EPISTAXIS AS A SERIOUS COMPLICATION OF HIGH FLOW NASAL CANNULA

Krwotok z nosa jako poważne powikłanie wysokoprzepływowej tlenoterapii donosowej

Krzysztof Kłos[1], Krzysztof Łukasz Piwowarek[1], Anna Skibińska[1], Artur Maliborski[2], Jerzy Kruszewski[1]

1. *Military Institute of Medicine – National Research Institute, Department of Internal Medicine, Infectious Diseases and Allergology, Poland*
2. *Military Institute of Medicine – National Research Institute, Department of Radiology, Poland*

Abstract

Introduction: High flow nasal cannula is a commonly known therapeutic option for acute respiratory failure in COVID-19 and other lung disorders. Together with non-invasive ventilation, it is a bridging therapy before invasive respiratory support, and often allows to avoid the latter. High flow nasal cannula has a favourable safety profile. However, the purpose of this case report is to draw attention to a rare yet potentially fatal complication of this therapeutic method. **Case report:** The paper describes a 63-year-old Caucasian male admitted to the Department of Infectious Diseases in April 2021 due to the critically severe course of COVID-19 with 90% lung tissue involvement as shown on computed tomography scans. From the beginning, the patient underwent high flow nasal cannula therapy. After 3 days of treatment, he developed massive nasal haemorrhage. Despite an immediate anterior nasal packing, the epistaxis led to rapid respiratory deterioration, which necessitated intubation and invasive ventilation. Cardiac arrest with pulseless electrical activity occurred in spite of measures taken. **Discussion:** The patient died after unsuccessful resuscitation. The risk of epistaxis, which may result in a critical deterioration of patient's respiratory capacity, must be taken into account when high flow nasal cannula is implemented. **Conclusions:** In view of increasing popularity of the discussed therapeutic method, there is an urgent need for cohort studies in order to assess risk factors and proper preventive measures in epistaxis resulting from the use of high flow nasal cannula.

Streszczenie

Wstęp: Wysokoprzepływowa tlenoterapia donosowa jest obecnie powszechnie stosowaną metodą leczenia ostrej niewydolności oddechowej w przebiegu COVID-19 i innych chorób płuc. Wraz z nieinwazyjną wentylacją mechaniczną stanowi ona leczenie pomostowe przed wdrożeniem respiratoroterapii inwazyjnej, częstokroć pozwalając na jej uniknięcie. Wysokoprzepływowa tlenoterapia donosowa cechuje się korzystnym profilem bezpieczeństwa. Prezentacja niniejszego przypadku ma jednak na celu zwrócenie uwagi na rzadkie, ale potencjalnie śmiertelne powikłanie tej metody terapeutycznej. **Opis przypadku:** W pracy przedstawiono opis przypadku 63-letniego mężczyzny rasy białej hospitalizowanego w oddziale chorób infekcyjnych w kwietniu 2021 roku z powodu krytycznie ciężkiego przebiegu COVID-19 z zajęciem 90% tkanki płuc w obrazach tomografii komputerowej. Od początku pobytu w Klinice u chorego stosowano wysokoprzepływową tlenoterapię donosową. Po trzech dniach leczenia doszło u niego do masywnego krwotoku z jam nosa, który pomimo niezwłocznego założenia tamponady przedniej doprowadził do gwałtownej dekompensacji oddechowej wymagającej intubacji i włączenia respiratoroterapii. Mimo podjętych działań doszło do zatrzymania krążenia w mechanizmie czynności elektrycznej bez tętna. **Omówienie:** Po nieskutecznej resuscytacji pacjent zmarł. Podczas stosowania wysokoprzepływowej tlenoterapii donosowej należy zatem uwzględnić ryzyko wystąpienia krwotoku z jam nosa, mogącego skutkować krytycznym pogorszeniem wydolności oddechowej. **Wnioski:** Z uwagi na rosnącą popularność omawianej metody terapeutycznej konieczne są badania kohortowe mające na celu ocenę czynników ryzyka wystąpienia krwotoku z nosa, a także sposobów zapobiegania temu poważnemu powikłaniu.

