Ventricular Tachycardia Following Ephedrine During Dexmedetomidine Dental Procedural Sedation

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We present the case of a 46-year-old man who received ephedrine for hypotension after surgery for a mandibular lesion under intravenous (IV) moderate sedation with dexmedetomidine (DEX) and experienced transient ventricular tachycardia (VT). The patient was scheduled to have cystectomy and multiple apicoectomies for the mandibular periapical infection and the simple bone cyst. Other than obesity, snoring, and a nonalcoholic fatty liver, he denied any other significant medical history, medications, or allergies. The surgery was successful; however, his blood pressure dropped after stopping the DEX infusion. Ephedrine was administered IV several times, which resulted in the onset of VT on the electrocardiogram (ECG). His blood pressure could not be measured at the time, but he was able to respond and breathe independently. A defibrillator was immediately made available. The ECG revealed a spontaneous transition from VT to atrial fibrillation with ST depression. Because he was unable to revert to a normal sinus rhythm, the patient was transferred to a general hospital, where he underwent additional testing. No abnormalities were observed in his heart or brain. After DEX administration, its long-lasting alpha-2 adrenoceptor agonist effects can cause vasodilation and inhibition of sympathetic activity, leading to hypotension in some patients. Should that occur, ephedrine can be used to increase blood pressure, but it may also provoke transient coronary artery spasms and lead to VT. Consequently, extreme caution should be exercised in patients who develop hypotension following DEX administration. We also recognize the significance of regular training sessions, such as advanced cardiac life support programs.

Key Words: Dexmedetomidine; Hypotension; Ephedrine; Ventricular tachycardia; Oral surgery.

Administration of dexmedetomidine (DEX) is associated with the onset of bradycardia, biphasic blood pressure responses (brief hypertension followed by hypotension), and other cardiovascular complications.[1–4] Cardiovascular agonists must be appropriately used for treatment in the event of such issues. However, literature regarding ventricular tachycardia (VT) caused by cardiovascular agonists in patients under DEX-induced sedation is scarce.

We present the case of a patient who received intravenous (IV) ephedrine to treat low blood pressure after surgery to address a mandibular cyst under IV moderate sedation with DEX and then experienced transient VT. The patient provided written informed consent to publish the details of this case report.

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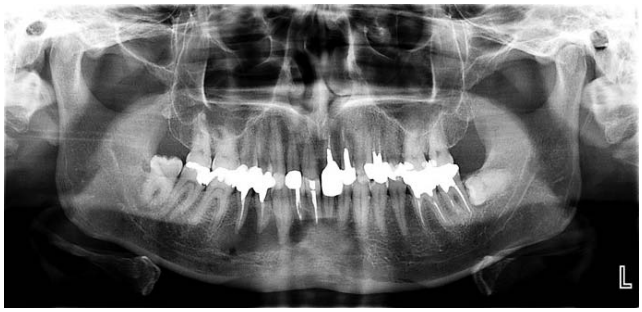
CASE PRESENTATION

A 46-year-old man (height 172.5 cm, weight 87 kg, body mass index 29.4 kg/m^2) presented with a 5-year history of swelling of the right anterior mandible. He had been monitored by a dentist but was referred to our hospital for evaluation and treatment. The unilocular radiolucency (oval-shaped lesion, approximately 1.3 × 3.8 cm; Figure 1) was initially diagnosed as a suspected simple bone cyst. However, because of a sinus tract with purulent discharge draining near the apex of the second incisor, a periapical infection was also suspected. Therefore, he was admitted to the hospital and scheduled for cystectomy and 5 apicoectomies (right mandibular central incisor to the right second premolar) under IV moderate sedation. His previous medical

Figure 1. Preoperative Panoramic Radiograph



Unilocular radiolucency approximately 1.3 by 3.8 cm noted in right mandible.

history included obesity and nonalcoholic fatty liver identified during a recent checkup along with sudden hearing loss in his left ear (at 36 years of age) and incomplete right Achilles tendon rupture (at 37 years of age), both of which were successfully treated with conservative measures. The patient denied any daily medications or allergies but reported sporadic snoring.

