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CLINICAL REPORT

Dexmedetomidine-induced atrioventricular block followed by cardiac arrest during atrial pacing: a case report and review of the literature

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Abstract Sinus bradycardia is a well-known consequence of stimulation of presynaptic α_2 adrenergic receptors due the adminstration of dexmedetomidine. One of the most serious adverse effects of dexmedetomidine is cardiac arrest. Some cases demonstrating such an arrest due to the indiscriminate use of this drug were recently reported. We continuously administered dexmedetomidine to a 56-year-old male patient at a rate of 0.3 μg/kg/h (lower than the recommended dose) without initial dosing for sedation in an intensive care unit. The patient had undergone open cardiac surgery and atrial pacing was maintained at a fixed rate, 90/min. The PQ interval in electrocardiography gradually prolonged during the infusion; finally, complete atrioventricular block and subsequent cardiac arrest occurred. Immediate cardiopulmonary resuscitation was carried out, including re-intubation, and recovery of spontaneous circulation was attained 15 min after the event. The patient was discharged from hospital on the 25th postoperative day without any neurological complications.

Keywords Dexmedetomidine · Cardiac arrest · Complication · Sedation

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Introduction

The administration of dexmedetomidine, an α_2 adrenergic receptor agonist, is becoming a popular regimen for the sedation of postsurgical patients, as it has useful anxiolytic and analgesic properties but does not induce marked circulatory and respiratory depression. One of the adverse effects of dexmedetomidine is bradycardia, and a sinus arrest incident related to the administration of this drug has been reported [1]. Here, we describe a case of severe atrioventricular block followed by cardiac arrest in a patient receiving a dexmedetomidine infusion despite undergoing atrial pacing after cardiac surgery.

Case report

A 56-year-old, 53-kg, 170-cm man with annuloaortic ectasia and aortic regurgitation was admitted to the hospital. The patient had been diagnosed with a gastric polyp and had undergone endoscopic polypectomy six months earlier. Follow-up examination suggested a residual malignant region and a total gastrectomy was scheduled; however, annuloaortic ectasia and moderate aortic regurgitation were found in preoperative evaluations. No other

abnormality was observed in the patient except for mild anemia (hemoglobin concentration: 12.1 g/dl), so 100 mg a day of iron were administered. Before the gastrectomy, a Bentall procedure was scheduled.

On the day of the operation, no premedication was prescribed. Anesthesia was induced by administration of midazolam 8 mg and fentanyl 100 μg, and orotracheal intubation was conducted after obtaining muscular relaxation with vecuronium 10 mg. A central venous catheter and pulmonary artery catheter were placed, and he was monitored via transesophageal echocardiography. General anesthesia was maintained through intermittent administration of midazolam and fentanyl. The total cardiopulmonary bypass time was 199 min and the aortic clamp time was 141 min. Surgical bleeding led to the loss of 1425 ml, and 533 ml of washed blood were re-infused using a cell-saver system. Supplemental transfusion of 960 ml fresh frozen plasma and 600 ml platelets was conducted. The intrinsic sinus rhythm was regained during re-warming, and 3 μg/kg/min of dopamine and dobutamine were administered to facilitate weaning from the cardiopulmonary bypass. He was moved to the intensive care unit with only a 3-μg/kg/min dopamine infusion. Heart rate at admission was 65/min (sinus rhythm), and atrial pacing was initiated at a heart rate of 85 through the temporal lead as a standard postsurgical regimen.

The day after the operation, the patient's trachea was extubated without any difficulties and no neurological complication was observed. The patient was completely alert and his vital signs were stable. His heart rate was

