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A newly diagnosed advanced HIV infection in an older female in Poland - challenging treatment of fungal pulmonary infections and the diagnostic process of FUO

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Abstract

This paper presents the diagnostic and therapeutic challenges encountered in a 53-year-old woman with advanced HIV infection. Upon admission, the patient exhibited severe symptoms of interstitial pneumonia and cachexia. During hospitalization, the patient was diagnosed with SARS-CoV-2 infection and a wide spectrum of opportunistic pulmonary infections, including *Pneumocystis jiroveci, Candida krusei*, and *Staphylococcus haemolyticus*. Another major diagnostic challenge posed the patient's prolonged fever, which persisted despite comprehensive treatment. This report underscores the importance of considering new HIV infections in older patients presenting complex clinical pictures, its significant mortality risk in older individuals, and the need for timely initiation and adjustment of antiretroviral therapy.

Key words

HIV; AIDS; Fever of Unknown Origin

Introduction

European Centre for Disease Prevention and Control (ECDC) and the WHO Regional Office for Europe indicate that the prevalence of diagnosed HIV infection in individuals above the age of 50 increases in eastern and central Europe. This concerning trend is associated with Russia's aggression on Ukraine, which led to the massive migration from territories that were already affected by the HIV epidemic [1,2]. Due to this difficult situation, healthcare providers must be vigilant, as there is a higher chance of encountering a patient who presents blur and unusual combination of clinical symptoms that might be a manifestation of AIDS comorbidities.

Case report

A 53-year-old woman was admitted to the Infectious disease department with exacerbated pulmonary symptoms, that suggested interstitial pneumonia, and in a state of cachexia with a BMI of 16. Physical examination revealed bright erythema and skin erosion in the area of the neck and cleavage, which was later revealed as a symptom of *Microsporum canis* skin infection.

A rapid antigen test showed that the patient is SARS-COV-2 positive. Upon admission, a chest radiographic image showed features of interstitial inflammation in the upper lobe and the peripheral part of the middle lobe of the right lung. Microbiologic tests established that the patient is infected with HIV type 1 subtype A, with a viral load of 74000 copies/ml. The CD4+ lymphocyte count in blood was recorded at 13 cells/ml and CD8+ lymphocytes – 117 cells/ml, establishing a 0,11 CD4/CD8 ratio. Polymerase chain reaction (PCR) and microscopic examination of sputum were conducted to diagnose the cause of pulmonary symptoms. Tests confirmed the presence of the *Pneumocystis jiroveci* DNA in sputum along with negative results in microscopic examination. Microbiological examination of sputum, accompanied by Quantiferon-TB Gold Plus test and blood cultures excluded *Mycobacterium tuberculosis* or other *Mycobacterium spp*. infections. In tests run on the patient's serum, the presence of *Cytomegalovirus* DNA on the level of 3153 IU/ml and anti-CMV IgG >250 AU/ml were confirmed. The additional serological tests did not indicate the presence of HCV, HBV, and *Toxoplasma gondii*. The patient's morphology showed mild anemia (HGB 10,9 g/dl), lymphopenia (0,35 K/µl), and a low level of monocytes (0,11 K/µl). Neutrophils (6,3 K/µl) and platelets (159 K/µl) counts were within normal ranges. Inflammatory parameters were low: CRP at 3,8 mg/l and procalcitonin at 0,05 ng/ml.

