Case reports

Beneficial effect of hyperbaric oxygen therapy in solving a nosocomial COVID-19 infection. Case report and short literature review

Cristina-Elena Micu^{1,2}, Raluca Andreea Smărăndescu^{1,3}, Ioan-Anton Arghir⁴, Mihaela Trencea^{4,5}, Bogdan Alexandru Barbu⁶, Claudia Mariana Handra^{1,6}

¹ Colentina Clinical Hospital, Occupational Medicine Department, Bucharest, Romania

² Doctoral School, Field: Medicine, "Ovidius" University, Constanța, Romania

³ Doctoral School, Field: Medicine, University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania

⁴ Faculty of Medicine, "Ovidius" University, Constanța, Romania

⁵ Medgidia Municipal Hospital, TB Outpatient Clinic, Medgidia, Romania

⁶ University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania

Corresponding author
Mihaela Trencea

mtrencea79@gmail.com

Abstract

The infection with the new coronavirus SARS-CoV-2 was declared a global health emergency in early 2020 and, two months later, became recognized as a pandemic, affecting the world's population regardless of age, ethnicity, geographical area. COVID-19 generally presents with altered general condition (fever, chills, marked fatigue, muscle aches, headache), respiratory manifestations from cough to dyspnea, acute respiratory distress, and multiorgan damage in critical forms. Manifestations can occur between 2 days and two weeks after exposure, the disease evolving from mildly symptomatic to moderate, severe, and even fatal forms. Our reported clinical case of COVID-19 is that of a 59-year-old nurse with diabetes and hypertension as risk factors. Accidental occupational exposure to SARS-CoV-2 infection occurred due to non-compliance with the existing dressing-undressing protective equipment protocols in facilities with treatment beds. We diagnosed a moderate-severe COVID-19, displaying bilateral lung damage and mild desaturation, complicated by bacterial superinfection with *Klebsiella* spp. The patient underwent antiviral, antibiotic, anticoagulant, cortisone treatment during hospitalization. In the first two months after discharge, we recommended seven hyperbaric therapy sessions to relieve respiratory symptoms and enhance regression of fibrotic lung lesions.

Keywords: SARS- CoV-2, COVID-19, nurse, occupational exposure, hyperbaric therapy

Introduction

COVID-19 is a disease caused by the new coronavirus SARS-CoV-2, which generally comprises the following symptoms: fever, chills, cough, difficulty breathing, fatigue, muscle aches, headache, anosmia, ageusia, odynophagia, nasal congestion, nausea, and digestive disorders. Symptoms may occur between two days and two weeks after exposure. COVID-19 infection progresses from asymptomatic forms to mild, moderate, severe, or even fatal symptoms.

The SARS CoV-2 virus was first identified in an outbreak of respiratory disease in Wuhan, China, and World Health Organization (WHO) reported it on 31.12.2019. On 30.01.2020, the WHO proclaimed SARS CoV-2 infection a global health emergency, and on 11.03.2020, it also declared COVID-19 pandemic. [1]

This infection should be suspected in patients with respiratory symptoms and newly established fever, especially in individuals who have been in an area with community-transmitted SARS-CoV-2 virus, who had recently contact with a suspected/confirmed person with COVID-19 or work in workplaces where there is a risk of contamination. The most exposed professional groups, according to the WHO, are represented by medical and auxiliary staff, care providers, ambulance personnel, police officers; for the diagnosis of the infection, it is necessary to confirm by RT-PCR test SARS CoV-2 or rapid antigen. [1]

Case Presentation

The 59-year-old female non-smoking patient, working as a nurse in an Internal Medicine department, was admitted to the Infectious Diseases Clinic with symptoms specific to SARS-CoV-2 infection and positive RT-PCR result SARS-CoV-2. The professional anamnesis evidenced the patient's total professional experience of 35 years in the same workplace, where she performs work in alternating shifts, including night shifts. The activity she carries out involves: taking the patient after hospitalization, collecting the usual and emergency tests (biochemistry, hematology, bacteriology, mycology, serology, urine biochemistry, immunology, coagulation, etc.), functional explorations, preparing the patient for specific investigations, patient care according to the care and treatment plan, such as administration of drugs orally or by injection (intramuscular, intravenous, subcutaneous), infusions (with or without branulas), application of dressings, cardio-

respiratory resuscitation (if necessary), measurement of vital signs and recording them in the patient observation sheet.

