

Pneumologia

Tobacco use as a contributing factor in HIV–TB co-infection – the multidisciplinary approach in the case of an immunosuppressed smoking patient

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Abstract

English:

Introduction: Tuberculosis-HIV co-infection remains a challenge to the clinician largely as a result of the potentiation mutual, which will result in deterioration of the immunological status and increased risk of mortality.

Case presentation: 37-year-old patient, smoker 5 pack-year (5PA), without pathological history, who is hospitalized in 2021 in an ear, nose and throat otolaryngology (ENT) service in the context of the appearance of laterocervical and axillary polyadenopathy, during the examination histopathologically resulting to be of tuberculous etiology. The transfer was made to the pneumophthisiology clinic where human immunodeficiency virus (HIV) testing was performed it was positive. It was decided to initiate antituberculosis and systemic corticoid treatment with initially favorable evolution, with the association following antiretroviral therapy. The patient develops motor deficits, and the brain magnetic resonance imaging (MRI) examination revealed the presence of two left hemispheric intracranial processes biopsied by neuronavigation, the result of which revealed histopathological changes highly suggestive of granulomatosis. In dynamics, the clinical examination carried out in an infectious disease service highlights the appearance of a pseudotumoral formation, with consistent right sterno-costal fluctuation, which is why it was decided to redirect the case to the thoracic surgery department, where drainage of the formation was practiced with the microbiological detection of *Mycobacterium tuberculosis*.

Discussions: The peculiarity of the case resides in the presence of multiple foci of extrapulmonary tuberculosis in a case of tuberculosis-human immunodeficiency virus (TB-HIV) co-infection, without lung damage, in a patient with apparent compliance to treatment.

Conclusions: Tuberculosis remains a challenge for the clinician, especially in the case of HIV co-infection, association with mortality and increased morbidity.

Keywords

tuberculosis • smoking • immunosuppression

Consumul de tutun ca factor care contribuie la co-infecția HIV–TB – abordarea multidisciplinară în cazul unui pacient fumător cu imunosupresie

Rezumat

Romanian:

Introducere: Co-infecția tuberculoză- HIV rămâne o provocare a clinicianului în mare parte ca urmare a capacității de potențare reciprocă, care va rezulta în deteriorarea statusului imunologic și creșterea riscului de mortalitate.

Prezentarea cazului: Pacient în vârstă de 37 ani, fumător (5PA), fără antecedente patologice, care se internează în anul 2021 într-un serviciu ORL în contextul apariției unor poliadenopatii laterocervicale și axilare, la examenul histopatologic rezultând a fi de etiologie tuberculoasă. S-a realizat transferul în clinica de pneumoftiziologie unde testarea HIV a fost pozitivă. S-a decis inițierea tratamentului antituberculos și corticoid sistemic cu evoluție inițial favorabilă, cu asocierea ulterioară a terapiei antiretrovirale. Pacientul instalează deficit motor, iar la examenul IRM cerebral s-au decelat prezenta a doua procese intracraniene emisferice

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stângi biopsiate prin neuronavigatie, rezultat ce a evidențiat modificări histopatologice înalt sugestive de granulomatoză. În dinamica examenul clinic realizat într-un serviciu de boli infecțioase pune în evidență apariția unei formațiuni pseudotumorale, cu consistență fluctuantă sterno-costală dreapta, motiv pentru care s-a decis redirectionarea cazului către secția de chirurgie toracică unde s-a practicat drenajul formațiunii cu decelarea microbiologică a *Mycobacterium tuberculosis*.

Discuții: Particularitatea cazului rezidă din prezența unor multiple focare de tuberculoză extrapulmonară într-un caz de co-infecție TB-HIV, fără afectare pulmonară, la un pacient cu aparentă complianță la tratament.

Concluzii: Tuberculoza rămâne o provocare a clinicianului mai ales în cazul co-infecției HIV, asociere cu o mortalitate și morbiditate crescută.

Cuvinte-cheie

tuberculoză • fumat • imunosupresie

Introduction

Tuberculosis is an infectious-contagious disease caused by *Mycobacterium tuberculosis*, which, despite the preventive and treatment measures developed over the last century, remains a burden for health services, especially in underdeveloped and developing countries [1].