Preoperative laboratory tests revealed elevated Aspartate aminotransferase (82 U/L, normal 5-40 U/L), Alanine aminotransferase (222 U/L, normal 7-56 U/L), and γ-Glutamyl Transpeptidase (116 U/L, normal 0-30 U/L) levels. However, these findings indicated mild hepatic dysfunction consistent with a nonalcoholic fatty liver, and no other abnormal values were noted.

His blood pressure, pulse rate, body temperature, and percutaneous oxygen saturation (SpO_2) were 132/92 mm Hg, 92 beats per minute (bpm), 36.4 °C, and 98% on room air, respectively, when he was admitted to the hospital. To reduce the risk of upper airway soft tissue obstruction caused by obesity as much as possible, IV moderate sedation with DEX was planned.

The patient was scheduled for surgery at 1300. He was instructed to fast beginning at 2300 the day before surgery and to start dry fasting at 1000 on the day of surgery, all of which was confirmed preoperatively.

The patient was sat in the dental chair in the treatment room at 1300. Standard anesthetic monitors for moderate sedation were placed, which included a noninvasive blood pressure cuff and pulse oximeter, as is customary in Japan. The patient's preoperative blood pressure, pulse rate, respiratory rate, and SpO_2 levels were 120/88 mm Hg, 70 bpm, 24 breaths/min, and 97%, respectively (Figure 2). An initial infusion of isotonic IV fluids (Solita T1, Aypharma, Inc; Na^+ 90 mEq/L, Cl^- 70 mEq/L, L-lactate 20 mEq/L, glucose 2.6 g/dL) was initiated after a 22-gauge IV catheter was placed in the left forearm. Simultaneously, supplemental oxygen 1 L/min was administered via nasal cannula.

A continuous infusion of DEX 6.0 mcg/kg/h was started at 1320. Following an IV bolus of hydroxyzine 15 mg, an IV infusion of cefmetazole 1 g diluted with normal saline (NS) 100 mL was administered. Pentazocine 12 mg was given as an IV bolus at 1328. The DEX infusion rate was reduced to 0.7 mcg/kg/h at 1330, at which point the patient's blood pressure, pulse rate, respiratory rate, and SpO_2 were 100/73 mm Hg, 60 bpm, 16 breaths/min, and 96%, respectively. At this time his Ramsay sedation score (RSS) was 3 to 4, which corresponded to moderate sedation. The patient began to snore following the loading dose of DEX. However, the snoring disappeared easily with verbal and surgical stimulation.

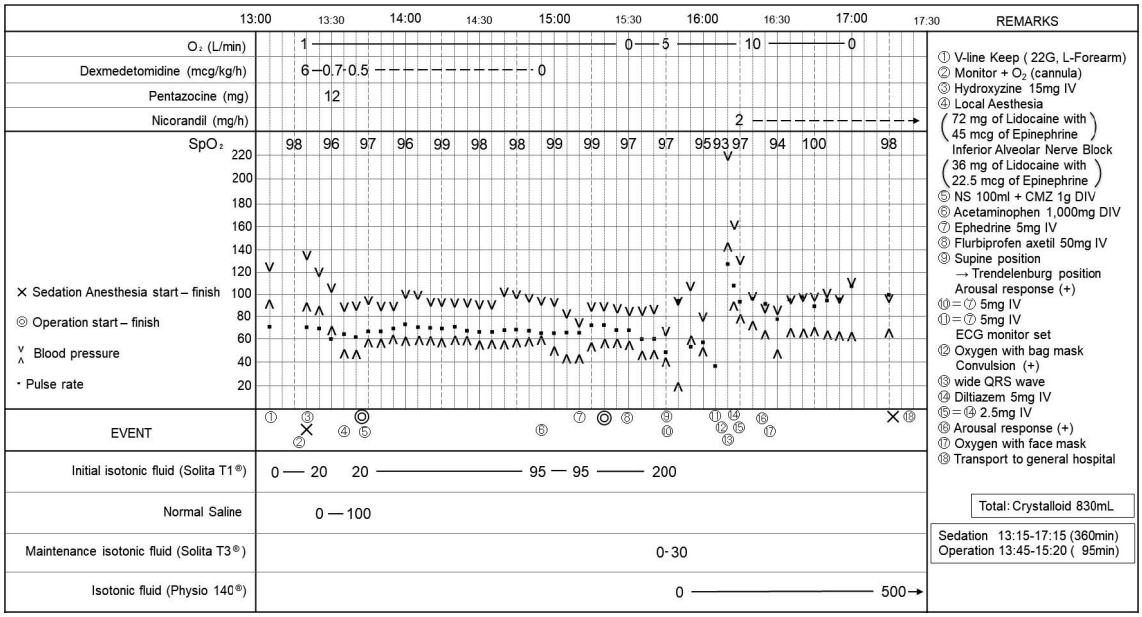
At 1335, 2% lidocaine with 1:80 000 epinephrine was used to perform infiltrative local anesthesia of the mandible, 3.6 mL, and a right inferior alveolar nerve block, 1.8 mL. The total dose of local anesthetics administered was 108 mg of lidocaine and 67.5 mcg of epinephrine. At 1340, the DEX rate was again reduced to 0.5 mcg/kg/h, and the surgery was initiated.

