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Case Report

Obesity and sleep apnea as a significant comorbidities in COVID-19 — A case report

Maja Nikolic[a], Stefan Simovic[b,c,*], Ljiljana Novkovic[b,d], Vuk Jokovic[e], Danijela Djokovic[f,g], Nemanja Muric[f,g], Danijela Bazic Sretenovic[b,h], Jovan Jovanovic[c], Katarina Pantic[d], Ivan Cekerevac[b,d]

[a] University of Kragujevac, Faculty of Medical Sciences, Department of Physiology, Serbia
[b] University of Kragujevac, Faculty of Medical Sciences, Department of Internal Medicine, Serbia
[c] Clinic for Cardiology, University Clinical Center Kragujevac, Serbia
[d] Clinic for Pulmology, University Clinical Center Kragujevac, Serbia
[e] Center for Vascular Surgery, University Clinical Center Kragujevac, Serbia
[f] University of Kragujevac, Faculty of Medical Sciences, Department of Psychiatry, Serbia
[g] Clinic for Psychiatry, University Clinical Center Kragujevac, Serbia
[h] Clinic for Internal Medicine, University Clinical Center Kragujevac, Serbia

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ABSTRACT

In our paper we aimed to increase the awareness among physicians, concerning coronavirus disease 2019 (COVID-19) severity, especially in patients with specific underlying comorbidities. Obesity is the second most common condition in hospitalized COVID-19 patients. Furthermore it has a major role in the development of obstructive sleep apnoea (OSA), which is highly involved in a severe COVID-19 development and its serious outcomes. Even though obese OSA patients had an increased pulmonary embolism (PE) risk, there is no enough evidence to support the interaction between obesity and OSA regarding PE development in the setting of COVID-19. Our patient is a 45-year-old obese male with COVID-19, who was admitted to the intensive care unit (ICU) with acute respiratory failure requiring high-flow nasal oxygenation. Clinical, laboratory and diagnostic findings pointed on severe COVID-19 form, complicated with PE. After recovery, the diagnosis of OSA was established. With this case, we wanted to alert the physicians on comorbidities, such as obesity and OSA, while those conditions, to some extent, may contribute to worse COVID-19 clinical presentation.

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Introduction

In hospitalized COVID-19 patients, obesity is the second most prevalent underlying condition present in nearly 60% of those 18–49 years old [1]. Moreover, it is recognized as a crucial factor for the development of obstructive sleep apnea (OSA), which, per se, carries the 3-fold higher risk for COVID-19 hospitalization [2]. In particular in obese COVID-19 patients, OSA may potentiate hypoxemia and cytokine storm [3], as well as the thromboembolic adverse events due to an level of coagulation markers [4]. However, there is still no enough evidence to support the interaction between obesity and OSA regarding COVID-19 severity and pulmonary embolism (PE) development.

Here we report a case of a severe COVID-19 disease course in a 45-year-old obese male with subsequently proven severe OSA.

Case report

A 45-year-old obese male (body mass index (BMI): 34 kg/m^2) was presented to our COVID-19 clinic, complaining of dyspnea, chest pain, dry cough, and 5-days lasting fever (up to 38.5 °C, despite the use of antipyretics). His past medical history revealed controlled arterial hypertension and *Helicobacter pylori* gastritis. After the initial evaluation and positive antigen test for COVID-19, our patient was immediately admitted to the intensive care unit (ICU) with signs of acute respiratory failure requiring high-flow nasal oxygenation (HFNO). On 1st day of hospitalization, his labora-

* Corresponding author at: Svetozara Markovica 69, 34000 Kragujevac, Serbia.
E-mail address: simovicst@gmail.com (S. Simovic).