The patient's initial treatment consisted of antiretroviral therapy (bictegravir, emtricitabine, and tenofovir alafenamide), antibiotherapy effective against *Pneumocystis jiroveci* (sulfamethoxazole and trimethoprim) and antiviral medications against SARS-CoV-2 (nirmatrelvir and ritonavir). Skin changes were treated with the unguent with clotrimazole. Due to the patients' state of cachexia high-protein and high-fat diet with necessary supplementation was applied. The administered combination of drugs gave a partial resolution of the symptoms. Imaging showed regression of the interstitial changes in the lungs. However, within a few days clinical state of the patient worsened again. A control CT scan showed bronchiectasis with pneumatoceles formations in the upper lobe of the right lung and progressions of interstitial changes in both lungs. Other radiological findings included

hydrothorax with a small amount of fluid in the right pleural cavity and lymphadenopathy of the mediastinum and pulmonary hilus nodes. Sputum and blood cultures were repeated. While blood cultures gave negative results, sputum cultures indicate the presence of *Candida krusei* and *Staphylococcus haemolyticus*. Additionally, an ELISA test performed on the patient's serum indicated the presence of Candida antigen with a concentration of 232.20 pg/ml. Thus, linezolid and caspofungin i.v. were introduced to the therapy. The implementation of the modified therapy resulted in a resolution of symptoms and changes radiological findings. The level of the Candida antigen concentration was reduced to 26,1 pg/ml. Due to the positive effects of the therapy, caspofungin i.v. was substituted with voriconazole p.o. Within a few days, pulmonary manifestations of the infection recurred, thus caspofungin i.v was reintroduced to the therapy, resulting in a renewed remission of the symptoms.

Meanwhile, the patient's morphology analysis showed severe pancytopenia. Consequently, red blood cell concentrates, fresh frozen plasma, cryoprecipitate, platelet concentrate, and a G-CSF were administrated, resulting in an improvement in hematological parameters. Pathology examination and myelogram revealed an image of cell-rich marrow with proliferation of granulocytic system with preserved maturation and deeply reduced red-blood cell system.

Following 28 days of linezolid administration, a decision was made to discontinue its use. The patient responded with a fever and an upsurge of inflammatory parameters. Such a clinical presentation gave a premise for expanded radiological diagnostics. In the dental panoramic radiograph, advanced carious changes and numerous missing teeth were found, therefore extraction of the decayed teeth was performed. Even though the procedure was successfully performed, the fever and inflammatory parameters did not decline.

Chest and abdomen CT scans revealed opacification in the lateral upper quadrant of the right breast and lymphadenopathy of the left subclavian, mesenteric, and retroperitoneal nodes. Because of CT findings, an ultrasound examination of breast with axillary, and neck lymph nodes check was performed. Change in the right breast was classified as a BIRADS 3, while the lymph nodes exhibited characteristics of cancerous metastasis. A lymph node biopsy was not performed due to the patient's refusal. At that time effectiveness of antiretroviral therapy was confirmed. After 2 months of the treatment, levels of the CD4+ lymphocytes reached - 208 cells/µl and CD8+ lymphocytes - 1323 cells/µl, while the HIV RNA level dropped to 247 copies/ml.

Discussion

HIV in older adults

Literature defines an older patient with HIV as an individual aged 50 years or older who is infected with the virus [3]. Data published by the European Centre for Disease Prevention and Control (ECDC) and the WHO Regional Office for Europe from Europe show, that diagnosis of new HIV infection in older adults increased over the years [1,4]. Even though women are a minority in newly reported HIV infections, the growth in reported cases is noticeable [1,4,5]. Reports underline a few factors that are responsible for such a growth in this particular age group, which are low perception and misconceptions about transmission risks, social stigma, along with poor risk assessment and sexual history collection by healthcare providers [3,4,6]. The source of the infection in our patient could not be determined, which is a typical medical interview in the older age group [4]. Literature suggests that in females the most common source of infection is heterosexual contact, compounded by common sexual risk behaviours and age-related changes in the female genitourinary system [4,7]. HIV infection in the elderly is characterised by rapid clinical progression with high initial plasma HIV RNA levels and a great decline of CD4+ lymphocyte cells, therefore most of the patients are diagnosed in an advanced clinical stadium of infection [1,5]. Symptoms of the retroviral infection can be misleading and may result in delayed testing for HIV. Patients may present weight loss, low-grade fever, fatigue, influenza-like symptoms, episodes of bacterial pneumonia, herpes zoster, neuropathies, dementia, and cervical or vulvar dysplasia or cancer [5,7]. In comparison to other age groups, older patients have a higher HIV-associated mortality rate and a greater chance of dying within a year after the diagnosis [8]. Even though HIV-related mortality declines over time, patients die from age-associated comorbidities, such as cardiovascular diseases, impaired renal function, metabolic, pulmonary, bone, and malignant diseases, at a higher rate than the general population [9,10]. In terms of AIDS treatment in older individuals, it is vital to consider not only changes in pharmacodynamics due to lower renal and hepatic function but also multimorbidity and polypharmacy [9,10].