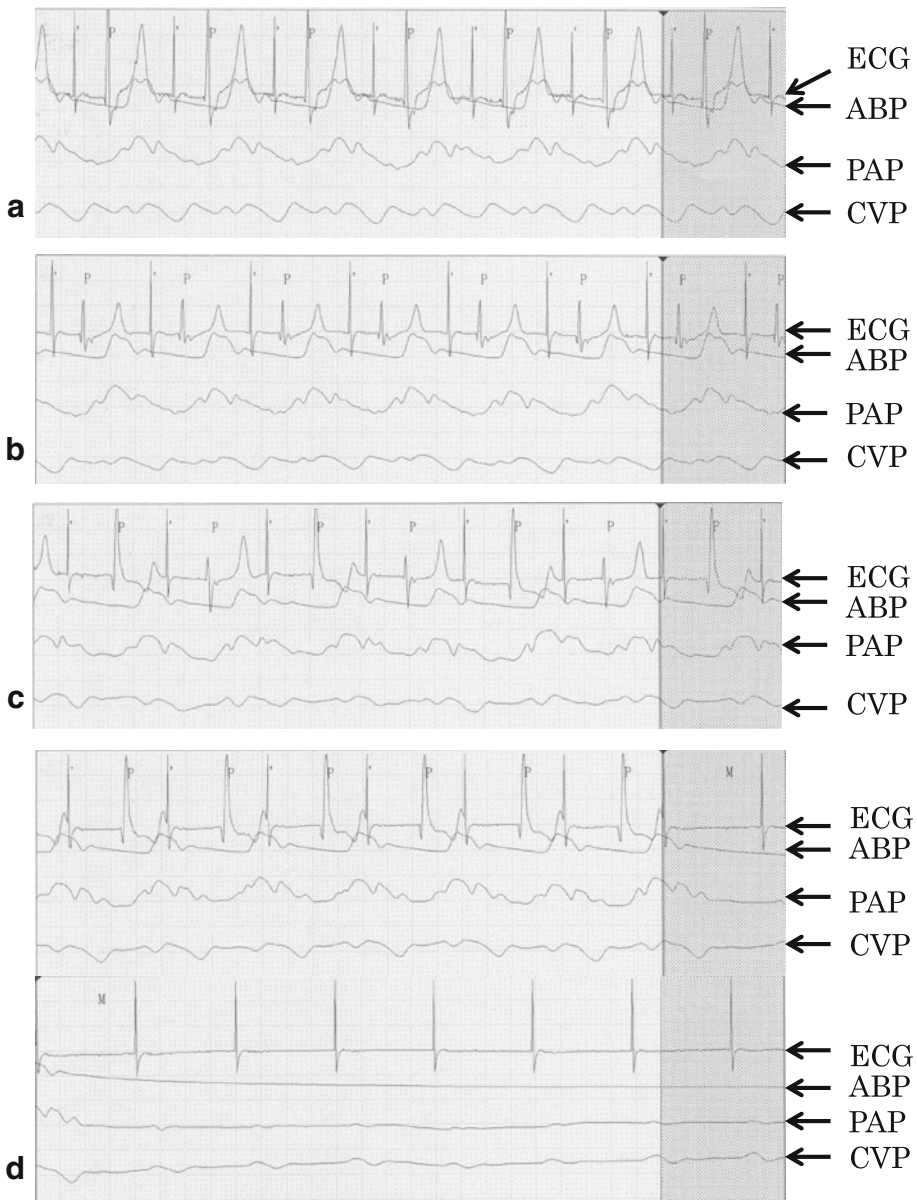

Fig. 1 Records of electrocardiogram and invasive pressure monitoring of the patient. **a** Immediately before the start of dexmedetomidine infusion, **b** 1 h later, **c** 5 h later, and **d** record of the cardiac arrest. *ECG* electrocardiogram, *ABP* arterial blood pressure, *PAP* pulmonary artery pressure, *CVP* central venous pressure

maintained by atrial pacing at 90/min. Small doses of dopamine (1 μg/kg/min), nicardipine (2 mg/h), insulin (2 unit/h), and fentanyl (25 μg/h) were continuously administered. From the evening of the first postoperative day, continuous administration of dexmedetomidine was started to obtain a hypnotic state. Dexmedetomidine was infused at a rate of 0.3 μg/kg/h without initial dosing. At the beginning of infusion, the interval between a pacing spike and a Q wave in the electrocardiogram was 242 ms (Fig. 1a). Three hours later, the interval was still 245 ms (Fig. 1b), but it had prolonged to 296 ms at 5 h after the beginning of administration (Fig. 1c).

