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LETTER TO THE EDITOR

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Severe SARS-CoV-2 pneumonia in a 58-year-old patient with HIV: a clinical case report from the Republic of Cyprus

To the Editor,

According to the ECDC, since December 31, 2019, and as of May 18, 2020, 4 679 511 cases of SARS-CoV-2 have been reported, including 246 979 deaths.[1] Between March 12, 2020, and May 18, 2020, in the Republic of Cyprus, a total of 917 confirmed cases have been reported. Only a few reports have been recently published regarding the course of SARS-CoV-2 in patients with human immunodeficiency virus (HIV). [2-4]

In our case study, we are presenting our experience from a 58-year-old Caucasian male patient with HIV who developed a severe SARS-CoV-2 infection. He was one of the first COVID-19 cases in the Republic of Cyprus.

The patient had malaise, fever, and dry cough on illness day 1 (March 20, 2020). Breathing difficulty developed on day 4, which led him to seek medical attention. The patient was transferred to Limassol General Hospital according to the Republic of Cyprus regional plan for COVID-19 suspected cases and was admitted to a dedicated ward.

On admission to our facility, the patient had a fever (38°C). The oxygen saturation was 92% while the patient was breathing ambient air, the respiratory rate 22 per minute, the blood pressure 117/72 mm Hg, and the heart rate 105 beats per minute. The patient was awake, alert, and fully oriented.

The patient's medical history is notable for HIV infection since 1995, followed in an outpatient HIV clinic. His most recent (August 2019) CD4 cell count was 1640 per μL, and viral load was undetectable under Elvitegravir, Cobicistat, Emtricitabine, and Tenofovir Alafenamide Fumarate. He had no comorbidities.

The results of laboratory tests upon admission were unremarkable except for a mildly elevated CRP (52 mg per litter). Specimens were collected in accordance with ECDC guidance[5] and included nasopharyngeal and oropharyngeal swab specimens for influenza A and B and SARS-CoV-2 (Table 1). Chest radiography was performed, which showed bilateral air space pacifications (Figure 1).

The patient was started on levofloxacin (750 mg once daily) and oseltamivir (standard dose, 75 mg twice a day), pending results from polymerase chain reaction (PCR) analyses. The first (hospital day 1) and a repeat (hospital day 3) upper respiratory specimen tested with reverse transcriptase real-time PCR (RT-PCR) for SARS-CoV-2 returned a negative result. COVID-19 was finally confirmed from a third nasopharyngeal/oropharyngeal sample on hospital day 6. Azithromycin (500 mg once daily) and Chloroquine (500 mg twice a day) was administered (Table 1). Influenza came out negative, and Oseltamivir was subsequently stopped.

The patient progressively developed severe acute respiratory distress syndrome (ARDS) (Figure 1) with a PO_2/FiO_2 ratio of 55 mm Hg on hospital day 7; he was electively intubated and admitted to the ICU (Table 1). Given the changing clinical presentation and concern about hospital-acquired pneumonia, piperacillin-tazobactam (4.5 g four times a day), and vancomycin (1750 mg loading dose followed by 1000 mg three times a day) were initiated. Nasal PCR testing for methicillin-resistant *Staphylococcus aureus* was negative, as were all other obtained cultures. Serial procalcitonin was tested negative. Due to persistent fever, the antimicrobial treatment was upgraded to meropenem (2 g three times a day) and gentamicin (400 mg once daily), and upon failure to respond, empirical antifungal treatment with caspofungin (70 mg daily) was administered. The patient responded and remained afebrile after hospital day 24.

The mechanical ventilation aimed at minimizing ventilator-induced lung injury (VILI).[6] Initially, we targeted a tidal volume of 6 mL/kg (predicted body weight), a plateau pressure lower than 30 cm H_2O, PaO_2 55 to 80 mm Hg, or SpO_2 88% to 95% and pH ≥ 7.25.[7] His oxygenation did not respond to recruitment manoeuvres. His lung mechanics displayed a near-normal static compliance of 40 $L\ cm{\cdot}H_2O^{-1}$, which allowed the use of an individualized, higher tidal volume ventilation strategy, based on observations that COVID-19 presents itself with impressive nonuniformity.[8] The oxygenation ratio was the worst on hospital day 9 (PO_2/FiO_2 185) (Figure 1) and gradually improved from that day forward. The patient did not need prone positioning.