Worldwide, it is estimated that the incidence in 2020 amounted to 9.9 million illnesses and the mortality was 1.5 million, with tuberculosis representing the infectious disease with the highest mortality after infection with the SARS-CoV-2 virus [2,3].

TB-HIV co-infection is common among the population suffering from only one of the comorbidities. The specialized literature estimates that in the absence of treatment, at the onset of HIV infection, the risk of developing tuberculosis is 2.5 times, while in the advanced stages, the risk increases 20 times, maintaining the risk of infection 4 times including during antiretroviral therapy [4].

Smoking is a preventable risk factor, considered to favor co-infection as a result of the inflammatory state it induces and the depression of the local immune system that increases the potential for reactivation of *M. tuberculosis* [5].

Presentation of the case

We present the case of a 37-year-old patient, a smoker 5PA, without occupational exposure and domestic respiratory noxes, without personal pathological history, and without documented allergies, who was hospitalized in November 2021 in an ENT service for the appearance of bilateral lateral cervical polyadenopathy and small axillae, mobile on the deep planes, painless, accompanied by weight loss and marked fatigue. A biopsy was performed from the level of the right axillary adenopathy, the histopathological examination being compatible with lymphadenoid tuberculosis (special Ziehl-Neelsen staining – BAAR positive). It is decided to

transfer the patient to the pneumology department for further investigations and the initiation of specialized treatment. During the hospitalization, the sputum examination was performed, with negative acid alcohol resistant bacilli (BAAR) both in the microscopy (Ziehl-Neelsen staining) and in the culture, which together with the nonspecific radiological imaging refuted a possible associated pulmonary tuberculosis (Figure 1).

Biologically, the presence of severe lymphopenia (170/ μ L) and severe microcytic hypochromic anemia (Hb: 6.3 g/dL) was detected, which is why a transfusion was performed. HIV testing was also carried out as part of the national diagnostic protocol, which had a positive result. At that time, an infectious diseases consultation was requested, which opined for the priority initiation of anti-tuberculosis treatment with the subsequent establishment of the optimal antiretroviral treatment. Anti-tuberculosis treatment was

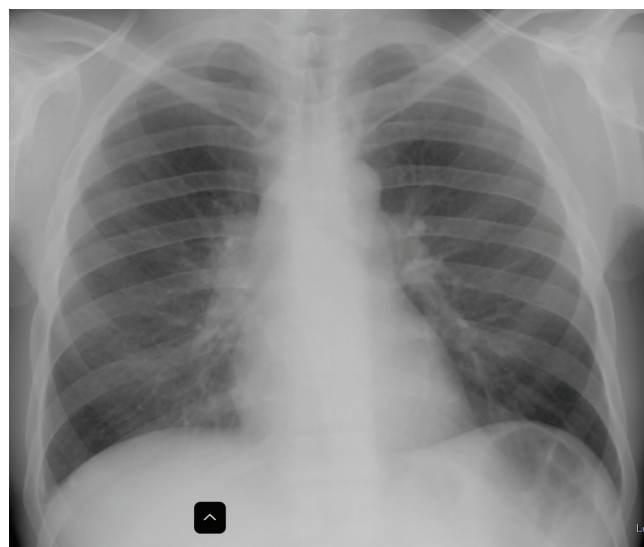


Figure 1. Normal chest x-ray.

instituted according to the weight, which was associated with cortisone treatment, vitamin B6, and liver protector, with initially favorable evolution of the general condition, which is why the patient was discharged, with the recommendation to continue the anti-tuberculosis treatment through the territorial dispensary and subsequently initiate the antiretroviral treatment.

In the infectious disease service where it was recorded, the persistence of later cervical and axillary lymphadenopathy was noted along with the appearance of multiple raised violaceous lesions on the limbs, anterior and posterior thorax, which is why the suspicion of Kaposi's Sarcoma was raised. Biologically, the persistence of microcytic hypochromic anemia (8.6 g/dL) and severe lymphopenia (180/ μ L) was noted. It was decided to initiate treatment with abacavir/lamivudine associated with raltegravir.

