

Pneumologia

Pneumocystis Pneumonia misdiagnosed as Pulmonary Tuberculosis in a patient with repeatedly false-negative HIV tests

Samuel Bodoarcă^{1,*}, Diana Bodoarcă², Emilia Tabacu¹, Irina Strâmbu^{1,3}

¹„Marius Nasta” Institute of Pneumophthysiology, Bucharest

²Emergency Clinical Hospital of Bucharest

³Carol Davila University of Medicine and Pharmacy, Bucharest

Abstract

English:

Pneumocystis jirovecii pneumonia, previously known as Pneumocystis carinii Pneumonia (PCP), is a fungal infection most commonly encountered in immunocompromised patients and, in some cases, can be life-threatening. Patients at risk include those with cancer, HIV positive, transplant recipients, and those under immunosuppressive therapies. There are no specific signs or symptoms for PCP and its differential diagnosis includes other viral or bacterial pneumonias and also Tuberculosis, the latter especially in high endemic areas. We present the case of a 32 year-old female patient who presented to the hospital for dyspnea and cough, treated for Pulmonary Tuberculosis, and eventually diagnosed with Pneumocystis Pneumonia, in spite of her multiple false-negative HIV tests.

Keywords

Pneumocystis jirovecii pneumonia • false negative HIV testing • tuberculosis • immunosuppression • AIDS

Pneumonie cu Pneumocystis confundată cu tuberculoza la o pacientă cu teste repetate HIV negative

Rezumat

Romanian:

Pneumonia cu Pneumocystis jirovecii, cunoscută anterior ca pneumonia cu Pneumocystis carinii (PCP), este o infecție fungică întâlnită cel mai frecvent la pacienți imunocompromiși și poate fi uneori amenințătoare de viață. Pacienții cu risc sunt cei cu cancer, HIV pozitivi, transplantați sau sub tratamente imunosupresoare. PCP nu are semne sau simptome specifice, iar diagnosticul diferențial include alte pneumonii virale sau bacteriene dar și tuberculoza, mai ales în regiunile cu endemie ridicată. Prezentăm cazul unei paciente de 32 de ani care s-a prezentat la spital pentru dispnee și tuse, tratată inițial pentru tuberculoză pulmonară, diagnosticată în cele din urmă cu pneumonie cu Pneumocystis, în pofida multiplelor teste HIV fals negative.

Cuvinte-cheie

Pneumonia cu Pneumocystis jirovecii • test HIV fals negativ • tuberculoză • imunosupresie • SIDA

Introduction

Pneumocystis jirovecii pneumonia, previously known as Pneumocystis carinii Pneumonia (PCP), is a fungal infection most commonly encountered in immunocompromised patients

and, in some cases, can be life-threatening. Patients at risk include those with cancer, HIV positive, transplant recipients, and those under immunosuppressive therapies [1].

*Corresponding author: Samuel Bodoarcă

E-mail: samuelbodoarca@yahoo.com

Open Access. © 2023 Bodoarcă et al., published by Sciendo

 This work is licensed under the Creative Commons Attribution-NonCommercial-NoDerivs 4.0 License.

In HIV infected individuals, *Pneumocystis pneumonia* is an AIDS defining illness. The rates of PCP in this group of patients declined significantly after the introduction of antiretroviral therapy, yet it remains an important cause of morbidity and mortality [2].

There are no specific signs or symptoms for PCP and its differential diagnosis includes other viral or bacterial pneumonias and also Tuberculosis, the latter especially in high endemic areas.

We present the case of a 32 year-old female patient who presented to the hospital for dyspnea and cough, treated for Pulmonary Tuberculosis, and eventually diagnosed with *Pneumocystis Pneumonia*, in spite of her multiple false-negative HIV tests.

