axillary lymphadenitis abscessed and fistulous on the anterior thoracic wall, basal decreased right lung vesicular murmur and moderate hepatosplenomegaly. A surgical drainage of the abscess is performed and also a lymph node biopsy.

Workup included blood tests that showed the following changes: C-reactive protein 270 mg%, fibrinogen 546 mg%, white blood cells count 11950/mm³, CD4+ 136/mm³, CD8+ 570/mm³, CD4+/8+ ratio = 0.24; platelets 13200-73000-32000/mm³, hemoglobin from 10.4 to 8.7g/dL, aspartate aminotransferase 101u/L, alanine transaminase 133u/L, gamma-glutamyl transferase 460 u/ L, IgG for *Cytomegalovirus* and *Toxoplasma gondii* positive and present HIV antibodies, HIV1 viral load 74990 copies/ml. Blood cultures, urine cultures, stool culture, nasal exudate were sterile from the bacteriological point of view. Candida present in pharyngeal exudate. Sputum examination was negative for *Mycobacterium tuberculosis*. Histopathological examination confirmed the diagnosis of tuberculous lymphadenitis, the culture for *Mycobacterium tuberculosis* from the harvested pus in the fistula was positive.

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CLINICAL ASPECTS

Figure no. 1. Lymph node granulomatous structures in different phases of evolution, in the presence of the central caseous necrosis, polymorphonuclear neutrophil, inflammatory elements, having epithelioid reaction and gigantic Langhans-type multinucleate cells. Around - lymphocytic inflammatory infiltrate. HE staining, 40x

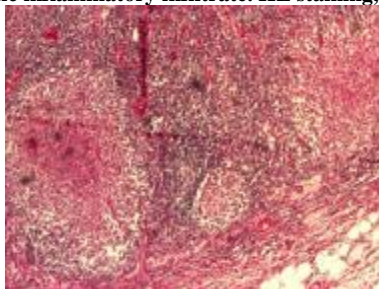


Figure no. 2. Gigantic Langhans-type multinucleate cells. HE staining, 100x.

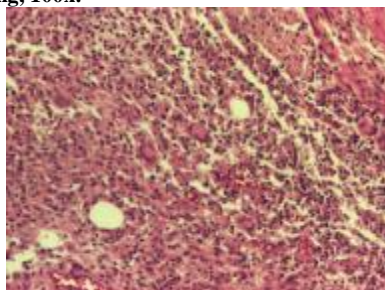


Figure no. 3. Gigantic Langhans-type multinucleate cells. HE staining, 100x.

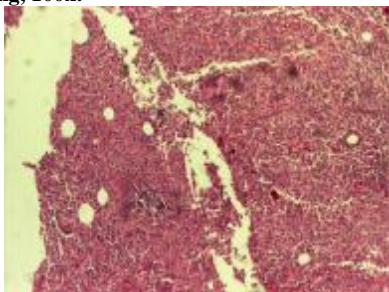
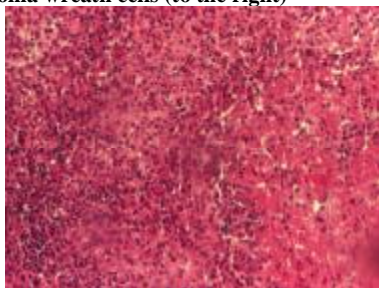


Figure no. 4. Central caseous necrosis with neutrophilic polymorphonuclear elements (right), epithelioid cell zone and the lymphoma wreath cells (to the right)



The thoracic-abdominal computerized tomography scan revealed a lymphadenopathy (block) of 35 mm diameter in the supraclavicular right fossa, paratracheal lymph nodes of 27-28 mm, left para-aortic nodes of the Baret's space and aortopulmonary window with central necrosis, hepatomegaly with the entire left lobe in the upper left abdomen and splenomegaly. The

appearance pleaded for lymphoma.

Another biopsy was performed from the right supraclavicular fossa lymphadenopathy from which the presence of *Mycobacterium tuberculosis* was confirmed again. The bone marrow biopsy revealed normal cellularity.

