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COVID-19 IN A PACIENT WITH HIV INFECTION – A CASE REPORT

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ABSTRACT:

A 28-YEAR-OLD FEMALE ADDRESSES HER FAMILY DOCTOR AFTER EXPERIENCING RESPIRATORY SYMPTOMS, AFTER SHE DECIDED TO SELF ADMINISTER A RAPID ANTIGEN TEST FOR THE DETECTION OF SARS-COV-2 INFECTION THAT YIELDED A NEGATIVE RESULT. AFTER PERFORMING A RT-PCR NASOPHARYNGEAL EXSUDATE THAT WAS POSITIVE FOR THE SARS-COV-2 INFECTION, THE PATIENT WAS REFERRED TO THE HOSPITAL FOR DETAILED EVALUATION AND SPECIALIZED TREATMENT. THE COURSE OF THE DISEASE AND THE RELATIVELY MILD ONSET OF COMPLICATIONS, WITH THE MAINTENANCE OF PHYSICAL ASTHENIA FOR 30 DAYS AFTER THE ONSET OF THE FIRST SYMPTOM AND THE ASSOCIATION WITH THE NEGATIVE OF THE RT-PCR TEST FOR SARS-COV2, DRAWS OUR ATTENTION AS A LONG COVID19 SYNDROME PATHOLOGICAL.

KEY WORDS: COVID-19, SARS-COV2, HIV, KOCH, HODGKIN, NHL.

INTRODUCTION

Coronaviruses are a family of viruses that are known to cause both respiratory and intestinal diseases in various species of animals and humans⁵. To date, 7 human coronaviruses have been identified, including the virus of the latest severe acute respiratory syndrome, coronavirus 2 (SARSCoV-2)⁶. At present, the virus has infected more than 268,189,593 people worldwide as of December 2021, killing 5,297,434 people, according to

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⁵ Dong Y, Liang X, Yu X. Prognostic value of the dynamic changes in extra vascular lung water index and angiotensin-2 in severe multiple trauma patients with acute respiratory distress syndrome. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue 2019;31:571–576

⁶ Niu P, Shen J, Zhu N, Lu R, Tan W. Two-tube multiplex real-time reverse transcription PCR to detect six human coronaviruses. Virologica Sinica 2016;31:85–88

the latest published data by the World Health Organization (WHO). The disease was identified as a pandemic by the WHO leading to thousands of deaths and hospitalizations worldwide⁷.

The human immunodeficiency virus (HIV) is a lentivirus within the family of Retroviridae, subfamily Orthoretrovirinae, that enters the body via mucous membranes, injured skin or by parenteral inoculation. This infection can progress with the marked reduction in CD4 cell numbers (<300/ μ l) and the immune response to respiratory microorganisms is suppressed⁸. Due to the ongoing COVID-19 pandemic, the investigation of comorbidities⁹ or concomitant infection with COVID-19 are extremely relevant¹⁰. To date, there is no current standard treatment available, and new treatments are currently under investigation, particularly in higher-risk populations¹¹.

The implementation of quarantine, social distancing and community isolation measures has reduced access to routine HIV monitoring. Even with the availability of HIV self-testing kits in some areas¹², testing remains a major challenge in environments with limited access to these kits. Therefore, increased efforts are needed to increase access and facilitate testing.

Timely link to HIV care could be impeded during the COVID-19 pandemic. People living with HIV who should have started antiretroviral therapy (ART) in hospital may be discouraged or delayed because hospitals are busy treating COVID-19 patients. In addition, as many public health authorities globally focus on controlling COVID-19, the allocation of

⁷ <https://www.worldometers.info/coronavirus/> Accessed: 2021-06-15; Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. *Lancet* 2020;395:565–574; Jia Z, Yan L, Ren Z, Wu L, Wang J, Guo J, et al. Delicate structural coordination of the Severe Acute Respiratory Syndrome coronavirus Nsp13 upon ATP hydrolysis. *Nucleic Acids Res* 2019;47:6538–6550; Wu Z, McGoogan JM. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. *JAMA* 2020. <https://doi.org/10.1001/jama.2020.2648>. Published online February 24, 2020