Case presentation

Patient P.A., a 32 year-old, never-smoker woman, with no known occupational or domestic respiratory exposure and no significant past medical history, presented to the emergency department of „Marius Nasta” Institute of Pneumophtisiology of Bucharest, for a 2-month history of progressively worsened shortness of breath and dry cough. She also described unintentional weight loss, approximately 13 kg over the past 2 years. The chest X ray performed in the emergency room revealed some alveolar infiltrates opacities predominantly at the lung bases, which raised the suspicion of Pulmonary Tuberculosis (TB) (Figure 1). The patient was referred to the local TB dispensary for diagnosis and treatment.

Three days later the patient presented to the local TB dispensary where two sputum samples were collected for microscopy, cultures and PCR – MTB/RIF GeneXpert – testing for TB. She was also tested for HIV infection and a hemogram was performed. In the same day she was started on Isoniazid 300 mg, Rifampicin 450 mg, Ethambutol 1200 mg and Pyrazinamide 1500 mg. The sputum smears were negative for Acid-Fast Bacilli and MTB/RIF GeneXpert tests also came back negative. The blood work showed lymphopenia (730/mm³) and an elevated erythrocyte sedimentation rate -ESR- (73 mm/h). The HIV test was negative. The patient was continued on TB medication for a month, yet she experienced no improvement of her symptoms. She was referred back to the „Marius Nasta” Institute for further investigations.

The physical examination at admission showed the patient was in a relatively good state, underweight (W 47 kg, H 155 cm), with normal color of the skin and mucosa, no palpable peripheral adenopathies, her oxygen saturation was 98% at rest and in the ambient air, blood pressure was 120/80 mmHg, with no abnormal breathing or heart sounds. Her blood work showed leukeopenia (3350/mm³), lymphopenia (580/mm³), and an elevated ESR (91 mm/h).

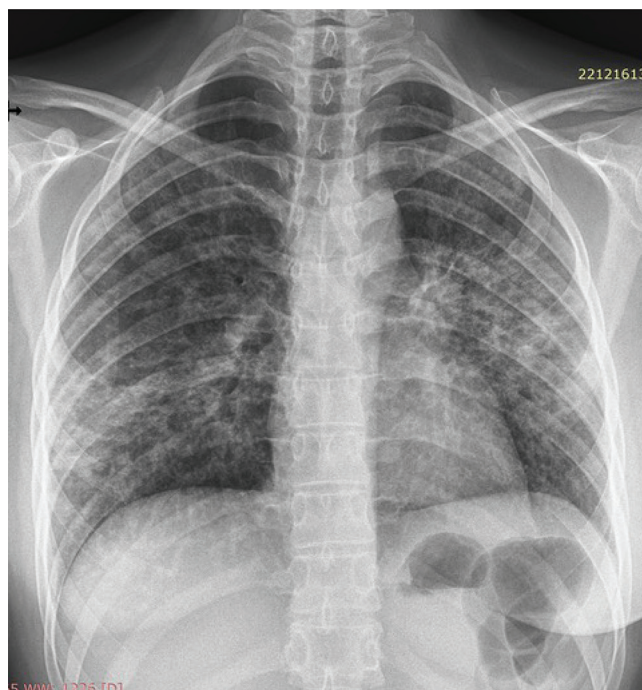


Figure 1. Postero-anterior chest X ray showing alveolar infiltrates opacities predominantly at the lung bases.

The patient's medical history was revisited and she revealed that her life partner, with whom she was in a relationship for more than 5 years, was a former heroine addict, HIV positive, yet clean and on antiretroviral treatment for more than 10 years, with apparently undetected viral load. The patient said she tested herself for HIV infection multiple times in the past and all those tests came back negative. Given this new information another HIV test was ordered, which also came back negative.

A chest CT scan was performed and revealed „ground glass” infiltrates predominantly in the upper lobes (Figure 2).

