Delayed HIV diagnosis of patients due to the COVID-19 pandemic

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Abstract
Introduction. The AIDS disease epidemic is still a global problem. To date, finding the connection between HIV and SARS-CoV-2 infection is very significant.

Case Report. A 51-year-old woman was admitted to the Neurology Department due to neurological symptoms lasting for 1.5 months. Imaging examinations of the CNS, chest CT and cerebrospinal fluid examination revealed significant abnormalities. Tests for HIV and SARS-CoV-2 were both positive. Klebsiella pneumoniae ESBL+ was detected in rectal swab as well as findings of Candida antigens and antibodies of Cryptococcus neoformans mycosis in serum. Due to these results, appropriate treatment was implemented but with with a time delay which resulted in the death of the patient.

Conclusion. HIV infection may be associated with an increased risk of severe SARS-CoV-2 infection causing an increase in mortality rate during the COVID-19 pandemic. Confirmation and early detection of HIV infection permits early and accurate diagnosis and faster treatment decisions.

Key words
COVID-19, Cryptococcus neoformans mycosis, delayed HIV diagnosis

INTRODUCTION
AIDS (Acquired Immunodeficiency Syndrome) is caused by HIV (Human Immunodeficiency Virus). The first cases of AIDS were recorded in 1981 [1]. According to UNAIDS (United Nations Programme on HIV/AIDS), in 2020, there were approximately 37.7 million people living with HIV worldwide [2]. So far, an effective vaccine to prevent the disease has not been developed. Currently, antiretroviral drugs (ART) are used, which are able to inhibit viral replication, this can improve the patient’s prognosis and quality of life, and may be used at an early stage of the infection. Delayed ART use associated with a late disease course may result in hospitalization for concomitant opportunistic infections [3]. Delayed diagnosis of HIV is diagnosed with a CD4 cell count <350/µl or an AIDS-defining event without regard to the CD4 cell count. Advanced HIV infection is diagnosed when the CD4 cell count is less than 200 cells/µl or an AIDS-defining event at the first control test [4].

The COVID-19 pandemic caused a negative impact of diagnosis and proper onset of pharmacological HIV treatment. A study by Kowalska JD et al. showed that HIV clinics in Central and Eastern Europe were functioning normally in only about 30% of the countries [5]. The study estimated that 19% of HIV-infected patients were unable to receive antiretroviral drugs as a result of the pandemic [6]. Due to the COVID-19 pandemic, HIV diagnosis and treatment were often delayed [2]. Initial diagnosis of HIV which occurs on time is essential in order to start treatment early and prevent further progression of the disease [7]. The presence of indicator diseases of AIDS should force HIV test. A great deal of data from randomized, controlled trials confirm the consequences of not treating HIV positive people with AIDS related diseases, which are presented below [8, 9,10].

CASE REPORT
A 51-year-old woman was reported to the Emergency Department with the following symptoms: weakness, dizziness, pain in the lumbar and sacral spine, abnormal gout, and fever. Due to neurological symptoms that lasted for 1.5 months, she was admitted to the Department of Neurology. During the admission, the patient’s Glasgow Coma Scale score was 15 (GCS 15). Meningeal symptoms, sensory disturbances, ataxia and paresis were absent. Laboratory tests showed several abnormalities (Tab.2). Imaging examinations of the central nervous system, spine and chest were performed which showed numerous small foci of ischemic strokes in CNS, most likely embolic, with a predominance on the right side. CT of the spine showed disc protrusion at the L5-S1 level. Chest CT showed an area of consolidation in the right lung and fluid on both sides of the chest. Cerebrospinal fluid examination performed on the 5th day of hospitalization revealed the following abnormalities: incomplete transparency, increased pleocytosis (28 cells/µl), increased protein level (175 mg/dl), and decreased glucose level (1.5 mg/dl). Antigen tests for the most common etiological factors of meningitis, such as S. pneumoniae, N. meningitidis, H. influenzae, and cerebrospinal fluid culture were negative. The results of microbiological tests for tuberculosis, syphilis, Lyme disease and COVID-19 were negative.
The patient's condition deteriorated on the 12th day of hospitalization. The patient was conscious but without verbal contact, opened her eyes in response to pain (GCS 6), with positive meningeal symptoms, transferred to the Department of Infectious Diseases. She was transferred to a unit dedicated for patients infected with SARS-CoV-2. Test for HIV infection was performed, which proved positive. Toxoplasma gondii antibodies. The remaining tests gave negative results. Due to late-stage HIV infection, the suspicion of CNS mycosis. Cryptococcus neoformans was found in the CSF and in the blood. Based on the results of clinical examination, treatment with amphotericin B, flucytosine, meropenem, co-trimoxazole and symptomatic treatment was initiated. As a result of increasing respiratory failure, the patient died after 35 days of hospitalization.