⁸ Jambo KC, Sepako E, Fullerton DG, Mzinza D, Glennie S, Wright AK, Heyderman RS and Gordon SB; Bronchoalveolar CD4⁺ T cell responses to respiratory antigens are impaired in HIV-infected adults. *Thorax*. 66:375–382. 2011

⁹ Branco ACCC, Sato MN and Alberca RW; The possible dual role of the ACE2 receptor in asthma and coronavirus (SARS-CoV2) infection. *Front Cell Infect Microbiol*. 10(550571)2020; Alberca RW, Pereira NZ, Oliveira LMDS, Gozzi-Silva SC and Sato MN; Pregnancy, viral infection, and COVID-19. *Front Immunol*. 11(1672)2020; Alberca RW; Asthma endotypes and COVID-19. *J Asthma*; Oct 1, 2020 (Epub ahead of print)

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¹¹ Marino A, Pampaloni A, Scuderi D, Cosentino F, Moscatt V, Ceccarelli M, Gussio M, Celesia BM, Bruno R, Borraccino S, Borraccino S, et al; High-flow nasal cannula oxygenation and tocilizumab administration in patients critically ill with COVID-19: A report of three cases and a literature review. *World Acad Sci J*. 2(23)2020; Chen H, Zhang L, He Z, Wang D, Liu L, Xhang W, Chen T, Dai Z, Han Z and Chen M; Systemic administration of human umbilical cord-derived mesenchymal stem cells effectively ameliorates the outcomes of a critically ill elderly patient with COVID-19 with multiple comorbidities: A case report. *World Acad Sci J*. 2(29)2020; Alberca RW, Teixeira FME, Beserra DR, de Oliveira EA, Andrade MMS, Pietrobon AJ and Sato MN; Perspective: The Potential Effects of Naringenin in COVID-19. *Front Immunol*. 11(570919)2020

¹² Tang W Wu D Opportunities and challenges for HIV self-testing in China. *Lancet HIV*. 2 18;5: e611-e612

resources for HIV care could be diminished and the circumstances surrounding the continuum of HIV care could worsen¹³.

Vaccination against the new Coronavirus in HIV-infected patients has become of vital importance¹⁴ due to the potentially lethal effects of COVID-19 in these patients compared to the general population¹⁵. However, to date, no large-scale study on the safety and efficacy of COVID-19 vaccines has been completed, especially in the HIV-positive population.

CASE REPORT

In April 2021, a 28 year old female patient decides seeing her family doctor after experiencing fever with a maximum value of 39.5 degrees C, chills, fatigue, difficulties breathing and productive cough dating 5 days prior to doctor evaluation. The patient self-administered antipyretics at home with a favourable evolution in the first days. She decided to self-administer a rapid antigen test for the detection of SARS-COV-2 infection that yielded a negative result. The test was repeated in the doctor's office with the same result and the decision was to perform a RT-PCR nasopharyngeal exudate due to the fact that the patient had been already vaccinated against COVID-19. The test was positive for the SARS-COV-2 infection. The patient was referred to the hospital.

This study has obtained approval from the Ethics Committee of the University of Medicine and Pharmacy of Craiova. The patient signed an informed consent, she was previously handed a form in which she was presented all the information related to the participation in the study and use of personal data. Clinical data and the collection of biological material were achieved after obtaining written informed consent from the patient.

From the anamnesis, we found that the patient was hospitalized in June 2016 at NHS Hospital in UK, where she was diagnosed and with HIV C3 category infection, pulmonary and meningeal tuberculosis, diffuse non-Hodgkin's lymphoma (NHL) with large cells and was initiated on specific treatment but the patient cannot provide details about its nature, and she also underwent brain surgery to remove NHL-derived tumors. Upon returning home in Romania, she was registered at the HIV Department of the Craiova Infectious Diseases Hospital and was initiated on oral antiretrovirals daily with Kivexa (Abacavir + Lamivudine) once a day and Isentress (Raltegravir) bid.