This was followed by a bronchoscopy with bronchoalveolar lavage (BAL). The cultures of BAL fluid were negative for bacteria and fungi. The BAL fluid smear was negative for acid-fast bacilli; MTB/RF GeneXpert of BAL fluid also came back negative. The microscopic examination of the BAL fluid identified frequent *Pneumocystis jiroveci* cysts. A diagnosis of *Pneumocystis jiroveci* pneumonia was thus established.

The anti-TB medication was discontinued and the patient was started on Trimethoprim-Sulfamethoxazole. The patient was referred for infectious diseases consult. She was confirmed to be HIV positive through RT-PCR and Western blot testing. Her CD4⁺ cell count was 7/mm³. She was started on anti-retroviral therapy.

The patient's symptoms progressively improved under treatment. A chest X ray performed 3 weeks later showed marked improvement (Figure 3).

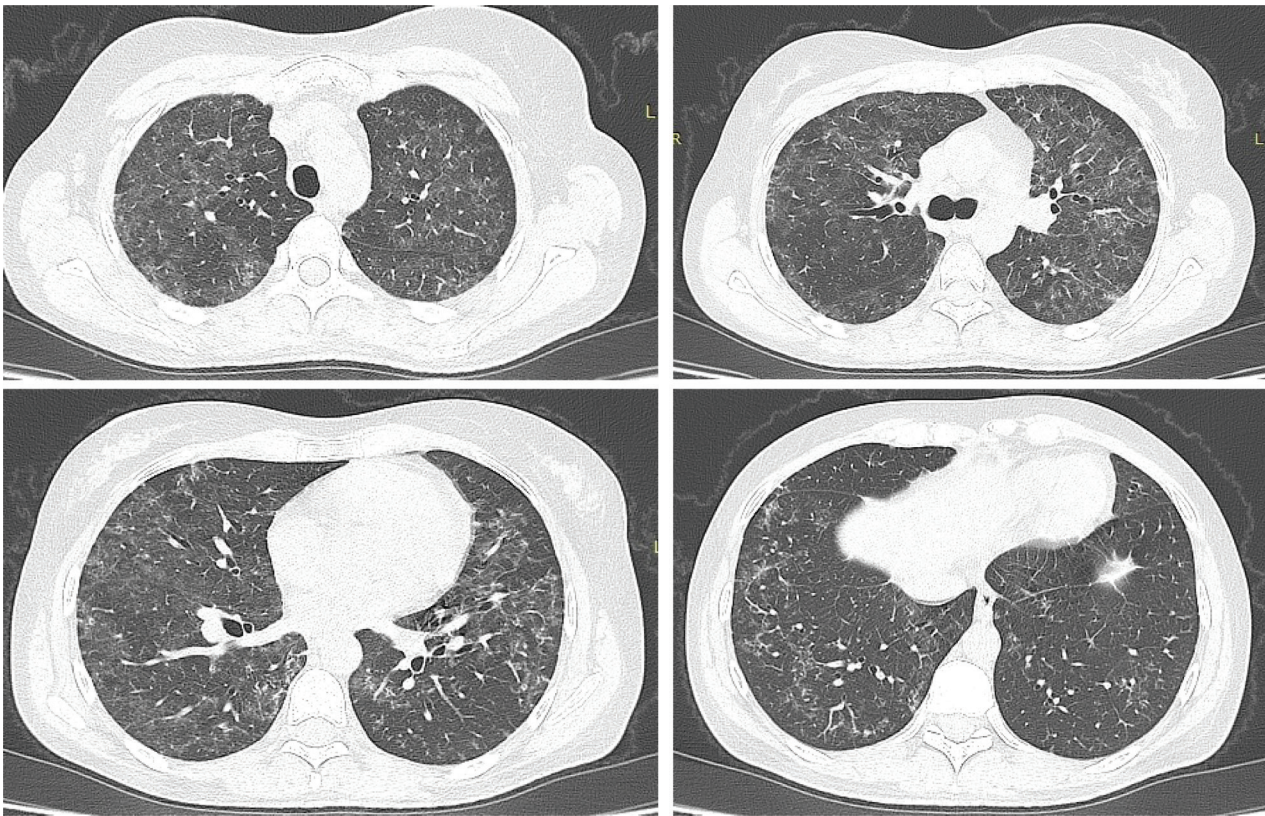


Figure 2. Chest CT scan showing ground glass infiltrates predominantly in the upper lobes.

