

## Propofol infusion syndrome & COVID-19 in a victim of multiple gunshot wounds: Diagnostic and therapeutic dilemmas

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### ABSTRACT

**Background:** COVID-19 has become a global pandemic. It has affected patients the world over, and when minimally symptomatic, it can be an incidental finding in trauma patients. It may also make the diagnosis of other rare conditions more difficult due to clinical finding superimposition.

**Case presentation:** A 23-year-old male was transferred to our Trauma Center in hemorrhagic shock after sustaining multiple gunshot wounds in the upper back. Imaging showed a retained projectile in the right pharyngeal area, a right upper lobe contusion, and a right hemopneumothorax; with additional infiltrates on both lungs suggestive of atelectasis. After intubation, a propofol infusion was started for sedation. Shortly thereafter worsening acidosis, refractory hypoxia, and hypotension with additional laboratory anomalies ensued, as the PCR screening for SARS-CoV-2 returned positive. The clinical findings suggested COVID-19 pneumonia with possible superimposed Propofol Infusion Syndrome. The drug was stopped, and the symptoms improved.

**Conclusion:** A high index of suspicion is necessary to manage unusual pathologies and difficult differential diagnoses, and this is especially true during the ongoing pandemic.

### Introduction

In December 2019, coronavirus disease-19 (COVID19) caused by the novel severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) emerged, and by March 2020 was declared a global pandemic. While COVID19 can cause systemic infection, the lungs are considered the primary affected organ resulting in diffuse alveolar damage causing respiratory insufficiency with possible progression to pulmonary fibrosis. People with COVID19 may also be asymptomatic carriers and the disease may be first detected on thoracic imaging as an incidental comorbidity during workup and treatment of a traumatic injury.

Studies have shown an increase in the number of gunshot wounds during the COVID19 pandemic, which has been attributed to both an increase in firearm purchases and behavioral changes secondary to social isolation, economic loss, and decreased access to non-emergent health treatment [1]. Trauma patients arriving with otherwise clear injury mechanisms that match the clinical findings might carry otherwise asymptomatic SARS-CoV-2 infection, which might complicate the diagnosis of rare conditions such as Propofol Infusion Syndrome. The following case exemplifies the type of diagnostic and therapeutic dilemmas that surgical intensivists might experience during the pandemic.

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## Case report

A 23-year-old male with no significant past medical history presented to our regional Trauma Center after sustaining two gunshot wounds to the back. He was transferred from a neighboring hospital where he received three units of blood, the medial bullet fragment was removed, and a chest tube was placed due to pneumothorax prior to transport. During the Primary Survey, he was alert, hemodynamically stable, and complained of right tonsil pain, shortness of breath, and chest pain. Exam showed a right-sided chest tube, right-sided neck swelling, gunshot wounds to the right scapula and mid-back and normal breath sounds bilaterally. CT angiography of the chest, abdomen, and pelvis revealed patchy pulmonary opacities throughout both lungs and a single dense parenchymal hematoma in the right upper lobe (Fig. 1). One bullet tract could be traced traversing and fracturing the medial right scapular body. The second bullet tract was visualized traveling superiorly and medially injuring the soft tissues of the neck and resulting in significant mass effect. CT angiography of the head and neck showed the projectile was located within the right parapharyngeal space adjacent to the oropharynx with associated moderate hemorrhage resulting in significant compression and deviation of the oropharyngeal airway (Fig. 2).

The patient was intubated for airway protection due to concerns for compression. A propofol (Diprivan, Fresenius Kabi USA LLC, Lake Zurich IL) infusion was started at 20 $\mu$ g/kg/min with a titration of 5–10  $\mu$ g/kg/min every 5 min as needed. Following intubation, the right external carotid artery was occluded after the origin of the superior thyroid, lingual, ascending pharyngeal and facial branches with no identifiable active contrast extravasation. After three hours of the infusion, the patient developed hypoxia, elevated ventilatory pressures, hyperkalemia, acidosis, increasing creatinine, increased CK, and hypertriglyceridemia. Repeat CT of the head, chest, abdomen, and pelvis was performed due to hypotension nonresponsive to fluid resuscitation. The chest showed extensive airspace disease increased from previous imaging, but no ongoing bleeding or extravasation could be identified. The patient was started on norepinephrine (Levophed, Hospira, Lake Forest IL) and received 2 units of packed red blood cells with an improvement in blood pressure. PCR testing ordered upon arrival to the SICU returned positive at that time. Blood gas analysis confirmed respiratory acidosis and hypoxemia and the patient was diagnosed with acute hypoxic respiratory failure and pneumonia secondary to COVID19. Remdesivir (Veklury, Gilead Pharmaceutical, Foster City CA) and Decadron (dexamethasone sodium phosphate USP) were started for treatment of COVID19; and after careful consideration, Propofol was discontinued and midazolam (Versed, Hospira, Lake Forest IL) was started for sedation. The hyperkalemia, acidosis, and increased creatinine improved one hour after discontinuation and normalized after 12 h.