In June 2022, the patient presents himself in a neurosurgery service in the context of the establishment of motor deficit in the level of the upper and lower right limb. During the clinical examination, the maintenance of the previously described lesions and the adenopathies was recorded, and neurologically, vivid osteotendinous reflexes, positive right Babinski sign, hemiparesis 3/5 brachial, and 4/5 crural and superficial hypoesthesia of the right hemibody were evident. A craniocerebral MRI was performed, which highlighted a space-replacing process developed at the left capsule-nuclear level (Figure 2), predominantly affecting the posterior capsular arm alongside a frontal interhemispheric frontal extraneuraxial space-replacing process coming into contact with the A3 segment (pericallosal artery) of the left anterior cerebral artery (with the maintenance of lesions at the 2023 evaluation). It was decided to perform the biopsy under neuronavigation guidance from the level of the expansive left capsule-nuclear process, which proceeded without major intra- and postoperative events. The histopathological examination of the biopsy piece identified a disorganized architecture, with aspects of demyelination, cellular vacuolations, lesions of vascular necrosis with polymorphous inflammatory infiltrate, and frequent foci of microgliosis alongside a granulomatous area, with central necrosis and adjacent epithelioid cells on a background of hypercellularity,

without mitotic activity. At that time, the appearance was considered possibly suggestive of a tuberculous lesion developed on the background of a viral encephalopathy, in the context of chronic immunosuppression. However, the anatomopathologist could not rule out the tumoral substrate of the lesions with certainty, which is why he requested an immunohistochemical examination, the report of which refuted the suspicion (Table 1).

The dispensary in the territorial tuberculosis (TB) service showed a poor response to the previously instituted anti-tuberculosis treatment, which is why, as a result of the lack of clinical improvement of the nodular formations corroborated with the patient's history, it was decided to modify the treatment scheme, choosing to increase the dose of rifampicin and replace ethambutol with moxifloxacin.

In May 2023, the patient was admitted to the infectious diseases service where he was taken into account for an altered general condition associated with the appearance of a pseudonodular formation, with fluctuating consistency in the upper ½ at the level of the left sternocostal angle, minimally painful. The biological assessment found a satisfactory immunological status under the previously instituted antiretroviral treatment: CD4 = 503/MMC, respectively, plasma Human immunodeficiency virus-Ribonucleic acid (HIV-RNA) = 66 c/mL.

A native chest computed tomography (CT) was performed that revealed the presence in the medial half of the pectoralis major and pectoralis minor on the left side, which showed a marked thickening, a multiloculated hypodense formation with septa and necrosis extended inside, with axial diameters of 103/44 mm, which does not exceed the muscular plane and does not infiltrate the subcutaneous cellular tissue or the underlying bony planes (sternum and left anterior costal arches), which presented benign CT features, most likely suggestive of a tuberculous cold abscess. It was recommended to continue the previously instituted treatment and refer to a thoracic surgery service to establish the therapeutic conduct of the abscess.

Table 1. Immunohistochemical result.

Zonal GFAP positive in hyperplastic astrocytes fost likely reactive
SYN negative
NFT negative
EMA negative
CD34 positive in small blood vessel
CD68 positive in rare macrophages
IDH-1 negative
Ki67 positive in 30 % pleomorphic inflammatory infiltrate
No elements are observe to suggest the association of umor proliferation with inflammatory elements

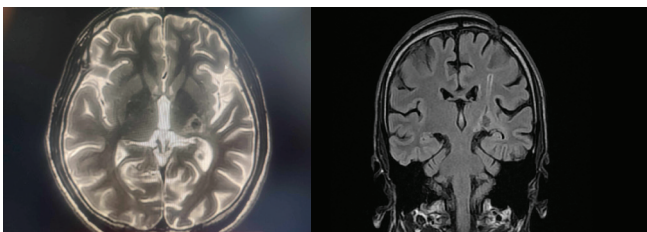


Figure 2. Space-replacing process developed at the left capsule-nuclear level.