Therapy was initiated with hydrazides 300mg/day, rifampicin 600mg/day, pyrazinamide 2000 mg/day, ethambutol 1600mg/day for 12 months, streptomycin 1g/day was associated for the first 3 weeks of treatment, then kanamycin 1g/day for 28 days, ciprofloxacin 2x500mg/day for three months, also the antiretroviral therapy was initiated with abacavir 600mg/day, lamivudine 300mg/day, efavirenz 600mg/day and enfuvirtide 2x90mg/day. The patient received Humaglobin® 5g/100ml for 5 days and platelet concentrate during the decrease of platelets below 50000/mm³. The patient had a slow favorable evolution with the axillary fistula closure after 9 months from the intervention; the regression of the hepatomegaly, splenomegaly and the paratracheal lymph nodes after 1 year from diagnosis and with the correction of CD4+ lymphocytes (300 cells/mm³) and an HIV viral load below 400 copies/ml.

DISCUSSIONS

Mycobacterium tuberculosis susceptibility to be acquired by HIV-infected patients is higher compared to the general population due to functional deficiencies of the alveolar macrophages in response to the TB infection; the reactivation of a latent TB infection is also possible 20-30 times more frequently than in immunocompetent individuals. The increased risk of TB infection doubles after the first year of HIV seroconversion (16), being the early expression of immunosuppression in HIV-infected patients. In the initial stages of HIV infection, the localized pulmonary TB is the most frequent, being attributed to a reactivation of an infection with *Mycobacterium tuberculosis*. In the advanced stages of the immunosuppression, the TB infection is a primary one, which is produced mainly by atypical mycobacteria. About 120 species of nontuberculous mycobacteria are known to be able to cause infections with lung, lymph node, bone, soft tissue and skin localization. Cases of renal and central nervous system impairment, keratitis and otitis media are also described.(17) For the cases associating a low CD4+ lymphocyte count (fewer than 100 cells/ μ L) the risk of disseminated *Mycobacterium avium* disease (MAC) or TB reinfection increases drastically.(18,19) On the other hand, there is rapid progression of HIV infection in patients that are co-infected with TB, progression which is attributed to the activation of the immune response and the expression of the CCR5 and CXCR4 receptors.(20) Initiating the antiretroviral therapy (ART) reduces the risk of TB infection by 57% in patients with CD4 counts of >350 cells/ml and 84% for patients with CD4 counts of <200 cells/ml respectively (21) but the risk remains still higher. Positive diagnosis with clinical suspicion in an immunocompromised patient can be confirmed by culture, lymph nodes biopsy or polymerase chain reaction. Nucleic acid amplification tests (NAATs), GeneXpert® Xpert® MTB/RIF test; negative TB skin tests most commonly do not exclude the diagnosis. Ganglion aspiration is positive only in 46-87% of cases, identifying granulomas.(22) Tuberculous lymphadenitis is the most common location of extrapulmonary TB, affecting mainly cervical lymph nodes, both in children and adults with HIV infection as an early manifestation of systemic infection. In our case, a young patient with previously undiagnosed HIV infection, the TB lymphadenitis location was unusual, catching several lymph node groups: axillary lymph nodes, abscessed and fistulous on the anterior thoracic wall in the presence of other lymph nodes like the one from the supraclavicular right fossa or from the mediastinum confirmed

CLINICAL ASPECTS

by bacteriological tests. Hepatosplenomegaly associated with mediastinal and peripheral lymphadenopathy raised questions in terms of differential diagnosis primarily with lymphomas unconfirmed by their anatomopathological examination and the bone marrow biopsy, confirming a disseminated TB infection most likely a primary one, in the absence of pulmonary TB (excluded by cultures and imaging studies). The unusual combination of tuberculostatic treatment is motivated by the increase incidence of multidrug resistance TB (MDR-TB defined as resistance to isoniazid, rifampicin) and extensively drug resistance XDR-TB (MDR-TB defined as resistance in association to any fluoroquinolones, and to any of the second-line injectables -amikacin, capreomycin and kanamycin) (23) in Romania, where there is a TB rate of over 50/100 000 and a resistance in isolates from 5 to 9.9%, according to the European Centre for Disease Prevention and Control (ECDC).

CONCLUSIONS

Tuberculous lymphadenitis is the most common location of extrapulmonary TB, affecting mainly cervical lymph nodes. In our case, TB lymphadenitis location was unusual, catching axillary lymph nodes groups.

Positive diagnosis in an immunocompromised patient with clinical suspicion can be confirmed by culture, lymph nodes biopsy or polymerase chain reaction.

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