The cystectomy and apicoectomies were completed successfully, and the DEX infusion was stopped at 1455 when the suturing started. Acetaminophen 1000 mg was infused IV over 15 minutes for postoperative analgesia. Because of a downward trend in the patient's blood pressure (73/48 mm Hg) and pulse rate (64 bpm), an ephedrine bolus 5 mg was administered IV at 1510. At 1515, his blood pressure was 83/58 mm Hg and his pulse rate was 73 bpm. The surgery was completed at 1520, for a total surgical time of 1 hour and 35 minutes. At this time his RSS was 2, corresponding to a cooperative, oriented, but tranquil level of sedation. The patient's SpO_2 was 97% to 98% at 1530, so supplemental oxygen administration was stopped, and after administration of an IV bolus of flurbiprofen 50 mg, the initial 200 mL of IV isotonic fluids was completed and subsequently replaced with maintenance isotonic fluids (Solita T3, Aypharma, Inc; Na^+ 35 mEq/L, Cl^- 35 mEq/L, K^+ 20 mEq/L, L-lactate 20 mEq/L, glucose 4.3 g/dL). Thus, the total volume of IV fluids administered before the emergency occurred was 330 mL (Solita T1 200 mL + NS 100 mL + Solita T3 30 mL).

At 1545, hemostasis was confirmed, and the patient was breathing normally with an SpO_2 of 98%. However, his blood pressure and pulse rate had decreased to 63/43 mm Hg and 48 bpm, respectively. He was able to respond, started receiving supplemental oxygen 5 L/min by a face mask, and was placed in Trendelenburg position. Another IV ephedrine bolus 5 mg was administered again at that time, resulting in a blood pressure of 90/22 mm Hg and pulse rate of 93 bpm.

He complained of nausea at 1550. Because a fluid deficit was suspected, the maintenance fluid was