Figure 3. Drain tube (suction tube) placed at the level of the cavity.

In June 2023, the patient was admitted to the thoracic surgery service for an anterior presternal thoracic tumor formation, which is in dimensional progression compared to the previous examination accompanied by previous chest pains. Radiologically, there were no changes in the lung parenchyma that would suggest a possible appearance of specific tuberculosis lesions compared to the imaging from 2021. Later, under general anesthesia with oro-tracheal intubation, an anterior thoracic incision is performed with myotomy of the pectoralis major muscle in a transverse plane with the evacuation of approximately 200 mL of purulent liquid, debridement, curettage, and betadine lavage, with the placement of a drain tube (suction tube) at the level of the cavity (Figure 3). The postoperative evolution was favorable with the drainage of the cavity progressively decreasing. On postoperative day 6, the cavity is washed with 10 mL of rifampicin suspension with 0.9% NaCl solution, with the subsequent suppression of drainage. The clinical–paraclinical evolution was favorable, which is why the patient was discharged with the recommendation to continue the previously instituted anti-tuberculosis and antiretroviral treatment.

Discussions

Despite the increased number of patients diagnosed with tuberculosis worldwide, extrapulmonary involvement remains a rather rare manifestation of *M. tuberculosis* infection, with a prevalence of 0.5%–5% of all tuberculosis cases [6].

Tuberculous lymphadenitis is the most frequent extrapulmonary manifestation, the patient profile diagnosed with the average age at onset between 23 years and 45 years, 78.3% having no personal pathological history, 69.9% presenting later cervical adenopathies, 54.2% showing symptoms, 7.2% having HIV co-infection, and only 18.1% with pulmonary infection [7].

Smoking is a risk factor frequently incriminated along with diabetes and alcohol consumption in the development of tuberculosis. Although pulmonary infection is more frequent in smoking patients (46.2%), the percentage is not negligible even in the case of those diagnosed with extrapulmonary manifestations (16.9%) because a lower rate of treatment success has been demonstrated and increased mortality in smokers [8].

It is estimated that one-third of the world's population has an infection with *M. tuberculosis* in a latent form, with a disease development rate of 10%, 50% of them more than 2 years after contact. However, HIV infection increases the risk of reactivation by up to 20 times and of infection by 5%–15% per year compared to 5%–10% during life in the case of an immunocompetent person [9].

The prevalence of TB–HIV is 14 million worldwide, with co-infection causing high mortality as a result of the potentiation phenomenon that the two have as a result of the common pathophysiological pathways they share [10]. Anti-tuberculosis treatment tends to have a lower success rate in patients with HIV (86.4%) compared to those with mono-infection (93.7%) [11]. The increased mortality in the case of co-infection (26%) determines a negative impact, estimating that 99% of the cases come from developing countries, which burdens the health systems [9,12]. The initiation of antiretroviral treatment is done after the anti-tuberculosis one, in case of simultaneous detection of the two infections as a result of the potential for the development of Immune Reconstruction Inflammatory Syndrome (IRIS), which involves an excessive immune response against *M. tuberculosis* [13].

Cerebral damage caused by infection with *M. tuberculosis* is very rare, worldwide representing approximately 1% of all tuberculosis cases. In contrast, patients with HIV co-infection have a rate of up to 10% [14,18]. Studies related to cerebral tuberculosis in HIV-infected patients are limited because it has a low incidence in developed countries and is insufficiently studied in developing countries [15]. A study published in 2020 that analyzed a group of 66 patients, all diagnosed with HIV, demonstrated that the prognosis of the patients at 18 months is favorable if the lesions do not completely disappear after the correctly instituted and followed anti-tuberculosis treatment (14). The tuberculous cold abscess represents a manifestation that occurs in 1% of the cases of extrapulmonary tuberculosis, being more frequent in immunosuppressed patients [16]. Optimal management in the case of cold abscess is difficult to achieve as a result of the limited published studies given the rare incidence of the pathology. Although there is no consensus, anti-tuberculosis treatment is recommended for 9–12 months along with surgical drainage, although some studies have opined only for drug treatment [17].

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