The physical examination demonstrated a slightly influenced general status, BMI = 23.95, post-operative scar on the scalp, paleness, tongue with whitish deposit, generalized, painless micropoliadenopathy pulmonary stetacoustics: bilateral wetties rales, spontaneous oxygen saturation = 92%, rhythmic heart sounds, BP = 108/70 mmHg, AV = 71 bpm, body temperature = 39.4°C. All other parameters of the physical examination were normal.

¹³ Jiang, H., Zhou, Y. and Tang, W., 2020. Maintaining HIV care during the COVID-19 pandemic. *The lancet HIV*, 7(5), pp.e308-e309

¹⁴ V.Padureanu, Maria Bogdan, Mihaela-Simona Subtirelu, Rodica Padureanu Adina Turcu-Stiolica, F. Petrescu Florentina Dumitrescu, Liliana Mititelu-Tartau. Perception of COVID-19 vaccination among healthcare professionals in Romania. *Med. Surg. J. - Rev. Med. Chir. Soc. Med. Nat.*, Iasi - 2020 - vol. 124, no. 3: 454-60

¹⁵ RW Eisinger, AM Lerner, AS. Fauci HIV/AIDS in the Era of COVID-19: A Juxtaposition of Two Pandemics *J Infect Dis* (2021), p. jia114 Apr 7; JM Tesoriero, CE Swain, JL Pierce, L Zamboni, M Wu, DR Holtgrave, et al. COVID-19 Outcomes Among Persons Living With or Without Diagnosed HIV Infection in New York State *JAMA Netw Open*, 4 (2) (2021), Article e2037069 Feb 1

Baseline investigation revealed **CBC**: WBC = $6.8 \times 10^3/\text{mm}^3$, LYM = $1.67 \times 10^3/\text{mm}^3$, LYM = 24.4%, MON = $0.5 \times 10^3/\text{mm}^3$, MON = 7.3%, NEU = $4.57 \times 10^3/\text{mm}^3$, NEU = 66.9%, EOS = $0.06 \times 10^3/\text{mm}^3$, EOS = 0.9%, BAS = $0.03 \times 10^3/\text{mm}^3$, BAS = 0.5%, RBC = $3.79 \times 10^6/\text{mm}^3$, HGB = 13.6 g/dl, HCT = 42.3%, MCV = $111 \mu\text{m}^3$, MCH = 35.9 pg, MCHC = 32.3 g/dl, RDW = 10.7%, PLT = $224 \times 10^3/\text{mm}^3$, MPV = $8.4 \mu\text{m}^3$, basophils = 1%, eosinophils = 1%, lymphocytes = 21%, segmented neutrophils = 70%, monocytes = 7%, blood smear = anisocytosis with macrocytosis, **Sedimentation rate** = 50 mm at 60 min and 84 mm at 120 min, **serum urea** = 24.2 mg/dl, **creatinine** = 0.65 mg/dl, **serum glucose** = 91.5 mg/dl, **triglycerides** = 81 mg/dl, **HDL cholesterol** = 43.4 mg/dl, **LDL cholesterol** = 112 mg/dl, **GOT** = 69.8 mg/dl, **GPT** = 75.1 mg/dl, **D-Dimers** = 579 mg/dl, **C-reactive protein** = 95 mg/dl, **fibrinogen** = 410 mg/dl, **procalcitonin** = 8.9 ng/ml, **INR** = 1.04, **prothrombin** = 97.6%, **Quick time** = 12.48 sec, **pH** = 7.39, **Na⁺** = 136 mmol/l, **K⁺** = 4.8 mmol/l. **CD4** = 560 cell / mm^3 ; **Viral Load-HIV** = undetectable; **HBs antigen** = negative; **HCV antibodies** = negative; **VDRL test** = negative; **Urine test** with normal results.