Figure 2. Sedation Record

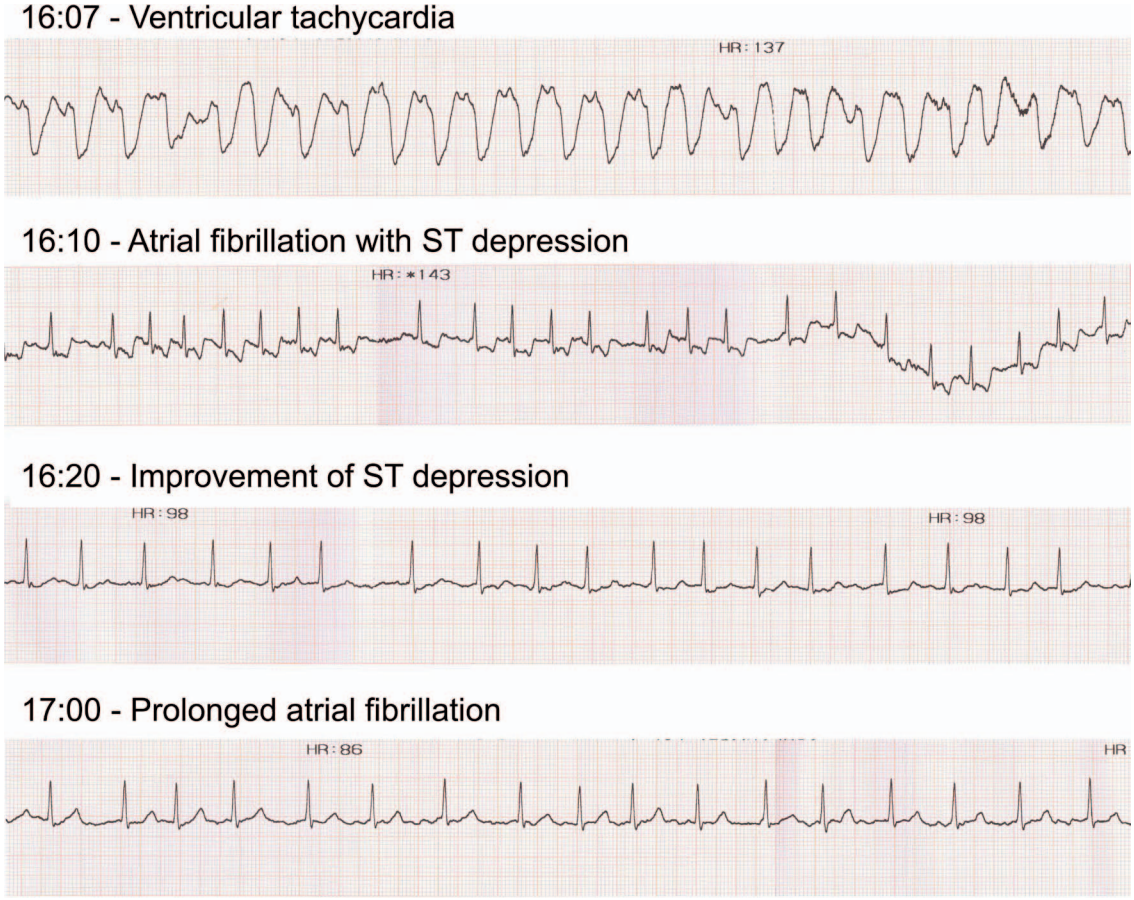


Sedation record detailing the patient's vital signs and treatment specifics.

switched to isotonic fluid (Physio 140, Otsuka Pharmaceutical, Inc; Na^+ 140 mEq/L, Cl^- 115 mEq/L, K^+ 4 mEq/L, acetate 25 mEq/L, Ca^{2+} 3 mEq/L, Mg^{2+} 2 mEq/L, glucose 1 g/dL), and rapid fluid resuscitation was initiated. His blood pressure and pulse rate dropped again at 1600 to 74/52 mm Hg and 57 bpm, respectively. At 1605, a third IV bolus of ephedrine 5 mg was given, and ECG monitoring was initiated. Sinus bradycardia was observed, which progressed to a rate of 39 bpm, and no measurable blood pressure was noted. The patient began snoring and lost consciousness. His SpO_2 temporarily decreased to 93% despite continued supplemental oxygen 5 L/min. A call for additional help was made, and a head tilt–chin lift maneuver was immediately performed, but the upper airway obstruction was incompletely released (ie, snoring noted). At 1607, VT at a rate of 137 bpm was noted on the patient's ECG. Figure 3 shows the changes in the ECG waveform over time. By this time, several dental anesthesiologists had responded to the emergency activation call, and a manual external defibrillator with ECG monitor was applied to the patient. The VT tracing was verified on both ECG monitors. The patient's blood pressure remained unmeasurable, and the pulse oximeter was not working; however, we verified the presence of a carotid artery pulse. The patient was able to respond slightly to verbal stimulation and was breathing on his own, although his level of consciousness as assessed using the Glasgow Coma Scale was 7 points (eye opening 2, verbal response 2, motor response 3). A bag-valve-mask was used successfully along with repositioning of the head tilt–chin lift position during assisted spontaneous ventilation as the mask fogged without snoring and the SpO_2 gradually increased. At 1610, the ECG waveform spontaneously transitioned from VT to an atrial fibrillation waveform with significant ST depression immediately before cardioversion was performed. The patient's blood pressure was 215/145 mm Hg, pulse rate was 127 bpm, and SpO_2 was 97% at that time. Following administration of IV diltiazem 5 mg, his blood pressure and pulse decreased to 155/93 mm Hg and 109 bpm, respectively. His blood pressure and pulse rate further normalized to 126/83 mm Hg and 91 bpm, respectively, after he received additional IV diltiazem 2.5 mg at 1615. Concurrently, an infusion of nicorandil (a potassium channel activator used to dilate coronary arteries for treating angina pectoris) was initiated at a rate of 2 mg/h. At 1620, the ST depression improved, and his blood pressure and pulse were 93/75 mm Hg and 96 bpm, respectively. The total infusion fluid volume following the emergency was 830 mL (Solita T1 200 mL + NS 100 mL + Solita T3 30 mL + Physio 140 500 mL).