Ten days before hospitalization, the patient had occupational exposure to SARS-CoV-2, by contact with a confirmed patient, after hospitalization with COVID-19. Following the anamnesis performed, the patient mentions that she didn't fully comply with protection measures: did not wear complete equipment, wore only one pair of gloves, one protective mask, no visor, wore personal belongings (mobile phone), did not wash and disinfect hands after every maneuver. After the onset of specific COVID-19 symptoms (dyspnea, cough with ineffective sputum, headache, diarrhea), the nurse performed the SARS-CoV-2 RT-PCR test, which was positive. She was hospitalized only seven days after the onset of symptoms in the Infectious Diseases Department.

From the patient's personal medical history, we noted intermittent asthma, bilateral basal pulmonary fibronodular sequelae of primary tuberculosis (an acute episode in childhood), type 2 diabetes, treatment with oral antidiabetics, and a history of recurrent pneumonia (2 episodes, in 2016, treated with antibiotics). On admission to the Infectious Diseases Clinic, the clinical examination showed non-febrility, altered general status, suffering facies, natural tongue, dyspnea on moderate exertion, and slight desaturation (94% SpO₂ without additional oxygen), crackles, and rales left mid-lung on auscultation; without other changes otherwise.

During hospitalization, paraclinical investigations revealed a moderate nonspecific inflammatory syndrome (ESR 40 mm/h, CRP 35 mg/dl, LDH 348 U/L), hyperglycemia, hypertriglyceridemia, uremic syndrome, and marked increases in ferritin (up to 894 ng/ml) starting from the 10th day of illness; otherwise, other biological markers were within normal ranges. The evolution in dynamics of the hematological and biological parameters is presented in Table 1.

Imaging investigations performed on day 8 of the disease (25/11/2021) revealed in the context of a viral pneumonia COVID-19, bilateral pulmonary damage in dynamic evolution with alveolar-fibro-interstitial lesions, a severity score of 9 (5 right lungs, four left lungs) corresponding to a slight degree of impairment (Figure 1a), and a tendency to consolidate in the posterior segment of right upper lobe and in the basal pyramid of lower lobe bilaterally (Figure 1b).

Figure 1. Dynamics of lung damage from lesions in frosted glass to consolidations and pulmonary fibrosis **Table 1.** Evolution in dynamics of hematological and biological parameters during hospitalization

	24.11	27.11	3.12	6.12	10.12	11.12
Leukocytes	$7.93 \cdot 10^9$	$5.84 \cdot 10^9$	$7.13 \cdot 10^9$	$10.52 \cdot 10^9$	$6.44 \cdot 10^9$	$5.61 \cdot 10^9$
Neutrophils	$7.01 \cdot 10^9$	$4.65 \cdot 10^9$	$5.86 \cdot 10^9$	$7.46 \cdot 10^9$	$4.21 \cdot 10^9$	$3.33 \cdot 10^9$
Lymphocytes	$0.69 \cdot 10^9$	$0.89 \cdot 10^9$	$0.9 \cdot 10^9$	$2.27 \cdot 10^9$	$1.53 \cdot 10^9$	$1.72 \cdot 10^9$
Erythrocytes	$4.3 \cdot 10^{12}$	$4.29 \cdot 10^{12}$	$4.63 \cdot 10^{12}$	$4.58 \cdot 10^{12}$	$3.89 \cdot 10^{12}$	$4.08 \cdot 10^{12}$
Hemoglobin (g/L)	13.2	13.3	14.3	14.1	12.1	12.6
Hematocrit	38.8	38.8	40.9	40.5	35.1	36.9
Platelets	$204 \cdot 10^9$	$273 \cdot 10^9$	$403 \cdot 10^9$	$348 \cdot 10^9$	$233 \cdot 10^9$	$245 \cdot 10^9$
ESR (mm/h)	40		20		40	
Fibrinogen (mg/dl)	560	420	310	278	390	492
CRP (ng/L)		4	2	3	35	23
ALT (U/L)	38	11	24			32
AST (U/L)	29.4		8	9.6		11.5
Total Bilirubin (mg/dl)	0.34		1.32			
Direct Bilirubin (mg/dl)	0.21	0.3	0.72	0.81		
Creatinine (mg/dl)	0.9	1.02	1.13	1.13	0.9	0.89
Urea (mg/dl)		48	59	48		21
Blood glucose (mg/dl)	186.1	254.9	437.3	381.2	387.1	323.4
Total Cholesterol (mg/dl)	124		281	310	229	
Triglycerides (mg/dl)			1060	1171	342	229
Creatin Kinase (U/L)	70		28	47		33
Lactate dehydrogenase (U/L)		348	277	283		254
D-Dimer ($\mu\text{g FEU/ml}$)					0.23	0.29
PT (sec)	12.6	12.9	11.4	12.7		11.8
INR	0.72	1	0.86	0.98		0.89
Serum amylase (U/L)				97		
Serum lipase (U/L)				241	116	151
Ferritin (ng/ml)		248.78	632.1	894.89	420.5	377.16
SARS-CoV-2 RT-PCR			positive			
SARS-CoV-2 IgG			13.09			
SARS-CoV-2 IgM			12.15			
Cytological examination of sputum	Klebsiella spp +					