Keywords: epistaxis; pneumonia; COVID-19; nasal cannula

Słowa kluczowe: krwawienie z nosa; zapalenie płuc; COVID-19; tlenoterapia donosowa

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Corresponding author:
Krzysztof Łukasz Piwowarek
Military Institute of Medicine – National Research Institute, Department of Internal Medicine, Infectious Diseases and Allergology, 128 Szaserów St.,
04-141 Warsaw
e-mail: kpiwowarek@wim.mil.pl

Introduction

The COVID-19 pandemic has given rise to a huge demand for techniques utilised in the treatment of acute respiratory failure, including mechanical ventilation. The limited capacity of healthcare systems in terms of ventilator sites and the unsatisfactory outcomes of this therapeutic approach have forced the search for new bridging therapies. The goal in this case is to postpone (or ideally avoid) the need for invasive ventilator therapy with all its known complications for as long as possible. The pandemic situation has given rise to the widespread use of non-invasive ventilation (NIV) and high-flow nasal cannula (HFNC). Although the latter technique was a particular novelty in the Polish healthcare system, its relatively easy use encouraged its utilisation even under pandemic conditions. HFNC allows for an intranasal delivery of a gas mixture heated to body temperature with fiO_2 up to 1.0 and humidity up to 100%. Depending on the manufacturer, the maximum flow rate ranges from 60 to 80 L/min. The mechanism of this therapeutic method consists in: 1) reducing dead space in the upper airways; 2) increasing the dynamic pressure in the airways; 3) reducing the metabolic cost of breathing and improving mucociliary clearance; 4) preventing bronchial obstruction in response to cold. The first two effects depend on the set flow rate, while the third and fourth result from the optimal physicochemical parameters of the respiratory mixture [1, 2].

In pre-pandemic times, hypoxemic respiratory failure was the main indication for HFNC. Although this method can be also used in hypercapnic respiratory failure, it is advisable to first attempt NIV in such cases, as in line with the current recommendations of the European Respiratory Society (ERS) [3].

HFNC is also recommended in patients:
- after extubation (postoperative in particular);
- as part of oxygenation before intubation;
- during NIV intervals;
- in the treatment of acute heart failure;
- in perioperative oxygen therapy during bronchofiberoscopy.

Treatment of severe respiratory failure in patients with contraindications to mechanical ventilation (do not intubate, DNI) is an important indication, the role of which has significantly increased during the COVID-19 pandemic [4].

Complications of HFNC, such as barotrauma, gastric distension, aspiration of secretions, or epistaxis, seem to be relatively rare in both adults and children. So far, they have not been considered a significant therapeutic problem; however, some cases had been reported even before the COVID-19 pandemic [5]. The literature estimates that 0.6–10% of patients develop epistaxis during HFNC therapy; however, the authors emphasise that these were retrospective case studies without randomisation [6, 7]. These reports concerned patients treated in intensive care units (ICUs) for reasons other than COVID-19.

This paper presents a case of a 63-year-old man hospitalised in the Department of Infectious Diseases in April 2021 due to a critically severe course of COVID-19, with 90% lung tissue involvement in computed tomography (CT). The patient was treated with HFNC due to acute hypoxemic respiratory failure, and developed severe nasal bleeding during treatment.

Case report

A 63-year-old man was admitted to the Department of Infectious Diseases as an emergency due to respiratory failure and pneumonia in the course of COVID-19. The patient was on chronic treatment for hypertension and type 2 diabetes mellitus (T2DM). He received amlodipine 10 mg/day, indapamide 1.5 mg/day, telmisartan 80 mg/day and metformin 1000 mg/day. He also reported a history of an episode of atrial fibrillation years ago, but he was not on anticoagulation, and he had no documentation to confirm arrhythmia. He denied chronic upper respiratory tract diseases and laryngological interventions. He did not report epistaxis in the past. On taking medical history, the patient complained of severe general weakness and muscle pain from a week before admission. Therefore, an outpatient antigen test for SARS-CoV-2 was performed, which was inconclusive. Also, he had developed dyspnoea two days before admission. Epidemiological history revealed exposure to a person infected with SARS-CoV-2 at work.