Monitoring of the patient continued until 1700. Because of the persistent atrial fibrillation waveform, we determined that additional tests were required. The attending oral surgeon and dental anesthesiologist decided to have the patient transferred to a nearby general hospital. After transportation at 1830, his ECG changed spontaneously to sinus rhythm from atrial

Figure 3. Changes in Electrocardiographic (ECG) Waveform Over Time



The waveform changed from ventricular tachycardia (VT) to atrial fibrillation with ST depression over time. No ECG record was available before the onset of VT.

fibrillation waveform. He was admitted to the general hospital's cardiology department and was being monitored until the next day. The patient underwent transthoracic echocardiography, a 12-lead ECG, and a computed tomography scan of the upper body on the day of transportation and all reports revealed no structural damage in his heart or brain. The next day, he was discharged home with no major problems.

DISCUSSION

Many drugs used in IV sedation reduce consciousness and can cause respiratory depression.[5] Posterior displacement of the tongue due to relaxation of the tongue's muscles during sedation is a common cause of upper airway obstruction. As a result, DEX was used for this patient to help reduce the risk of decreased consciousness and respiratory depression.[6] However, snoring began soon after the DEX infusion was started, raising the possibility of sleep apnea syndrome. In patients with sleep apnea syndrome, nonsustained VT due to sleep-related hypoxia can be induced and is especially common during non–rapid eye movement (non-REM) sleep.[7,8] The duration of non-REM sleep increases with DEX.[9] Obese patients or those who often snore may be at high risk of developing VT when they become hypoxic under IV sedation with DEX. Our patient was obese (body mass index of 29.4 kg/m^2) and likely to experience obstruction/narrowing of the upper airway under sedation. Given that he snored even after discontinuing the DEX following the completion of the surgery, transient hypoxia due to upper airway obstruction resulting from the sustained effects of DEX may have induced VT.

ST-segment elevation is commonly observed immediately before the onset of tachyarrhythmias/lethal arrhythmias, such as ventricular fibrillation (VF) and VT.[10] A third of patients with coronary artery spasms (CAS) develop lethal arrhythmias (ie, VF or VT), and any stimulus under shallow anesthesia, use of an

adrenergic agonist, vasovagal reflex, hypotension, and hyperventilation can all lead to perioperative CAS.[10]

Although we could not confirm the development of CAS on ECG, several items corresponding to known CAS triggers, like lighter planes of anesthesia, hypotension, ephedrine use, and altered sympathetic tone, were detected in our patient.[10] Notably, a systematic review[10] and a case report[11] indicated the occasional occurrence of VT induced by ephedrine among other adrenergic agonists. In our patient, it is possible that the myocardial oxygen demand exceeded the supply because of the increased heart rate attributed to ephedrine-induced β-receptor stimulation that occurred while under a state of hypoxia and hypotension. However, there was no record of a preoperative ECG for our patient, so this is only speculation, and the possibility that CAS was induced by multiple IV boluses of ephedrine cannot be ruled out.