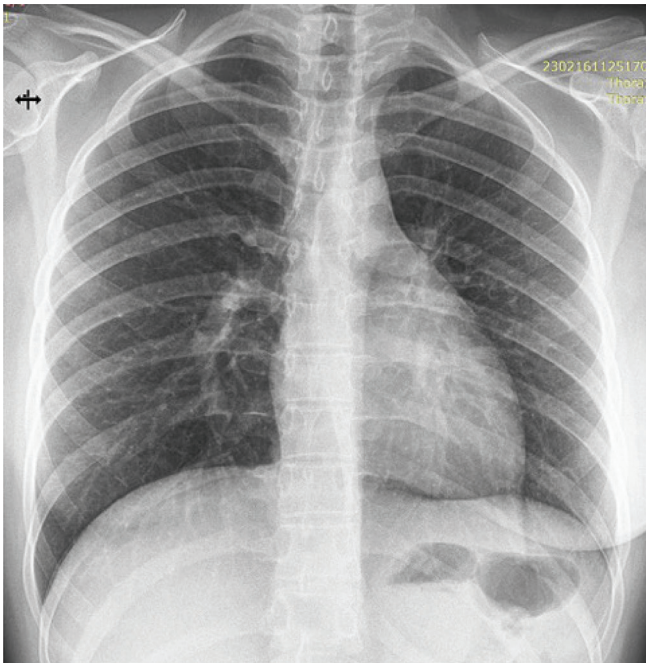


Figure 3. Postero-anterior chest X ray showing marked improvement of the lesions after 3 weeks of treatment.

Discussion

Pneumocystis pneumonia remains an important opportunistic infection in immunocompromised patients, including those HIV positive, for whom it is an AIDS defining illness [2,3].

Pneumocystis pneumonia is classically described as an acute or subacute illness, consisting of nonproductive cough, dyspnea, fever, and leading to some degree of respiratory failure in most cases [1,4]. Its radiographic features consist of bilateral fine reticular opacities, determining a “ground glass” aspect, which in the right clinical context help raise the suspicion for this diagnosis [5].

Although most of the time it is encountered in individuals known to be HIV positive, sometimes a Pneumocystis pneumonia can lead to the recognition of an unrevealed HIV infection [6].

The differential diagnosis includes other viral or bacterial pneumonias and also tuberculosis, especially for those cases with a more insidious clinical course and radiographic changes suggestive of tuberculosis, including cavitary lesions. This can lead to a delay in making the diagnosis and starting the treatment [4].

Our patient presented for shortness of breath and cough for approximately 2 months and she was not hypoxemic at any moment. Given her insidious clinical course, her history of weight loss and the high endemic level of Pulmonary Tuberculosis in Romania [7], she was suspected to have tuberculosis. After sputum collection, the patient was started on TB medication. Her sputum smear and GeneXpert came back negative for TB and she was continued on TB medication, while the sputum cultures were in progress. She was tested for HIV infection in accordance with the national protocol [7] and the test was negative.

Her HIV tests were repeatedly negative, including the one ordered during her hospitalization. The chest CT scan showed “ground glass” lesions predominantly in the upper lobes and her *Pneumocystis Pneumonia* diagnosis was confirmed through bronchoscopy with BAL, which revealed *Pneumocystis jirovecii* cysts at microscopy. The HIV infection was then confirmed through RT-PCR and Western Blot testing. Her CD4+ count showed severe immunosuppression (7/mm³).