On hospital day 14, the patient demonstrated a marked elevation of D-dimer to 70 386 ng/mL (from 8854 ng/mL on day 6), accompanied by a rise in pCO_2 and demand for ventilation. Despite a negative venous duplex ultrasound that excluded acute deep venous thrombosis, enoxaparin dose was increased to therapeutic, based on the procoagulant pattern of patients with COVID-19. Central Venous Catheters were replaced with peripheral, in line with our thrombosis prevention and infection control bundles.[9] D-dimers and gas exchange gradually normalized over the next days. A thrombus in the previously cannulated internal jugular vein was documented on hospital day 30.

Upon initiation to wean the patient from the mechanical ventilation, he developed severe hyperventilation, with high respiratory drive, large tidal volumes, and potentially injurious transpulmonary pressure swing, increasing the risk of patient self-inflicted lung injury (P-SILI). Sedation and controlled mechanical ventilation were reinitiated, allowing the lung more time to recover. In that perspective,

TABLE 1 Patient demographics and clinical characteristics

Patient Demographics	
Age in years	58
Gender	M
SARS-CoV-2 exposure	Hotel personnel
Comorbidities	HIV
Year of HIV diagnosis	1995
Last CD4 cell count (cells per µL)	1641
Last CD4: CD8 ratio	NA
ART-regimen before admission	Elvitegravir, Cobicistat, Emtricitabine, Tenofovir Alafenamide Fumarate
Clinical findings on admission	
Symptoms	Dry cough, fever, difficulties on breathing, since three days
Diagnosis	Lower respiratory infection
Vital signs upon admission	
Temperature	38° C
Blood pressure (mm Hg)	117/72
Respiratory rate (breaths per min)	22
Heart rate (beats per min)	105
O_2 saturation in ambient air	92%
PaO_2/FiO_2 ratio	328
Chest x-ray findings	Bilateral air space opacifications

Hospitalization	Day1	Day 2	Day3	Day 4	Day5	Day 6	Day7	Day 8	Day9	Day 10	Day 11	Day 12	Day13	Day 14	Day 15	Day 16
Respira-tory status	2lt O2			3lt O2			NRM and intubation FiO2 60%	60%	60%	35%	30%	40%	45%	40%	30%	30%
PO2/FiO2 (mmHg -wors values)	351	348	318	226	256	224	55 After intubation Worst value: 115	190	185	194	243	295	275	310	236	243

Hospitalization	Day 17	Day 18	Day 19	Day 20	Day 21	Day 22	Day 23	Day 24	Day 25	Day 26	Day 27	Day 28	Day 29	Day 30	Day 31	Day 32
Respira-tory status	35%	35%	35%	30%	25%	25%	25%	25%	25%	25%	25%	25%	25%	25%	2 lt O2 Tracheostomy	Nasal 2 lt O2
PO2/FiO2 (mmHg -wors values)	280	228	242	283	304	296 nable to extubate	294	304 PCR for SARS-COV19 Negative	376	380	472	384	420	398	444	439

TABLE 1 (Continued)

