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Oropharyngeal hemorrhage in patients with COVID-19: A multi-institutional case series

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ABSTRACT

Background: Patients with COVID-19 who are intubated and require mechanical ventilation have been observed to have oropharyngeal bleeding necessitating otolaryngology intervention.
Methods: We report five cases of oropharyngeal hemorrhage in COVID-19 patients on mechanical ventilation requiring evaluation by otolaryngologists at George Washington University Hospital (GWUH) and Boston Medical Center (BMC) from March to April 2020. Institutional Review Board at both institutions exempted this study from informed consent because there were no identifiable patient characteristics, photographs, or imaging studies included.
Results: All five patients were managed conservatively; four required packing with Kerlix gauze by an otolaryngologist. Two patients had the additional requirement of extracorporeal membrane oxygenation (ECMO) and associated anticoagulation. Three patients improved with oropharyngeal packing; two had persistent bleeding. Three patients expired. Endotracheal tubes were repositioned less frequently due to the COVID-19 pandemic.
Conclusions: Intubated patients with COVID-19 may have an increased risk of oropharyngeal hemorrhage. This may be due to anticoagulation, prolonged intubation, or decreased frequency of endotracheal tube repositioning. Otolaryngologists should wear appropriate PPE when managing this hemorrhagic complication.

1. Introduction

SARS-CoV-2 is a novel coronavirus that causes Coronavirus Disease (COVID-19), which has disseminated rapidly worldwide [1]. The major morbidity and mortality associated with this virus is acute viral pneumonia leading to acute respiratory distress syndrome (ARDS). Approximately 20% of individuals with COVID-19 will develop severe respiratory disease and require hospitalization. Among those individuals, 25% require intensive care management and mechanical ventilation [1]. Emerging evidence suggests that anticoagulation in COVID-19 patients improves survival and decreases the high incidence of venous thromboembolism observed in these patients [2,3]. Additionally, COVID-19 patients often require vasopressor administration. These factors may result in increased risk of hemorrhagic complications, such as oropharyngeal bleeding. At our institutions, we have observed an increase in this complication since the beginning of the COVID-19 pandemic.

This case series describes the clinical course of five SARS-CoV-2-infected patients on mechanical ventilation with oropharyngeal bleeding who required management by otolaryngologists. Institutional Review Board at both institutions exempted this study from informed consent because there were no identifiable patient characteristics, photographs, or imaging studies included.

2. Case reports

2.1. Case 1 (BMC)

An 87-year old female presented with ARDS secondary to COVID-19 and was intubated with a 7.0 endotracheal tube (ETT). On hospital day (HD) 11, she developed acute kidney failure and was started on continuous renal replacement therapy (CRRT). Thereafter she developed

Abbreviations: BMC, Boston Medical Center; GWUH, George Washington University Hospital; HD, hospital day

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oral bleeding and large clots were removed from the oropharynx and the ventilator circuit. Evaluation by otolaryngologists found clots in the oral cavity and oropharynx, but no bleeding source. The otolaryngologist packed her oral cavity and pharynx with saline-soaked Kerlix gauze and she was started on antibiotic prophylaxis. Her hemoglobin (Hgb) decreased to 6.4 mg/dL and she was transfused with 1 unit (U) of packed red blood cells (pRBCs). Kerlix gauze packing was removed on HD 15 without further bleeding. Thereafter, she was extubated and remains in critical condition, but without further bleeding or ventilatory support.

2.2. Case 2 (BMC)

A 65-year-old male was admitted with COVID-19. On HD 5, he developed ARDS and was intubated with an 8.0 ETT and placed on mechanical ventilation. On HD 7, his Hgb decreased from 12 mg/dL to 8 mg/dL without bleeding source identified on physical exam. On HD 9, blood clot was suctioned from floor of the mouth and oropharynx. The otolaryngology service packed his oral cavity and pharynx with Kerlix gauze. Aspirin was discontinued though he continued on subcutaneous heparin. Due to saturation of the gauze packing, it was removed on HD 10 and there were clots in the oral and nasal cavities. No source of bleeding was identified. Kerlix gauze packing was replaced and CT angiogram demonstrated a contrast blush along the superior margin of the packing and near the left palatine tonsil, indicating extravasation. Desmopressin was given for uremic platelets and declining Hgb (9.3➔8.3 mg/dL). On HD 12, he began CRRT due to acute kidney failure and started on heparin gtt. On HD 13, oral packing was removed with no clots appreciated and the ETT was replaced due to mucous clogging the tube. On HD 14, oral bloody secretions were observed with a decrease in Hgb (7.7➔ 6.7 mg/dL) and he was given 1 U of pRBCs. The ETT tube was changed on HD 15 due to variable tidal volumes. He remained intubated and in critical condition with intermittent oropharyngeal bleeding that did not require additional otolaryngology intervention. He developed multi-system organ failure and expired on HD 31.