Table 1. Examples of indicator diseases

| Respiratory                | Neurology                                    |
|---------------------------|----------------------------------------------|
| Pneumonia, recurrent (≥2 or more episodes in 12 months) | Cerebral toxoplasmosis                       |
| Tuberculosis pneumonia    | Cryptococcal meningitis                      |
| Histoplasmosis, disseminated/extra pulmonary | Primary cerebral lymphoma                    |
| Candidiasis, bronchial/lungs | Progressive multifocal leukoencephalopathy |
| Mycobacterium avium complex (MAC) or Mycobacterium kansasii, disseminated or extrapulmonary | Dementia                                    |
| Herpes simplex            | Aseptic meningitis or encephalitis          |
| bronchitis/pneumonitis    | Guillain–Barré syndrome                     |
| Bacterial pneumonia       | Leukoencephalopathy                         |
| aspergillosis             | Peripherial neuropathy                      |
|                           | Cerebral abscess                            |
|                           | Space occupying lesion of unknown cause      |
|                           | Transverse myelitis                         |

| Oncology and Haematology  | Dermatology/Dermatovenerology                |
|---------------------------|----------------------------------------------|
| Non-Hodgkin lymphoma      | Kaposi’s sarcoma                             |
| Lung cancer               | Herpes simplex ulcer(s)                     |
| Malignant lymphoma        | Severe or recalcitrant seborrheic dermatitis |
| Anal cancer or anal intraepithelial dysplasia |          |
| Seminoma Head and neck cancer |    |
| Castleman’s disease       | Multidermatomal or recurrent herpes zoster   |
| Unexplained leukocytopenia/thrombocytopenia lasting ≥4 weeks | Candidiasis |

| Gastroenterology          | Ophthalmology                                |
|---------------------------|----------------------------------------------|
| Cryptosporidiosis diarrhoea, > 1 month | Cytomegalovirus retinitis                     |
| Candidiasis, oesophageal | Any unexplained retinopathy                  |
| Hepatitis B or C infection | Infective retinal diseases including herpes viruses and toxoplasma |
| Oral candidiasis          |                                              |
| Oral hairy leukoplakia    |                                              |
| Chronic diarrhoea of unknown cause |                                              |
| Salmonella, Shigella or Campylobacter enteritis |  |
| Weight loss of unknown cause |                                              |

| Ear, nose and throat      | Other                                        |
|---------------------------|----------------------------------------------|
| Candidiasis tracheal/oesophageal | Any lymphadenopathy of unknown cause       |
| Lymphoepithelial parotid cysts | Mononucleosis-like syndrome (primary HIV infection) |
| Lymphadenopathy of unknown cause | Pyrexia of unknown origin                     |
| Mononucleosis-like illness | Any sexually-transmitted infection           |
| Chronic parotitis         |                                              |

| Table 2. Laboratory tests results |
|-----------------------------------|
| **ON ADMISSION**                  | **19TH DAY OF HOSPITALIZATION** |
| CRP                              | 177.7 mg/l                     |
| PCT                              | 0.27 mg/l                      |
| WBC                              | 3.69 K/µl                      |
| NEU                              | 3.03 K/µl                      |
| PLT                              | 292 K/µl                       |
| HBG                              | 4.67 g/dl                      |
| CREATININ                        | 0.27 mg/dl                     |
| AST                              | 53.9 IU/L                      |
| ALT                              | 73.8 IU/L                      |
| D-DIMERS                         | 6.011 ng/ml                    |
| IL-6                             | 377.9 pg/ml                    |
| FERRITIN                         | 831.1 µg/l                     |
CONCLUSION

Due to the presented clinical case, attention should be paid to early detection and treatment of HIV infection. Confirmation of HIV infection permits taking diagnostics focused on diseases characteristic for infected people. During a pandemic, it is especially important to maintain the continuation of HIV treatment due to the negative consequences of its neglect [17]. Another important aspect is the prevention of SARS-CoV-2 infection among immunosuppressed people, such as those with HIV. Despite numerous research studies about the impact of HIV infection on the course of COVID-19, there are still questions without unambiguous answers. This highlights the need to deepen knowledge on this topic by conducting further researches.

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