Chest X-ray: Multiple bilateral infiltrates, areas of lobar and segmental condensation, diffuse reticulo-nodular pattern; decreased diffuse pulmonary transparency, hilum with increased size and opacity, diffusely contoured, lung damage approximately 70%; (Fig 1)



Fig.1. Chest X-ray. Anteroposterior erect view

Due to the neurosurgical medical history we decided to perform a neurological examen that recommended a brain MRI for clinical monitoring. The result showed a discrete regressive appearance of the round-oval tumor formation of 33.7/23.5 mm vs. approx. 40/30 mm, located in the right frontal lobe, tangent to the large right sphenoidal wing, with minimal perilesional edema and discrete compressive effect on the frontal horn of the right lateral ventricle; regressive aspect of the round-oval tumoral formations with intense capture of the contrast media, located in the right cerebral peduncle of 6.2/3.2 mm vs. approx. 12/11

mm, respectively right posterior parietal 2.1 mm vs. approx. 4 mm, with the appearance of possible lymphoma determinations; (Fig 2)

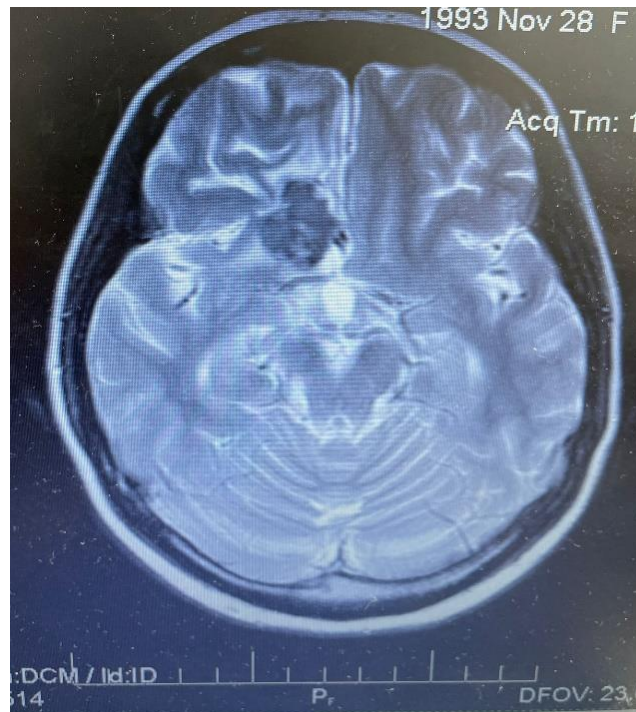


Fig.2. Brain MRI: round-oval tumor, located in the right frontal lobe.

We also performed a pneumophtisiology exam that recommended a sputum examination for Koch Bacillus microscopy with negative result, sputum culture examination to identify Mycobacterium tuberculosis with negative result.

The continuous decrease in oxygen saturation from the beginning of hospitalization required the introduction of additional oxygen on nasal cannula starting with a flow of 5 liters O₂/min, correcting, and stabilizing after about 1 hour at 98%. Considering the clinical, paraclinical evaluation and corroboration of the anamnestic data, it was established the introduction of symptomatic medication with bromhexine hydrochloride 24 mg/day for the improvement of productive cough, antibiotic therapy with ceftriaxone intravenous administration 2g/day every 12 hours, intravenous corticosteroid with 8 mg/day, anticoagulant in prophylactic dose with enoxaparin 0.4 ml 1 ampoule/day (evening), ranitidine 50mg/2ml 1 ampoule/day for gastric protection, antiviral treatment - remdesivir 200 mg on the first day, then 100 mg/day for the next 4 days. Beginning the 3rd day of hospitalization, she was administered vitamin B injection (B1, B6) and C to support immunity, taking into consideration her medical history.