2.3. Case 3 (BMC)

A 66-year-old female presented with ARDS secondary to COVID-19 and was intubated with a 7.5 ETT. On HD 6, she had a prolonged partial thromboplastin time (PTT) (139–170) and was transfused with 2 U of fresh frozen plasma (FFP). She additionally developed acute kidney failure and began CRRT. On HD 7, she had copious blood in her oral cavity. On exam, a posterolateral tongue ulceration was identified adjacent to the ETT. The otolaryngology service packed the oral cavity and pharynx with Kerlix gauze. Another unit of FFP was given while heparin and aspirin were held. Substantial bleeding persisted despite packing and she required transfusion of 1 U pRBC and 2 U of FFP. Bleeding resolved on HD 9 and packing was removed. Her respiratory condition deteriorated and she expired on HD 12.

2.4. Case 4 (GWUH)

A 44-year-old male developed ARDS secondary to COVID-19 and was intubated with a 7.5 ETT at an outside hospital (OSH). He was transferred to GWUH for extracorporeal membrane oxygenation (ECMO). On HD 1, the patient was placed on veno-venous (VV) ECMO and started on anticoagulation (heparin gtt transitioned to bivalirudin). On HD 7, bivalirudin dose was increased for sub-therapeutic PTT and his activated coagulation time (ACT) goal was increased to 180–200. The patient subsequently developed bleeding from bilateral nares and oral cavity on HD 6. The ICU team superficially packed his oral and nasal cavities with gauze, held bivalirudin, and started antibiotic prophylaxis. Upon otolaryngology evaluation on HD 8, the patient was not bleeding around packing. No further intervention was performed due to concern for clot destabilization and manipulation of mucosal membranes. His bivalirudin gtt was resumed at a lower dosage, oral packing was removed on HD 11, and bleeding resolved. On HD 15 the patient was started on vasopressin. The patient had another limited oropharyngeal bleed that did not require additional otolaryngology intervention. On HD 21, he developed a rectal bleed (possibly related to prolonged use of rectal tube), requiring rectal packing and embolization by interventional radiology. He remains on ECMO, currently HD 28.

2.5. Case 5 (GWUH)

A 62-year-old female presented for ECMO evaluation due to severe ARDS secondary to COVID-19. She was intubated at the OSH with a 7.5 ETT but was re-intubated with an 8.0 ETT due to cuff leak. On HD 1, she developed acute kidney failure and started on CRRT. She was placed on VV ECMO and started on epinephrine and heparin gtts. Heparin was switched to bivalirudin while on ECMO in order to maintain her ACT goal of 180–200. On HD 8, she developed bleeding from her oral cavity and bilateral nares. Hemoglobin dropped from 7.8 mg/dL to 5.5 mg/dL, requiring 2 U pRBCs and 1 U of platelets. The ICU team placed superficial oral and nasal gauze packing and started antibiotic prophylaxis. Otolaryngology was consulted on HD 9 for persistent bleeding. The packing was removed and each nare was packed with 8 cm Merocel nasal packs. The superficial oral pack was removed, multiple clots were suctioned, and a small ventral tongue abrasion was visualized. Saline-soaked Kerlix gauze was tightly packed into her oral cavity and pharynx. Despite these interventions, the patient experienced persistent bleeding requiring multiple transfusions of pRBCs and platelets. Due to multi-system organ failure, the family and ICU team decided to withdraw supportive care and the patient expired on HD 11.

3. Discussion

We report a case series of five patients at two tertiary care institutions with ARDS secondary to COVID-19, who developed upper aerodigestive (oral cavity, oropharyngeal, nasal) bleeding. All patients had some anticoagulation with bilvarudin, heparin and/or aspirin, and required vasopressor administration at a time point prior to bleeding (Table 1).