SARS-COV-2 sample		- Nasopharyngeal		- Nasopharyngeal		+ Nasopharyngeal																		- bronchial secretions					- bronchial secretions			
Laboratory results																																
White blood cell count (×10³/μL)	8.58		7.62	7.62		12.83	10.30	7.54	8.86	13.63	12.99	12.11	15.15	12.25	12.23	13.55	11.18	11.15	12.08	12.51	13.23	11.94	13.78	14.07	12.25	11.01	10.88	8.96	8.83	8.73	11.6	9.93
Antimicrobials	Levofl	Levofl	Levofl	Levofl	Levofl	Levofl																										
	Oselt	Oselt	Oselt	Oselt	Oselt	Oselt																										
						Chloro	Chloro	Chloro	Chloro	Chloro	Chloro	Chloro	Chloro	Chloro	Chloro	Chloro	Chloro	Chloro	Chloro													
						Azithr	Azithr	Azithr	Azithr	Azithr	Azithr	Azithr																				
						Taz-Pip	Taz-Pip	Taz-Pip	Taz-Pip	Taz-Pip	Taz-Pip	Taz-Pip																				
										Vanco	Vanco	Vanco	Vanco	Vanco	Vanco	Vanco	Vanco	Vanco	Vanco	Vanco	Vanco	Vanco	Vanco									
												Caspof	Caspof	Caspof	Caspof	Caspof	Caspof	Caspof	Caspof	Caspof	Caspof	Caspof	Caspof	Caspof	Caspof							
												Merop	Merop	Merop	Merop	Merop	Merop	Merop	Merop	Merop	Merop	Merop	Merop	Merop	Merop							
												Gent	Gent	Gent	Gent	Gent																
Lymphocyte (%)	34.7					11.9	20	25.6	16.3	12.5	12.6	16	11.6	13.4	21.9	18.7	19	28	28.6	22.7	23.5	24.4	21	20.5	21.1	22.8	25.2	31.9	33.4	27.9	26.4	31.6
Platelets (×10³/μL)	187		214	238	187	152	183	188	217	298	344	322	368	381	485	540	518	565	515	470	431	387	371	399	418	456	487		514	509	539	537
Procalcitonin												**Neg <0.1 ng/ml**		**Neg <0.1 ng/ml**					**Neg <0.1 ng/ml**													
D-dimer (ng/mL)						8854								70836	43593											8658		6630	7383		7314	5146
LDH (U/L)	458					644	562	580	707	589	671	591	714	686	752	763	753	873	694	630	591	622	525	467	428		431	487	504	513	514	511
C-reactive protein (mg/L)	52		98	172	167	210	270	304	305	309	293	293	248	192		115	119	124	156	110	112	125	107	72	60	44	35	25	23	24	21	16
Ferritin (ng/mL)				436			590		861			1034	1150	928	629		619	610	590	600	720	701	639		489		609		572	572	563	
ART						ART before admission maintained through hospitalization																										
Other antiviral treatments						Olsetamivir for 6 days Chloroquine 500mg x2, for 14 days																										
Other antibiotics						Azithromycin 500 x1, for 7 days Levofloxacin 750 x1, for 6 days Piperacillin-Tazobactam 4,5 x 4, for 7 days Meropenem 2gr x 3, for 14 days Gentamicin 400mg x 1, for 5 days Vancomycin 1gr x 2, for 14 days Antifungal: Caspofungin 70mg x1, for 14 days																										
Tocilizumab or corticosteroids						None																										
Ward of admission						Day one to day 7 medical ward hospitalization		ICU admission day 7 to day 31																			ICU discharge & transferred to the medical ward					
Invasive or non-invasive mechanical ventilation						Invasive ventilation day 7 to day 31 (25Days)																										
Outcomes						Improved, fully alert on discharge, no positive cultures																										