The incidence of hypotension due to DEX administration reportedly occurs in 42.8% of the intensive care unit patients overall.[3] The mean blood pressure at the initiation of DEX administration decreased to $\leq$70 mm Hg in many cases. A possible explanation is the vasodilation and inhibition of sympathetic nervous system (SNS) activity attributed to DEX's alpha-2 adrenergic agonist activity.[12] DEX-induced decreases in blood pressure frequently occur when the circulating blood volume decreases.[13] Therefore, circulating blood volume should be maintained appropriately during DEX sedation.

DEX can cause a biphasic blood pressure response (transient hypertension with reflex bradycardia followed by hypotension and normalization of heart rate). A study by Bloor et al[4] reported that administration of a 1 mcg/kg DEX bolus initially caused an increase in blood pressure at 2 minutes after administration combined with a reflexive decrease in heart rate, followed by a subsequent decrease in blood pressure at 4 minutes after administration. Hypotension and bradycardia peak about 1 hour after the commencement of the infusion.[4] Both effects are thought to result from the inhibition of central sympathetic outflow. Stimulation of the presynaptic alpha-2 adrenoceptors by DEX decreases norepinephrine release, which is considered another possible mechanism of its subsequent cardiovascular effects.[2] In Japan,[14] administration of DEX is generally initiated at a rate of 6 mcg/kg/h for 10 minutes, followed by a maintenance dose of 0.2 to 0.7 mcg/kg/h. In North America,[15] it is generally initiated at a rate of 1 mcg/kg over 10 minutes, followed by a maintenance dose of 0.2 to 0.7 mcg/kg/h. Therefore, although there were differences in the protocol of DEX administration, they were likely insignificant. The other drugs used in this case were pentazocine and hydroxyzine. However, reports of VT related to these drugs are scarce. Given that these drugs were administered over 2 hours before VT onset, we felt the relationship between these drugs and the onset of VT was likely minimal.

Typically, when hypotension occurs after a patient receives DEX, the first step is to reduce the DEX continuous infusion rate and then consider fluid loading the patient. If the patient's blood pressure remains low, DEX should be discontinued and cardiovascular support via a sympathomimetic agent considered.[3] The frequency of vasopressor use during noncardiac surgery is higher in patients who receive DEX than in those who do not. A case report by Klinger et al[16] indicated that patients receiving DEX more frequently received single boluses or continuous infusions of phenylephrine or single boluses of atropine than those who did not. Phenylephrine causes peripheral vasoconstriction, which elevates blood pressure; however, reflex bradycardia often occurs with phenylephrine use. Phenylephrine should be appropriate for patients with hypotension and normal sinus rhythm or sinus tachycardia; however, it may further slow the heart rate in patients with hypotension and bradycardia. Therefore, using either atropine or ephedrine as the initial cardiovascular agonist in our case would have been appropriate given the presence of hypotension with bradycardia.

In our patient, IV sedation was initiated without ECG monitoring because he had no history of ischemic heart disease. The Japanese Guidelines for IV Sedation in Dentistry (revised 2017)[17] state that "consciousness, ventilation, oxygenation, and circulation (pulse rate and blood pressure) should be monitored continuously (intermittently in some cases; degree of recommendation: A; evaluated by the Working Group on Guidelines Development). ECG should be considered in patients with cardiovascular or respiratory disease (degree of recommendation: B; evaluated by the Working Group on Guidelines Development)." This suggests that it is not always essential to assess the ECG for patients without a concomitant cardiovascular or respiratory issue. In this case, IV sedation was initiated without ECG monitoring because the patient had no history of cardiopulmonary disease. However, we cannot deny the possibility that the patient may have experienced an ST-segment elevation or transient CAS before the onset of VT. Therefore, it is suggested that ECG monitoring be performed for all patients undergoing sedation or receiving vasoactive IV drugs, even if the patient has no history of medical issues. This case report also supports that capnography or End-tidal carbon dioxide ($EtCO_2$) monitoring via nasal cannula should be employed alongside ECG monitoring for all patients undergoing moderate sedation. Capnography can help detect disruptions in ventilation much faster than pulse oximetry, especially if supplemental oxygen is being administered. In an emergency like this,

capnography also assists in validating the quality of bag-valve-mask ventilation. Furthermore, during cardiac arrest, it helps verify the quality of cardiopulmonary resuscitation and ventilation.