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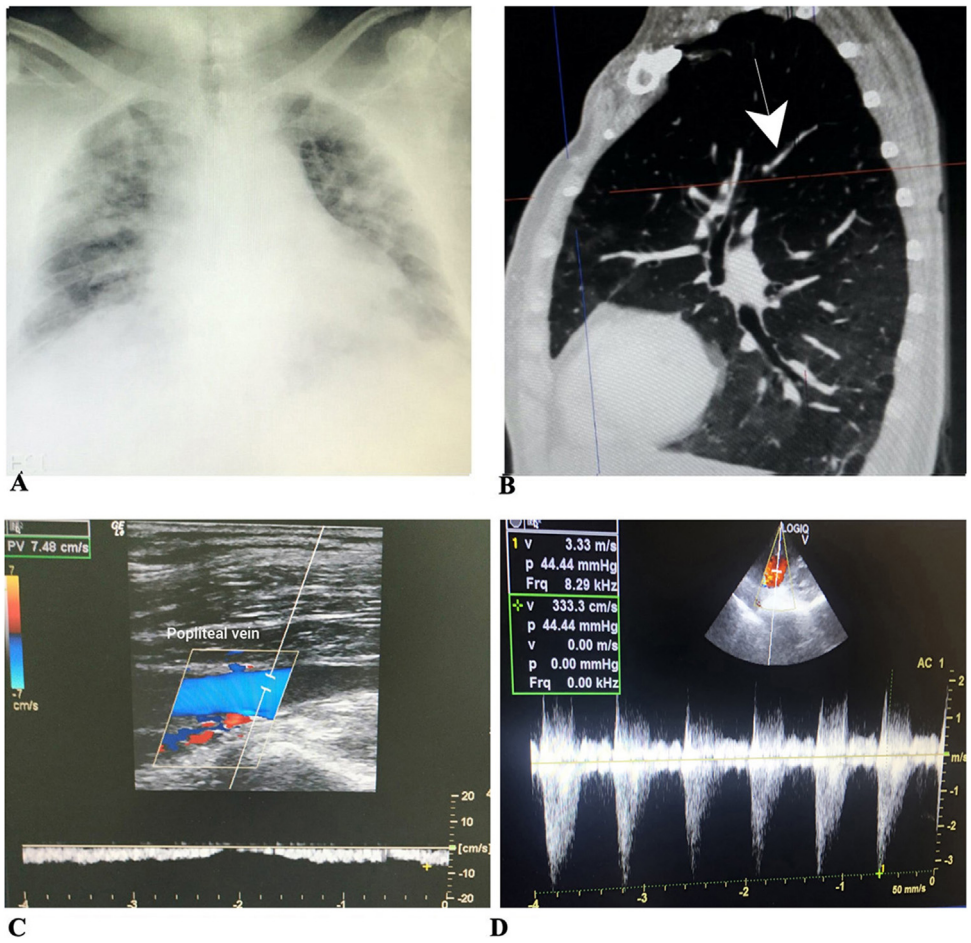

Fig. 1. (A) The chest X-ray on admission showing bilateral consolidations and ground-glass opacifications. (B) The CTPA showing multiple bilateral segmental and subsegmental filling defects. (C) The Color Doppler of lower extremities showing no signs of DVT. (D) The transthoracic Doppler echocardiography revealing increased RVSP (49 mmHg).

tory results showed elevated proinflammatory and prothrombotic markers (Leukocytes 12.83 $\times$ 10^9 /L, Lymphocytes 6.4%, C-reactive-protein 159 mg/L, Ferritin 962 ng/mL, LDH 732 U/L, and D-dimer 5.1 ng/mL), while the chest X-ray revealed bilateral consolidations and ground-glass opacifications (Fig. 1A). Since our patient had an increased risk for PE (current symptoms, comorbidities, and high D-dimer values), on the 2nd day of hospitalization we performed the computed tomography pulmoangiography (CTPA), which detected multiple segmental and subsegmental filling defects (Fig. 1B). The Color Doppler of lower extremities did not show any signs of deep vein thrombosis (DVT) (Fig. 1C), while transthoracic echocardiography revealed a dilated right ventricle (RV: 31 mm) and increased right ventricular systolic pressure (RVSP: 49 mmHg) (Fig. 1D). During the hospitalization of 24 days, out of which 4 days at the ICU, our patient received HFNO, antibiotics, a therapeutic dose of low-molecular-weight heparin, and corticosteroids. After recovery, he was discharged with Apixaban.

Additionally, during the current hospitalization, specific symptoms predictive for OSA were noticed (deep snoring with breathing pauses). He later reported frequent daytime sleepiness and nocturia in the past 2 years. On discharge, according to the previously mentioned symptoms and comorbidities (obesity, hypertension), we conducted an evaluation for OSA using the STOP-BANG Questionnaire [5]. The score was 7/8, and we recommended a sleep study-polygraphy, which was, due to epidemiological situation, performed one month after hospitalization. Our patient was diagnosed with a severe form of OSA (Fig. 2A) (Apnoea-Hypopnoea Index (AHI): 66.3; minimal oxygen saturation was 62%) and increased amount of visceral fat (33.7%) on body density scan (DEXA) (Fig. 2B). He started to use positive airway pressure (PAP) therapy during sleep and was advised for implementing dietetic and hygiene measures.

Discussion

This case emphasizes the importance of a high degree of alertness among physicians for severe COVID-19, particularly in patients with specific comorbidities, such as obesity and OSA.

One recent study demonstrated that among various pre-existing respiratory comorbidities, only OSA was significantly associated with COVID-19 adverse outcomes (ICU admission, need for mechanical ventilation, and mortality) [6]. Furthermore, frequent companions of OSA, such as obesity and hypertension in our case, are also strongly related to severe COVID-19 [3]. However, the relationship between undiagnosed and untreated OSA and adverse outcomes in COVID-19 is lacking, which led some authors to hypothesize even a worse outcome in this patient population [7].