The patient continued to have a high fever of over 38.6 degrees C after 5 days of antibiotics, which imposed the change of antibiotic treatment to meropenem 1g at 8 hours associated with azithromycin orally 500 mgs per day. After 3 doses of antibiotics the fever disappeared with an improve of the patient's health status. The slow favourable evolution of the patient, especially the need to increase oxygen from 5 liters O₂ / min to 20 liters O₂ / min within 5 days of hospitalization also raised the need to increase the dose of dexamethasone to 16 mg / day associated with enoxaparin 0.4 ml 1 ampoule every 12 hours. Following the next days we identified an increase in serum transaminases (GOT = 102 mg/dl, GPT = 124.2

mg/dl) so the patient has to undergo an abdominal ultrasound (liver with left hepatic antero-posterior diameter of the left lobe = 40 mm, cranio-caudal diameter = 97 mm, caudate lobe antero-posterior diameter = 22 mm, right hepatic lobe- prerenal diameter = 144 mm; Cholecyst 81 mm, main biliary duct- normal calibre, pancreas normal appearance; Right kidney 109 mm long axis, RPI (renal parenchymal index)= 15.7 mm. Left kidney 116 mm long axis, RPI = 18.7 mm; Spleen = 109/32 mm, with the presence of a infracentrimetric calcification. Urinary bladder-normal parameters. No peritoneal effusion. We decided to introduce intravenous infusion of aminosteryl-N-hepa 8% 1 vial per day associated with aspatofort 2 ampoules per day in isotonic glucose solution within one hour, medication administered 7 days. A 7-day follow-up was performed and serum transaminases reached almost normal levels (GOT = 53,2 mg/dl, GPT = 44, 5 mg/dl). The patient's health has improved considerably, although fatigue was persisting even on the 15th day of admission. After 21 days of hospitalization, even though the RT-PCR for the detection of SARS-CoV2 infection was still positive, we decided to discharge the patient with the decision to isolate at home. Although the patient had associated multiple illnesses with episodes of unfavourable evolution, during hospitalization it was possible to stabilize the health condition with the cure of COVID 19. Even though the patient had been already vaccinated against COVID-19, she still developed a severe illness with lung damage of 60%. Before discharge, only fibrous sequelae could be identified on the chest X-Ray with complete resolution of the previous findings. She was discharged with the recommendation to continue antiretroviral (HIV) treatment, Vitamin C 1000 mg once a day, Vitamin D 2000 IU once a day for 7 days, and Silymarin 1000 mg and Essential Phospholipids 300 mg tid for 30 days.

At 45 days follow-up visit, we repeated the RT-PCR SARS-CoV2 that was negative, and the biological and clinical reassessments were also within normal parameters, with the resolution of hepatic impairment and fatigue.

CONCLUSION

HIV patients that are closely monitored to keep the value of CD4 above 500 cells copies per ml and undetected VL-HIV are likely to have an easy to moderate form of COVID 19. Some studies develop the idea that HIV patients could have a lower risk to develop severe COVID19 because of the activity of the antiretroviral drugs particularly protease inhibitors or maybe because of the dysregulation that occurs which might limit the cytokine cascade response¹⁶. Specific data from literature, showed that patients with HIV that tested positive for SARS-CoV-2 tended to develop a long COVID syndrome. We need further investigations to fully understand the mechanisms behind this disease and also to identify the risk factors.

COVID 19 remains a still unknown disease worldwide with multiple complications, with a risk for death due to incorrect decisions of the patients to see a doctor at symptom debut. Global research needs to focus on the possibility of a quick, safe, inexpensive, and easy-to-use diagnosis for patients that will allow them to focus on their health following the right treatment recommended by healthcare professionals.

¹⁶ Elfiky A.A.; Ribavirin, Remdesivir, Sofosbuvir, Galidesivir, and Tenofovir against SARS-CoV-2 RNA dependent RNA polymerase (RdRp): a molecular docking study. Life Sci.2020;253(February) doi: 10.1016/j.lfs.2020.117592

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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