During hospitalization, we instituted antiviral therapy with Lopinavir/Ritonavir 2 cp x 2/day PO, low molecular weight heparin (Clexane 0.4 ml x 2 /day s.c.), systemic corticosteroid therapy (Dexamethasone iv), proton pump inhibitor i.v., hepatoprotective, probiotic, lipid-lowering (Lipantil 145 mg, one cp/day), personal anti-diabetic medication and oxygen therapy on a facial mask with the increased flow (6-8 l / min) to correct desaturation. At the indication of the diabetologist, Slow Insulin Lantus 20 IU / day s.c. (evening) on the 10th day of treatment. For bacterial superinfection with *Klebsiella* spp., Antibiotic therapy was combined with Piperacillin / Tazobactam 4.8/8 h i.v., antifungals (Fluconazole i.v). Despite the

increase in ferritin that could have been a marker of the cytokine storm, the evolution was favorable. On the 16th day of the disease, we discharged the patient in improved condition with a positive control RT-PCR SARS-CoV-2 test and recommendations for hyperbaric therapy (considering the incipient fibrotic lesions at the lung level) and pneumology monitoring in the territorial clinic. After discharge, the patient underwent seven courses of hyperbaric treatment. The CT chest investigation performed subsequently highlighted the quasi-total regression of fibrotic lesions (Figure 1c), and the spirometry performed on February 22, 2021, had normal values (Figure 2).

Figure 2. Spirometry performed hyperbaric post-oxygen therapy

The epidemiological investigation supported the nature of occupational exposure by non-compliance with hygiene rules and wearing incomplete personal protective equipment, given that the nurse was the only family member diagnosed with COVID-19

infection. Four other medical staff who came in contact with the index case (2 doctors and two nurses) at work also confirmed Occupational SARS-CoV-2 disease.

Discussions

COVID-19 is a disease with an increased risk of infectivity and unpredictable evolution. Thus, the forms initially considered light can progress rapidly to aggravation, with the need for hospitalization.

The most common manifestation is viral pneumonia. Symptoms of pneumonia include fever, cough, shortness of breath, muscle aches, and headache. The average recovery time is two weeks for mild forms and 3-6 weeks for severe illness. [1] A severe complication, especially in patients with comorbidities, may be acute respiratory distress syndrome (ARDS), with a variable frequency between 20-40%. [1] This complication has been associated, in the literature, with age > 65 years, diabetes and hypertension. [1] In July 2020, the WHO estimated that 1.5 million health workers had become infected with COVID-19, three times more than at the beginning of January of the same year. [2] As of February 11, 2020, in China, 3.8% of all confirmed cases of SARS-CoV-2 infection were among medical staff. [3] In Italy, the most affected country in Europe, the prevalence of diseases among medical staff was 10%, and in Lombardy (the most affected region), COVID-19 infection became almost a nosocomial infection. [4] Reports from health professionals show a reasonable and adequate level of hand hygiene in hospitals in Spain before the pandemic. At the same time, the wearing of masks by medical staff and patients has been poor, and 23.6 % of all workers included in the study reported COVID-19 infection as dependent on contact with hospitalized patients. [5] In the United States, 8-10% of all SARS-CoV-2 infected health workers required hospitalization. [6] A study conducted in the Chinese city of Tongji on a batch of 54 medical staff hospitalized for COVID-19 between January 7 and February 11, 2020, showed that the majority (72.2%) came from clinical departments, compared to 3.7% coming from emergency departments. The age difference was associated with the clinical form, as follows: for severe conditions, the mean age was higher (47 years) than in non-severe forms of the disease, where the mean age was low (38 years). [3]