The increased incidence of oropharyngeal hemorrhage is likely multifactorial in these patients. Patients are intubated for prolonged periods of time and may be at increased risk for injury from ETT. Medical device-related pressure ulcers (MDRPU) are defined as localized tissue damage from the prolonged, unrelieved pressure from a

Table 1
Patient characteristics and relevant factors related to intubation and bleeding risk.[a]

Case	Sex	Age (years)	BMI (kg/m^2)	ETT size (mm)	Days after intubation to bleed	Vasopressor administration	Anticoagulation therapy
1	F	87	42.33	7	11	NE, DDAVP	ASA, heparin
2	M	65	24.38	8	4	NE, DDAVP	ASA, heparin
3	F	66	44.38	7.5	7	NE, DDAVP	ASA, heparin
4	M	44	29.25	7.5	7	NE, vasopressin	Bivalirudin, heparin
5	F	62	48.62	7.5, 8.0	9	NE, epinephrine	Bivalirudin, heparin

[a] BMI, body mass index; ETT, endotracheal tube; NE, norepinephrine; DDAVP, desmopressin; ASA, aspirin.

medical device [4]. The incidence of ETT-associated MDRPUs among surgical and ICU patients ranges from 7% to 45% [4]. The time points at which pressure ETT-associated ulcers become clinically visible are variable and patient-dependent with a range of 2–13 days [5]. Protocols for prevention of ETT-caused pressure ulcers include risk assessment, routine ETT repositioning in the mouth, and cushioning skin areas in contact with the ETT [5]. Some manufacturers recommend repositioning every 2 h and this is the standard of care at our institutions under normal circumstances [6].

However, the SARS-CoV-2 pandemic has led to a shift from traditional airway management protocols in an effort to protect healthcare workers and minimize transmission as multiple studies have demonstrated that manipulation of mucosal surfaces leads to aerosolization and dissemination of the virus [7–9]. Nurses report prolonged intervals between repositioning and manipulation of the ETT. Also, clinicians are performing laryngoscopy less often, making it difficult to find and repair the source of ETT-associated bleeding [10].

The requirement for vasopressor and anticoagulation therapy leads to an increased risk of oropharyngeal hemorrhage in this cohort [11]. For patients requiring ECMO, hemorrhagic complications occur in up to 45% of patients [12] and the incidence of oropharyngeal bleeding is as high as 30% [13]. One case series observed an oropharyngeal bleed rate of 42% in patients with ARDS secondary to H1N1 [14]. There are many reasons for this, including anticoagulation therapy, increased ACT goals, thrombocytopenia and platelet dysfunction, among others [15–17]. Patients on ECMO and CRRT often require additional anticoagulation to prevent clots in the circuits [18]. Bleeding presents a unique challenge in patients with COVID-19 on ECMO, given the anticoagulation requirements, as well as concern for mucosal manipulation or ventilator circuit disruption.

Emerging literature suggests that anticoagulation therapy improves survival in patients with COVID-19 [2,3]. A recent study from the Icahn School of Medicine at Mount Sinai in New York City demonstrated that in-hospital mortality for patients requiring mechanical ventilation was significantly decreased among those who received anticoagulation therapy (29% vs. 63%). There was a small increase in hemorrhagic complications in the anticoagulation group, though not statistically significant [3]. As such, we anticipate an increase in the number of patients on mechanical ventilation treated with anticoagulation and the potential increase in hemorrhagic complications.

Management of these individuals during the COVID-19 pandemic requires careful consideration. Any manipulation of the aerodigestive tract, including packing and suctioning, increases risk of viral aerosolization and requires enhanced personal protective equipment (PPE), including N95 respirators and/or powered air-purifying respirators (PAPRs) [19]. Given this risk, conservative management with saline-soaked Kerlix gauze packing (with proper PPE) was selected for treatment of oropharyngeal hemorrhage. This was sufficient in reducing or eliminating bleeding in three of five patients reported without requiring additional manipulation of mucosal membranes. Therefore, we recommend this conservative approach as an initial step in management of oropharyngeal hemorrhage in patients with COVID-19. Health care teams should continue to follow existing guidelines for airway management [20] without compromising COVID-19-specific safety precautions [10].

Declaration of competing interest

None.

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