On the day of admission, the emergency medical service called by the patient found severe respiratory failure, with 67% saturation while breathing atmospheric air. After applying an oxygen mask with a reservoir bag, with an oxygen flow of 15 L/min, saturation increased only to 91%. During diagnosis at the Hospital Emergency Department, chest CT showed massive interstitial densities manifesting as ground-glass opacification in both lungs, with thickening of the interlobular septa, minor parenchymal consolidations and band-like densities, including subpleural bands, as well as bronchiectasis – COVID-19 CT score of 23/25 and CO-RADS 5. Additionally, a subpleural nodule of 7 × 6 mm in size, an enlarged heart, a hypodense focus of 6 × 3 mm in the left thyroid lobe, as well as a hiatal hernia of the diaphragm and signs of fatty liver were described (fig. 1).

The patient was in serious condition on admission to the ward. Physical examination revealed signs of respiratory failure and obesity (body weight about 115 kg and height 180 cm). Electrocardiogram showed regular sinus rhythm. Laboratory tests revealed significantly elevated C-reactive protein (CRP) and ferritin, neutrophilia with lymphopenia, hyperglycaemia, mild hypernatremia and a moderately increased transaminase activity. IL-6 was also elevated (297.6 pg/mL; reference range 0–150 pg/mL). The coagulation profile did not show any significant abnormalities during hospital stay, with aPTT of 27.5 s (reference range 23–35 s), Quick index of 88% (reference range 80–120%), and D-dimers of 0.6 µg/ml (reference range 0–0.5 µg/mL). Genetic testing with reverse transcription polymerase chain reaction (RT-PCR) confirmed SARS-CoV-2 infection.

Antiviral therapy with remdesivir at a dose given in the SmPC, parenteral broad-spectrum antibiotic therapy with ceftriaxone at a dose of 2000 mg/day with clarithromycin 1000 mg/day, as well as enoxaparin at an interme-