At the beginning of 2020, the population of Wuhan was 11,212 million. Of these, 117,100 were health workers: 43,100 doctors, 57,700 nurses, and 16,300 other categories of medical staff. Of the total health workers infected with SARS CoV-2, 72.28% were women, more than half (52.06%) were nurses, 33.62% were doctors, and 14.33% were the average staff. The rate of SARS-CoV-2 infection was higher among nurses, perhaps also because nurses come

into contact with patients longer than doctors. The extended work schedule and protective equipment in the early stages of the COVID-19 pandemic were insufficient. [7]

The lack of equipment components, non-compliant equipment, lack of reserves for personal protective equipment (PPE) were the factors responsible for the increased number of illnesses in the medical staff. [3] Because the disease is highly contagious, much of the medical staff has not been adequately protected in many parts of the world, or not all staff have complied with PPE, as in our reported clinical case. An increased number of medical workers contracted infections in the first six months of the pandemic [8], and many died from SARS-CoV-2 disease. [9]

Another study conducted in India, in hospitals in the Mumbai region, between April 6 and August 20, 2020, showed that, out of 3711 health workers included in the study, 74.32% were in the first line of care of COVID-19 patients. The total prevalence of infection was 4% among medical staff, 85% of cases were symptomatic, and 15% were asymptomatic, and the most common comorbidities in symptomatic forms were hypertension and diabetes. [10]

In February 2020, Iran launched the Center for the Prevention and Control of the New COVID-19 Disease to detect coronavirus incidence in the Fars province (the most populous region of Iran). The retrospective cross-sectional study conducted among medical staff in 44 state and private hospitals revealed 51.3% of cases among nurses. [11]

Concerning PPE, 1,6% of infected healthcare professionals did not wear a protective mask, 18,7% did not wear gloves at work, and 73,3% of patients admitted to infectious contact at work. [11]

Nurses and other health care workers have experienced trauma and stress in caring for patients with severe COVID-19, so these workers are vulnerable to the psychological impact of this health crisis, being at risk of burnout through depression, anxiety, insomnia, exhaustion. and post-traumatic stress. [12]

To date, no specific antiviral drug is effective in preventing or treating COVID-19. Those with severe forms of the disease appear to have an inadequate immune response so that severe lung damage can occur due to an excessive inflammatory response of the host. According to the recommendations under the conditions of oxygen therapy, oxygen has no toxic effect in humans in therapeutic concentrations. However, in 75% of cases, prolonged inhalation of oxygen can cause many side effects, such as nausea, dizziness, cough with dyspnea, and convulsions,

requiring patients to be exposed to air as soon as possible.

Hyperbaric oxygen therapy (HOT) has beneficial effects in reducing inflammatory conditions by modulating oxidative stress, including lipid peroxidation and increasing antioxidant enzymes. HOT stimulates cell regeneration by increasing the amount of oxygen available to tissues and is therefore used as adjuvant therapy to correct hypoxemia caused by respiratory failure. Thus, the increased amount of oxygen in tissues maintains cellular metabolism in hypoxic tissues and stimulates cell regeneration and the formation of new blood vessels by neovascularization. The principle of this therapy is that the tissues need oxygen to function correctly, and by providing an oxygen supplement, it reaches a significant amount in the cells and tissues due to the increased pressure in the hyperbaric chamber. Studies in humans have confirmed the benefits of hyperbaric oxygen therapy in various inflammatory conditions. [13] At least ten sessions are recommended for a positive result, up to 20, depending on the severity of the condition. We evaluated all COVID-19 patients before starting hyperbaric oxygen therapy to avoid complications and continuously monitored them throughout treatment. [13]

The beneficial effects of hyperbaric oxygenation are facilitating the diffusion of oxygen to damaged or insufficiently vascularized tissues, stimulating their healing; improving the immune system by activating lymphocytes to fight viral infection; rapid reduction of inflammation and edema through vasoconstriction caused by hyperoxia. [14]

If treatment is safely administered, complications such as eardrum damage, transient diplopia, pneumothorax (caused by barotrauma) are rare. The only absolute contraindication to HOT is

pneumothorax. Studies in patients with COVID-19 treated with hyperbaric oxygen therapy have shown improved survival and successful prevention of mechanical ventilation. [14]