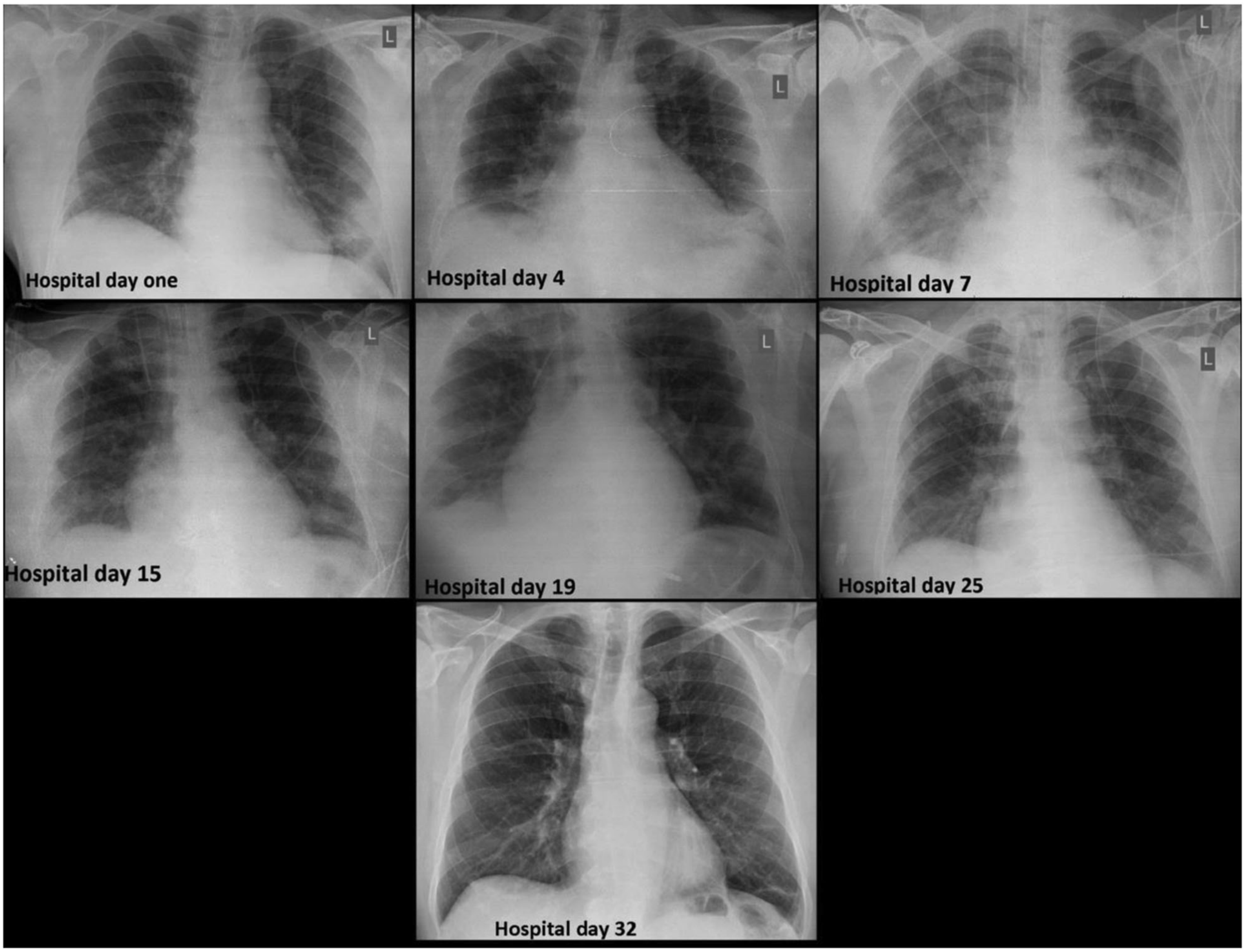

FIGURE 1 Chest X-rays of the patient

percutaneous dilatational tracheostomy was performed on hospital day 24 after bronchial secretions resulted in negative for SARS-CoV-2. Despite the prolonged sedation and mechanical ventilation, the patient regained consciousness relatively quickly and remained oriented and cooperative during the entire stay. He was weaned off the ventilator on hospital day 29, and decannulation was performed on hospital day 31. The patient was discharged from the ICU the following day and transferred to a clinic for rehabilitation. So far, he makes a quick and uneventful recovery.

Standard antimicrobial treatment was used in combination with Chloroquine and azithromycin, based on studies that showed promising results.[10] The patient remained on his previous ART (on tenofovir-containing regimen),[3,4] given his excellent virologic and immunologic condition. Remdesivir, Lopinavir/Ritonavir, Tocilizumab, and corticosteroids were not used due to inconclusive data about their efficacy and safety.[11] COVID-19 characteristics such as serial false-negative upper respiratory specimens, deterioration between days 7 and 10, near-normal lung compliance, hyperventilation, prolonged need for mechanical ventilation, and increased risk for thrombotic complications, were observed in our patient, in line with findings from other case studies. The absence of comorbidities, the virologic and immunologic condition, as well as the use of standard antimicrobial treatment in combination with chloroquine and azithromycin and the maintenance of previous ART instead of adaptation ART seem to have an impact on patient's recovery despite his age. The early initiation of antimicrobial treatment may be translated into a lower risk for opportunistic infections.

CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

AUTHOR CONTRIBUTIONS

S.I., D.K., and V.R. have been involved in the writing of the manuscript. C.T.M. and D.M. are members of the ICU team and read the manuscript.

ETHICS STATEMENT

A single case report. The patient has given his informed consent.

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