One of the major concerns among severely ill COVID-19 patients is PE. According to the present literature, CTPA-confirmed PE was detected in up to 30% of COVID-19 patients [8]. Even though, the exact mechanism underlying the PE development on the top of COVID-19 has not been elucidated yet. Meanwhile, several pathophysiological mechanisms, including inflammation-mediated overreactivity of the immune system (cytokine storm), were proposed as triggers of the prothrombotic state in COVID-19

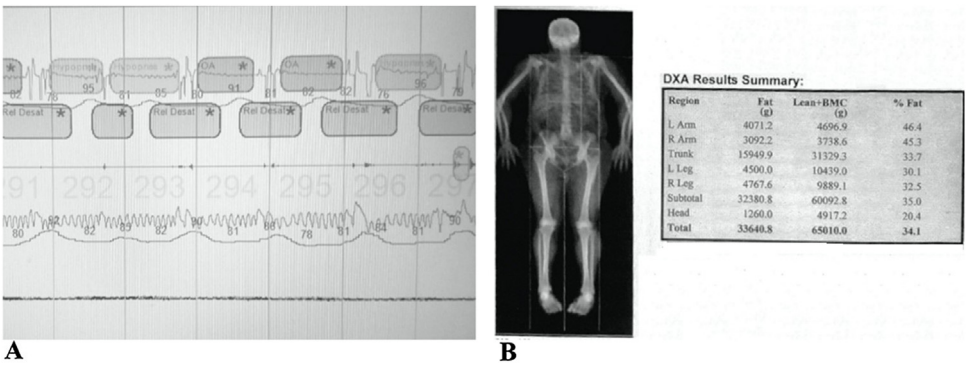

Fig. 2. (A) The polygraphy showing the periods of hypopnea and apnoea, and intermittent hypoxia. (B) The DEXA screening showing increased amount of total and visceral fat.

patients [9]. Also, impaired coagulation process in these patients, reflected by elevated D-dimer values, was associated with disease severity and progression [10]. The pathophysiological aspects of the specific underlying conditions in COVID-19 patients, to some extent, may contribute to this unfavourable profile.

It has been reported that obese COVID-19 subjects (BMI > 30 kg/m^2), as in our case, were at 2.7-fold higher risk for PE [8], which could be related to obesity-mediated hemostatic and coagulation abnormalities observed in COVID-19 patients [11]. Furthermore an excessive accumulation of visceral fat, as in our case, is a known marker of low-grade inflammation, and has been associated with an increased need for ICU treatment and worse COVID-19 clinical presentation [12]. On the other hand, intermittent hypoxia, as a feature of OSA, can also interact with the COVID-19-related endothelial dysfunction and parenchymal impairment, contributing to COVID-19 adverse events [13]. The low-intensity inflammation in obese OSA subjects, followed by elevated proinflammatory cytokines, such as IL-6 and TNF-α, promotes viscosity, raises the levels of clotting factors, leading to increased PE risk [14]. Our patient did not have signs of DVT, and it corresponds to literature reports regarding a huge discrepancy between the PE and DVT occurrence, which also pose a question of whether the occlusion of pulmonary vessels is a consequence of pulmonary thromboembolism or "in situ" thrombosis [15].

The pulmonary thromboembolism, in the majority of patients with severe COVID-19 pulmonary disease, affected the segmental/subsegmental arteries in consolidated lung segments, as in our case, thus some authors postulated a pulmonary thrombosis as a key pathophysiological substrate of pulmonary occlusion, rather than thromboembolism [16]. Moreover, it has been suggested that increased incidence of PE in COVID-19 patients reflects the interaction between endothelial dysfunction and systemic inflammation, resulting in coagulopathy [17], which may serve as an explanation for the very low rate of DVT in these patients. One question remains open, could there be a link between a synergistic effect of OSA, obesity and COVID-19 resulting in PE?

Conclusion

With this case, we aimed to increase the awareness among physicians concerning COVID-19 patients with specific comorbidities, such as obesity and OSA. A timely recognition of OSA is of great importance, especially in obese males who tested positive for COVID-19. The identification of underlying conditions and their possible synergism resulting in the severe form of COVID-19 may improve survival by implementing an adequate preventive and therapeutic strategy in these patients.

Contributions of the authors

Maja Nikolic — writing the manuscript, research of the literature.
Stefan Simovic — supervision, text editing.
Ljiljana Novkovic — supervision.
Vuk Jokovic — supervision.
Danijela Djokovic — supervision, text editing.
Nemanja Muric — text editing, research of the literature.
Danijela Bazic Sretenovic — text editing.
Jovan Jovanovic — text editing.
Katarina Pantic — text editing.
Ivan Cekerevac — supervision.

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Ethical approval and informed consent

Our work has been conducted in accordance with ethical principles (Declaration of Helsinki). The statement of informed consent for publication was obtained from the patient.

Conflict of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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