Conclusions

Given the occupational exposure and the lack of protective equipment or the use of non-compliant equipment (inadequate protective masks, lack of disinfectants, etc.), medical workers have an increased risk of illness. The healthcare professionals are the most exposed to SARS-CoV-2 infection during the pandemic, so assessing the rate of disease and the characteristics associated with occupational exposure is essential for effective organizational management to improve the protective measures needed for this vulnerable group. Ensuring safety and early identification of cases among healthcare workers is vital to limit the nosocomial transmission of SARS CoV-2. There is a need for health staff education related to hygiene, awareness of medical staff regarding the importance of personal protective equipment and equipping hospitals with protective materials to provide safety to medical personnel. Adherence to protective measures is essential to reduce the number of infections and stop the spread of the virus. We present the case of a 59-year-old patient, a nurse in a medical department, with occupational exposure to SARS-CoV-2, who triggered, at her workplace, an outbreak with four other infected medical staff. Although the patient was at risk of developing a severe form due to metabolic and cardiovascular comorbidities, the disease progressed towards clinical improvement. Hyperbaric therapy is helpful for fibrotic lesions appearing after COVID-19.

References

1. Coronavirus Disease 2019 (COVID-19): Practice Essentials, Background, Route of Transmission. 2021 May 20 [cited 2021 May 28]; Available from: <https://emedicine.medscape.com/article/2500114-overview>
2. Health Workers Should Be Top Priority for Vaccines: Nurses' Group [Internet]. Medscape. [cited 2021 Jul 17]. Available from: <http://www.medscape.com/viewarticle/934630>
3. Chu J, Yang N, Wei Y, Yue H, Zhang F, Zhao J, et al. Clinical characteristics of 54 medical staff with COVID-19: A retrospective study in a single center in Wuhan, China. *J Med Virol*. 2020;92(7):807–13.
4. Felice C, Di Tanna GL, Zanusi G, Grossi U. Impact of COVID-19 Outbreak on Healthcare Workers in Italy: Results from a National E-Survey. *J Community Health*. 2020 Aug 1;45(4):675–83.
5. Rivera-Izquierdo M, Valero-Ubierna M del C, Martínez-Diz S, Fernández-García MÁ, Martín-Romero DT, Maldonado-Rodríguez F, et al. Clinical Factors, Preventive Behaviours and Temporal Outcomes Associated with COVID-19 Infection in Health Professionals at a Spanish Hospital. *Int J Environ Res Public Health*. 2020 Jun;17(12):4305.
6. CDCMMWR. Characteristics of Health Care Personnel with COVID-19 — United States, February 12–April 9, 2020. *MMWR Morb Mortal Wkly Rep* [Internet]. 2020 [cited 2021 Jul 26];69. Available from: <https://www.cdc.gov/mmwr/volumes/69/wr/mm6915e6.htm>
7. Zheng L, Wang X, Zhou C, Liu Q, Li S, Sun Q, et al. Analysis of the Infection Status of Healthcare Workers in Wuhan During the COVID-19 Outbreak: A Cross-sectional Study. *Clin Infect Dis*. 2020 Nov 19;71(16):2109–13.
8. Gholami M, Fawad I, Shadan S, Rowaiee R, Ghanem H, Hassan Khamis A, et al. COVID-19 and healthcare workers: A systematic review and meta-analysis. *Int J Infect Dis*. 2021 Mar 1;104:335–46.
9. Erdem H, Lucey DR. Healthcare worker infections and deaths due to COVID-19: A survey from 37 nations and a call for WHO to post national data on their website. *Int J Infect Dis*. 2021 Jan 1;102:239–41.
10. Mahajan NN, Mathe A, Patokar GA, Bahirat S, Lokhande PD, Rakh V, et al. Prevalence and Clinical Presentation of COVID-19

among Healthcare Workers at a Dedicated Hospital in India. J Assoc Physicians India. 2020 Dec;68(12):16–21.

11. Sabetian G, Moghadami M, Hashemizadeh Fard Haghighi L, Shahriarirad R, Fallahi MJ, Asmarian N, et al. COVID-19 infection among healthcare workers: a cross-sectional study in southwest Iran. Virol J. 2021 Mar 17;18(1):58.

12. A Pandemic Crisis: Leadership and the Millennial Nurse [Internet]. Medscape. [cited 2021 Jul 17]. Available from: <http://www.medscape.com/viewarticle/935364>

13. Senniappan K, Jeyabalan S, Rangappa P, Kanchi M. Hyperbaric oxygen therapy: Can it be a novel supportive therapy in COVID-19? Indian J Anaesth. 2020 Oct;64(10):835–41.

14. Paganini M, Bosco G, Perozzo FAG, Kohlscheen E, Sonda R, Bassetto F, et al. The Role of Hyperbaric Oxygen Treatment for COVID-19: A Review. Med Biomed Updat. 2020 Jul 22;1289:27–35.