The effectiveness of anti-retroviral treatment may be disturbed by the emergence of HIV drug-resistance mutations. A recently published study, which evaluated cases from Polish infectious-diseases centres showed, that despite the massive migration movement from Eastern European countries, no increased risk of transmission of multidrug-resistant strains of HIV was observed [11].

Fever of Unknown Origin

Fever of Unknown or Uncertain Origin (FUO) remains a frequent clinical problem in patients infected with HIV. The definition of FUO includes fever higher than 38.3°C on several occasions, lasting for more than 3 weeks with no clear origin, despite appropriate investigation [12]. The most common cause of FUO is disseminated opportunistic infection and it usually appears in AIDS. In this case, fever appeared during the attempt to withdraw the linezolid. The patient's positive response to ART, indicated by the increase of CD4+ lymphocyte count and decrease of HIV RNA suggests that the fever was not caused by HIV infection itself [12]. Causes of fever of unknown origin in patients with AIDS feature mycobacterial infections, pneumocystis pneumonia, cytomegalovirus infection, endemic mycoses, visceral leishmaniasis, cryptococcosis, toxoplasmosis, aspergillosis, lymphomas, drug allergy [13]. Evaluation of the patient should concentrate on obtaining a precise medical history, information about recent travels, and analysing the possibility of occurrence of the causes described above [13]. The investigation should include incubating appropriate blood cultures, especially toward mycobacterial infection, however, it was not a fever's origin in this case [13]. Radiological diagnostics should include abdominal, thoracic, and cerebral CT, while the most convenient way to evaluate the whole body is fluorodeoxyglucose PET [13].

In this case, findings in the breast were assessed as BIRADS 3, however, the presence of lymphadenopathy in CT scans may have indicated a malignancy [14] [15]. Nonetheless, breast neoplasms rarely manifest with fever [15]. Yet another potential source of the fever could be determined through pathologic examination of bone marrow and changed lymph nodes[16].

In this case only trepanobiopsy was performed. Biopsy of the lymph nodes performed in patients with HIV usually reveals tuberculous or reactive lymphadenitis, however, it can also uncover lymphomas, which frequently manifest themselves through the fever [17]. It is also important to assess less apparent sources of fever, such as suspected pathology in the oral cavity, such as dental caries, apical periodontitis, or acute apical abscess [18]. However, our patient did not respond with the resolution of fever and decline of inflammatory parameters, even after appropriate dental treatment. In this case, the origin of the fever remains unknown.

Conclusion

This case shows challenges encountered during the diagnostics and therapeutical processes of AIDS. It also presents that in older patients with opportunistic infections, diagnosis of a new

HIV infection should always be taken into consideration. It is a reminder for healthcare professionals, not to exclude older people from the diagnostic process. That is an especially vital message these days, with a rising total number of reported HIV infections in Central and Eastern Europe [1].

Disclosure

Author's contribution

Conceptualization: JSR; Investigation: WH, JW, PH, AK, JR, IW; Resources: JSR;
Data curation: JSR; Writing - rough preparation: WH, JW, PH, AK, JR, IW;
Writing - review and editing: JSR; Visualization: WH, JW, PH, JSR; Supervision: JSR; Project administration: JSR
All authors have read and agreed with the published version of the manuscript.

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Conflict of interest

None.

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