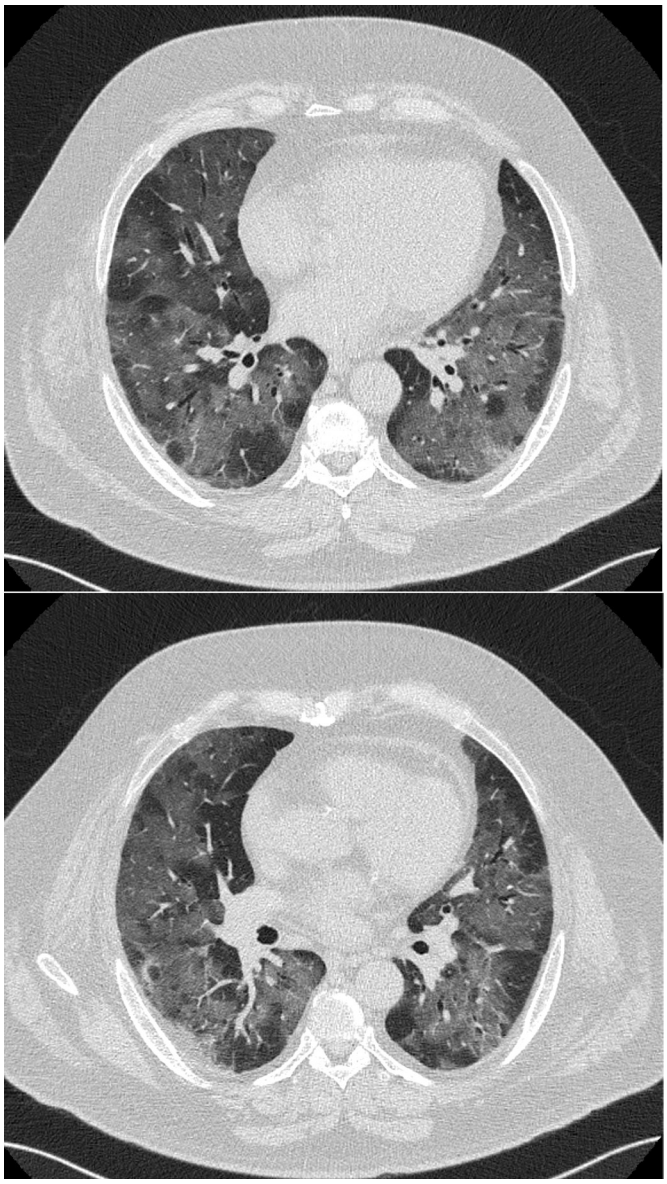

Figure 1. Massive interstitial ground glass opacities, with thickened interlobular septa and small peripheral parenchymal consolidations

diate dose of 60 mg/day, anti-inflammatory dexamethasone 8 mg/day, and fluid therapy were started. Two units of convalescent plasma were transfused. Insulin therapy, as well as medications that the patient was taking regularly, except for metformin, were included.

The patient was undergoing oxygen therapy on admission, with a flow of 15 L/min using a face mask with a reservoir bag. Despite these measures, desaturation below 90% occurred. Due to the increasing hypoxemic respiratory failure, it was considered advisable to initiate HFNC. Nasal oxygen cannulas (NAC) were fitted to the patient's anatomy (1L, size L; fig. 2) and the therapy was implemented using the Respircare Hifent HUMID-BH system (Shenyang RMS Maisi Medical Technology Co., Ltd., China), with flows of 60-80 L/min, fiO_2 approx. 0.95 and a temperature of the gas mixture of 37°C (fig. 3).

On day 4 of hospital stay, in the evening, the patient developed massive nasal haemorrhage, which was ini-

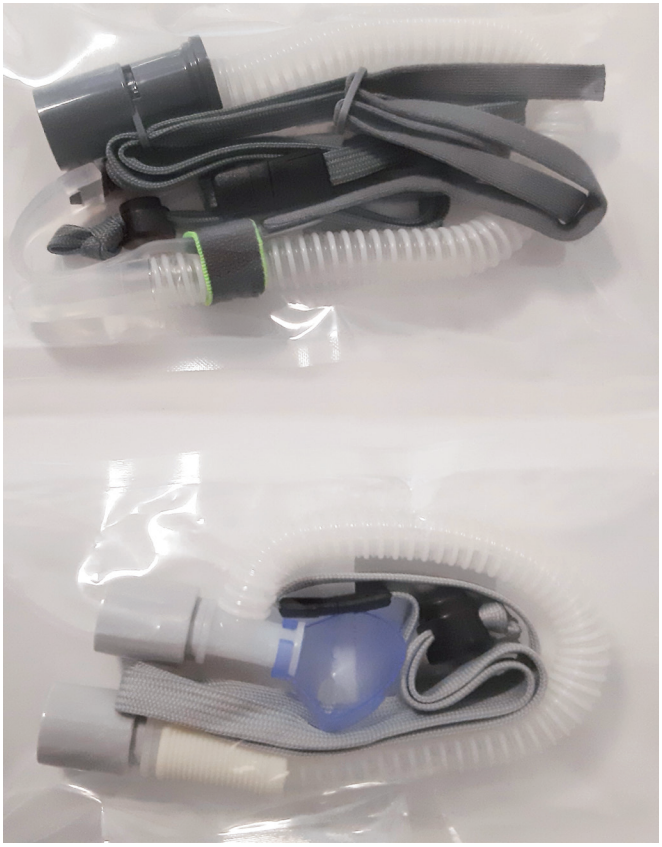

Figure 2. Nasal cannulas of various sizes used during high-flow nasal cannula therapy