In this case, preoperative fasting, which also included abstaining from drinking water, may have resulted in modest volume depletion in our patient, potentially leading to a decrease in circulating blood volume. Then, at 1545, the blood pressure and the pulse rate decreased to 63/43 mm Hg and 48 bpm, respectively. After a second IV bolus of ephedrine 5 mg (10 mg total), the blood pressure and pulse rate changed to 90/22 mm Hg and 93 bpm, respectively. Both systolic blood pressure and pulse rate increased, by 43% and 93%, respectively, when ephedrine was administered. This improvement suggests that ephedrine led to an increase in cardiac workload and oxygen consumption. In contrast, it is also possible that the 50% reduction in diastolic pressure may have reduced coronary artery perfusion, leading to cardiac ischemia. Additionally, the inhibition of SNS activity due to the DEX, the shallow level of anesthesia/moderate sedation, and the third IV bolus of ephedrine 5 mg (15 mg total) may have induced CAS. Furthermore, the lack of surgical stimulation and the resumption of snoring due to the upper airway soft tissue obstruction that occurred as a consequence of the posterior displacement of the tongue caused by the relaxation of tongue muscles due to impaired consciousness decreased the SpO_2 to 93%. Although SpO_2 was within an acceptable range, some hypercapnia might have occurred because of snoring or hypoventilation. Eventually, the hypercapnia and CAS might have triggered VT. Immediate bag-valve-mask–assisted ventilation with 100% oxygen may have improved the hypercapnia, which may have caused the spontaneous transition of the VT waveform on the ECG to an atrial fibrillation waveform. Monitoring of $EtCO_2$ would have enabled early detection of ventilatory disturbances, in particular hypercapnia. Therefore, in patients under moderate sedation, continual use of an ECG and capnography should be considered as critical monitors regardless of the presence or absence of medical comorbidities.

VT improved before cardioversion was performed in this case even though a manual external defibrillator was present and prepared. VT is likely to persist or progress to a lethal arrhythmia. In advanced cardiac life support (ACLS),[18] when a sudden change in the patient's condition is noted, their level of consciousness should first be assessed before the emergency response system is activated, and the patient's pulse and respirations should also be checked. If no pulse is detected, the ECG waveform should be reviewed while chest compressions and artificial ventilations are performed. If pulseless VT is confirmed, defibrillation should be performed immediately. On the other hand, if VT with a pulse is confirmed, the patient should be subjected to oxygen administration and IV cannulation, and acute symptoms (hypotension, impaired consciousness, shock signs, ischemic chest discomfort, and acute heart failure) must be examined. If no symptoms (stable) are noted, either adenosine or amiodarone should be administered intravenously. If acute symptoms (unstable) are noted, or the drugs used are ineffective, cardioversion should be applied under sedation. For both cases, supplemental oxygen/ventilation and obtaining IV access are necessary. In this case, cardioversion was indicated because the patient exhibited VT with a pulse accompanied by an acute symptom of hypotension (unstable) under moderate sedation. To prepare for emergencies, we realized how important it is to regularly participate in ACLS training.

CONCLUSION

Herein, a notable blood pressure decrease was observed after discontinuation of sedation using DEX. Ephedrine was intravenously administered several times, which may have caused CAS. Furthermore, our patient concomitantly experienced transient hypoxia and hypercapnia associated with narrowing of the upper airway during sleep due to obesity, possibly leading to VT onset. When IV sedation is performed, factors such as obese patients, DEX use, and modest fluid deficits may increase the risk of developing VT. If several types of drugs are used in IV sedation, ECG and $EtCO_2$ should be monitored and attention paid to waveform changes. Additionally, regular participation in emergency training sessions like ACLS is also important.

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