The patient was evaluated by Otolaryngology and no acute intervention was deemed necessary for the bullet fragment in the parapharyngeal soft tissues as no mucosal surfaces were disrupted. Approximately 48 h after being admitted to the hospital the patient self-extubated and was maintained with bilevel positive airway pressure. His pneumothorax resolved and the chest tube was removed. The right neck swelling was managed conservatively with airway protection and pain medications. Repeat thoracic radiographs showed continued improvement of the bilateral patchy ground glass opacities. The patient continued to improve clinically and was discharged after a total of 6 days in the hospital. He has since been lost to follow-up.

## Discussion

Propofol infusion syndrome (PIS) is a rare complication of propofol administration with risk factors including high dose infusion (>4 mg/kg/day or 67 $\mu$ g/kg/min) for a prolonged period (>48 h), critical illness of respiratory or central nervous system origin, use of vasopressors and glucocorticoids and carbohydrate depletion [4,5]. Clinical features of PIS include metabolic acidosis, acute kidney injury, rhabdomyolysis, hypotension, bradycardia, ventricular tachycardia or fibrillation, asystole, hyperkalemia, hyperlipidemia, and hepatomegaly [6]. The patient in this current report did develop acidosis, increased creatinine, hyperkalemia, and elevated CK after

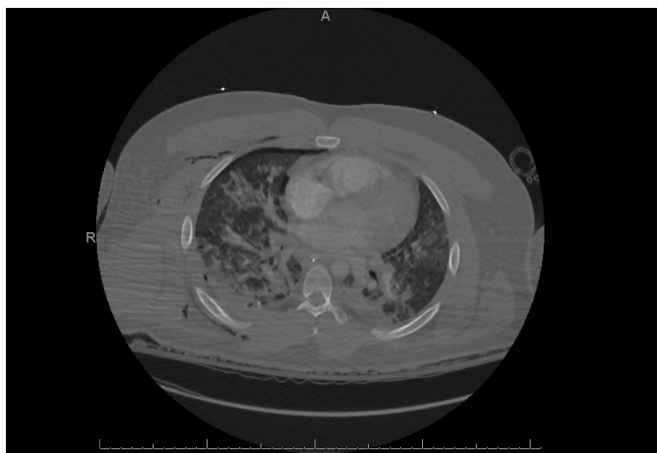


Fig. 1. CT angiography of the chest showing extensive airspace disease with patchy interstitial infiltrates.



**Fig. 2.** CT angiography of the head and neck. The bullet can be visualized within the right parapharyngeal space with surrounding soft tissue swelling and edema resulting in deviation of the trachea.

the initiation of a propofol infusion, and these abnormalities resolved shortly after discontinuation of the infusion which supports a likely reaction to propofol (although the patient did not develop bradycardia and had been on a low dose for a short period).

Blood loss and changes secondary to his traumatic injuries were also a consideration as his hypotension improved after a transfusion and the use of pressors however no source of bleeding could be found. The pulmonary changes were initially thought to be due to atelectasis and contusions secondary to trauma; however, in retrospect the findings were better explained as a result of his viral pneumonia.

Trauma patients commonly have CT scans shortly after presenting to the emergency department to fully assess the extent of their wounds while labwork and COVID19 results may take hours to return. Chest CT has been shown to have a high sensitivity when compared to real-time PCR (97 %) for the diagnosis of COVID19 [2]. The most common finding with COVID19 pneumonia is bilateral ground glass opacity, multifocal, round, with lower lobe and peripheral predominance [3]. Atelectasis and lung consolidation can occur secondary to thoracic lesions such as pneumothorax and pleural effusion and may look similar to COVID19 infection. Patients may also have COVID19 pneumonia in addition to other pulmonary problems. In epidemic areas, suspicion of COVID19 should be a consideration based on chest CT results. Radiologists can then inform providers quickly so they may utilize the appropriate isolation precautions and initiate therapy in a timely manner.

Patients with COVID19 that require mechanical ventilation often require deep and prolonged sedation, and propofol is commonly used. PIS is not well understood and clinical features can overlap with those of COVID19 infection making diagnosis challenging. The reported mortality rate for PIS ranges from 18 % to 48 % and prompt recognition and intervention is important [6,7]. A retrospective study on the safety of continuous infusion propofol in mechanically ventilated adults with COVID19 found a 3.2 % incidence of possible PIS with a 7-day mortality rate of 25 % in patients with a creatine kinase level  $\geq$  5000 U/L [8]. PIS in the patient in this case study was initially suspected based on the acute development of metabolic acidosis, hyperkalemia and increased creatinine. Monitoring for multi-organ involvement along with CK may help with early detection and intervention. Given the high mortality rate, considerations should be made for alternative hypnotic drugs for the sedation of patients diagnosed with COVID19. One potential drug could be dexmedetomidine (Precedex), an alpha-2 adrenergic receptor agonist that has been approved by the U.S. Food and Drug Administration (FDA) for sedation in mechanically ventilated patients during the first 24 h [9]. However, no study has been able to show a clear advantage of dexmedetomidine over propofol, and vice versa [9,10].

## Conclusion

While the presence of hypotension and laboratory evidence of shock are usually indicators of the need for continued resuscitation in trauma patients, unusual causes such as PIS must be ruled out on clinical grounds. Expected pulmonary findings of contusion and atelectasis in victims of penetrating trauma to the chest might mask otherwise asymptomatic COVID-19 lung findings, which has implications for the management of the patient; including the use of mechanical ventilation.

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## Declaration of competing interest

None of the authors have any competing interests to declare.

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