Figure 3. System for high-flow nasal cannula therapy

tially controlled locally with intranasal packing with epinephrine and etamsylate, prepared *ex tempore*, using Adrenalina WZF 0.1% (Polfa Warszawa SA, Poland) and Cyclonamine 12.5% (FSP "Galena", Poland), respectively. However, the subsequent deterioration of the patient's respiratory function and desaturation of up to 85% in pulse oximetry indicated that HFNC was considered insufficient. A bridging attempt was made to apply continuous positive airway pressure (CPAP) using the Trilogy Evo device (Philips, USA) and a full-face mask with fiO_2 = 1.0 and positive end expiratory pressure (PEEP) of 10 cm H_2O. Satisfactory saturation values of 91–92% were achieved, but the patient reported mask intolerance. Additionally, the patient's blowing of cold compresses and clots from the nasal cavities led to bleeding recurrence. An otorhinolaryngologist was called in and applied an anterior nasal packing to both nasal cavities, which effectively controlled the bleeding. However, he was unable to determine the site of bleeding due to the rapidly deteriorating condition of the patient.

At the same time, due to the exhaustion of non-invasive treatment options for respiratory failure, an anaesthesiologist was called in to intubate the patient and initiate mechanical ventilation (Puritan Bennett, USA). Despite the suction of blood clots from the respiratory tract and optimisation of the ventilator settings, hypoxia rapidly increased, with electrocardiography showing increasing Pardee waves as a manifestation of type 2 myocardial infarction. Soon, a sudden cardiac arrest occurred in the mechanism of pulseless electrical activity (PEA). Resuscitation was initiated in accordance with the current protocol of the Polish Resuscitation Council [8]. Despite measures taken, the rhythm went into permanent asystole and finally, after unsuccessful resuscitation, the patient was pronounced dead.

Discussion

Patients with SARS-CoV-2 infection are a specific group frequently presenting with coagulopathy. Although it usually manifests with higher rates of thromboembolic events, an increased tendency to haemorrhages, including epistaxis, has also been described [9–12]. The aetiology may be both systemic and local. The first group includes the use of coagulation factors and the impact of anticoagulant therapy, i.e. low-molecular-weight heparins, routinely used in COVID-19. This has been confirmed in a case series by Dell'Era et al. [13]. The authors emphasise that prolonged oxygenation with a nasal cannula contributes to increased nasal dryness and is a risk factor for crusting, which weakens the nasal mucosa, exposing patients to nasal haemorrhages.

Interestingly, the coagulation profile did not show any significant deviations from the norm in the discussed case. However, given the anticoagulant treatment with low-molecular-weight heparin used during hospital stay, it is difficult not to consider its potential impact on the occurrence of bleeding. In turn, the inflammation of the nasal mucosa associated with a viral infection, which also seems to be the cause of damage to the olfactory nerve endings and anosmia, may have been a local factor in this case [14, 15]. Therefore, even in the absence of obvious rhinological problems, there may be a tendency to bleed from the submucosal plexuses.

It therefore seems that both systemic and local factors played an important role in the presented case. Their overlap had a dramatic effect on the patient, as the bleeding into the upper respiratory tract irreversibly deteriorated arterial blood oxygenation. It is worth noting that the patient's respiratory reserve was critically low due to 90% lung involvement.

Current international guidelines for the management of sepsis recommend the use of NIV or HFNC in patients with severe hypoxia requiring non-invasive oxygen therapy to avoid complications of intubation. The authors emphasise that self-limiting complications associated with HFNC are possible, but usually do not require treatment discontinuation [16].

Although there are no absolute contraindications to HFNC, its use should be carefully considered in patients with impaired consciousness, as measured with the Glasgow Coma Scale, reduced upper airway reflexes, claustrophobia, risk of aspiration, unstable hemodynamics or epistaxis [1, 2]. However, in the case discussed, it was the HFNC therapy itself, overlapping with the above-mentioned coexisting local and systemic factors, that may have contributed to the bleeding.

Conclusions

When using HFNC, the risk of epistaxis should be taken into account as it may lead to a critical deterioration of respiratory function in the patient. Due to the growing popularity of this treatment approach, cohort studies are needed to assess the risk factors for epistaxis, as well as methods to prevent this serious complication.

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