The *Pneumocystis Pneumonia* was not taken into account at first given her relatively good state, with normal oxygen saturation at all times and her multiple, repeatedly negative HIV tests. It should be emphasized that despite HIV screening tests having a high sensitivity and specificity, it is reported a prevalence of 3.1% false positive results and 0.4% false negative results [8]. Factors associated with misdiagnosis are cross-reactivity, quality of the tests used, errors in collecting the specimens, errors in documenting and reporting information, acute/early infection [8,9]. It has rarely been reported that severe immunosuppression might lead to false negative HIV tests [10], which could be the case for our patient.

Pulmonary Tuberculosis seemed a more plausible diagnosis at first. The patient was started on TB medication before any sputum tests came back. Although the tests were negative, the diagnosis was not reconsidered until 1 month of treatment being completed. The lack of improvement in patient's clinical state made necessary additional tests.

Conclusion

Pneumocystis pneumonia can sometimes be misdiagnosed as Pulmonary Tuberculosis, especially in areas with high TB burden. Even if a TB diagnosis seems plausible in a clinical and epidemiological context, it is always preferable to have some sort of confirmatory test in support of the diagnosis. On the other hand, in our case the repeatedly false-negative HIV tests made *Pneumocystis Pneumonia* seem an improbable

diagnosis, which was eventually confirmed through bronchoscopy with BAL. Thus, the patient was treated for TB in spite of negative sputum tests and the *Pneumocystis* diagnosis was delayed because of multiple false-negative HIV tests.

The possibility of false-positive and false-negative results of laboratory tests should be taken into account.

Funding

None.

Institutional Review Board Statement

Not applicable.

Informed Consent Statement

Informed consent of the patient was obtained.

Data Availability Statement

Data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

None.

References

1. Truong J, Ashurst JV. *Pneumocystis jirovecii* Pneumonia. [Updated 2023 Jan 21]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK482370/>
2. Solano L MF, Alvarez Lerma F, Grau S, Segura C, Aguilar A. [*Pneumocystis jirovecii* pneumonia: Clinical characteristics and mortality risk factors in an Intensive Care Unit]. *Med Intensiva*. 2015 Jan-Feb;39(1):13-9
3. Bartlett JG. Pneumonia in the patient with HIV infection. *Infect Dis Clin North Am* 1998;12:807-20.
4. Sarkar S, Dubé MP, Jones BE, Sattler FR. *Pneumocystis carinii* pneumonia masquerading as tuberculosis. *Arch Intern Med*. 1997 Feb 10;157(3):351-5

5. McGuinness G, Gruden JF. Viral and Pneumocystis carinii infections of the lung in the immunocompromised host. *J Thorac Imaging* 1999;14:25-36.
6. Kayik SK, Acar E, Memis L. Pneumocystis Jirovecii Pneumonia in Newly Diagnosed HIV Infection: A Challenging Case Report. *Turk Patoloji Derg.* 2020;1(1):246-250. doi: 10.5146/tjpath.2020.01480
7. Ghid metodologic de implementare a programului național de prevenire, supraveghere și control al tuberculozei și altor mico-bacterioze, monitorul oficial al romaniei, 4 aprilie 2022
8. Johnson CC, Fonner V, Sands A, et al. To err is human, to correct is public health: a systematic review examining poor quality testing and misdiagnosis of HIV status. *J Int AIDS Soc* 2017;20(Suppl 6):21755. <https://doi.org/10.7448/IAS.20.7.21755>.
9. Wolpaw, B.J., Mathews, C., Chopra, M. *et al.* The failure of routine rapid HIV testing: a case study of improving low sensitivity in the field. *BMC Health Serv Res* **10**, 73 (2010). <https://doi.org/10.1186/1472-6963-10-73>
10. Chuwa F, Kivuma B, Ndege R; KIULARCO Study Group. Repeated false-negative HIV rapid test results in a patient presenting to care with advanced HIV disease: A case report. *IDCases.* 2023 Feb 14;31:e01719. doi: 10.1016/j.idcr.2023.e01719. PMID: 36845910