5 h and 30 min after the start of infusion, the interval had increased to 340 ms (not shown). Finally, complete atrioventricular block without an escape rhythm (asystole) developed (Fig. 1d). Blood pressure and heart rate immediately before the arrest were 98/56 mmHg and 79/min, respectively. The electrocardiogram showed only pacing spikes. Immediate cardiac life-support procedures, including external chest compressions and orotracheal intubation followed by mechanical ventilation, were promptly initiated. The total dose of dexmedetomidine was approximately 83 μg and infusion was discontinued immediately. Epinephrine (1 mg bolus), dopamine (up to 5 μg/kg/min), norepinephrine (up to 0.05 μg/kg/min), and sodium bicarbonate (200 ml of 8.4 % solution) were administered. A capture beat was observed 15 min after the start of resuscitation. Arterial blood pressure increased to 152/98 mmHg immediately after the event. Mild hypothermia was initiated to prevent brain injury over the subsequent 2 days. On the 6th postoperative day, the patient was weaned from mechanical ventilation and moved to a general ward the following day without any complications. He was discharged from the hospital on the 25th postoperative day.

Discussion

As far as we are aware, this is only the second case report of dexmedetomidine-related sustained cardiac arrest in Japan [2]. We found 15 cases of dexmedetomidine-induced cardiac arrest in the literature, including 6 cases reported by Bharati et al. [3] (Table 1). The simulated concentration was calculated using RUGLOOP©, version 3.14 (DeSmet and Struys, Department of Anesthesia, University Hospital Ghent). Sudden complete atrioventricular block without an escape rhythm, asystole, is the one of most severe complications during the perioperative period. Ingersoll-Weng et al. [4] were the first to describe a case of severe bradycardia progressing to asystole in a patient with myasthenia gravis who received a dexmedetomidine infusion. However, the asystole may have been induced by an autonomic response to sternal retraction. The cardiac arrest lasted <2 min and the cardiac rhythm promptly returned. Thus, the etiology of that cardiac arrest differed [5, 6] from those of the patients reported by Shah et al. [1], Nagasaka et al. [2], and us.

A typical case of dexmedetomidine-induced severe cardiac arrest was reported by Shah et al. [1]. The patient was administered dexmedetomidine for sedation purposes. The infusion rate was 3 μg/kg/h and the arrest developed 15 min after the beginning of infusion. This rate would be appropriate for rapidly achieving a pharmacokinetic steady state, but immediately after the initial dosing, the plasma concentration of the dexmedetomidine could have been up to 1.7 ng/ml. Depression of cardiac function would have been induced when the plasma concentration of dexmedetomidine exceeded 1.2 ng/ml [7].

In our case, dexmedetomidine was continuously administered at a rate of 0.3 μg/kg/h. We had attempted to diminish the excess sympathetic activity during the postoperative period using a small dose of dexmedetomidine. The plasma concentration of dexmedetomidine would have increased gradually over the subsequent hours, and the calculated plasma concentration of dexmedetomidine at the cardiac arrest event may have been 0.32 ng/ml [7]. This concentration is smaller than that recommended for achieving a sufficient state of sedation, but dexmedetomidine is synergistic with other hypnotic and analgesic drugs [8]. Despite the simulated low plasma concentration, the patient's cardiac complication was severe and sustained. In the previous cases, the concentration of dexmedetomidine was inconsistent (Table 1).

There is no clear explanation for the relationship between the cardiac arrest and a low concentration of dexmedetomidine. An undiagnosed disorder of the cardiac conduction system in the patient could be suspected. It is well known that coronary artery disease, cardiomyopathy, acute or chronic infective endocarditis, and autoimmune disorders are the most common causative factors of complete atrioventricular block. However, intensive examination, including interventional radiology, could not identify any other systemic disorders. Risk of cardiac arrest is not necessarily associated with the blood concentration of dexmedetomidine (Table 1).

The 16 cases can be sorted into two groups. The first group showed preceding hypotension followed by a fatal cardiovascular collapse and cardiac arrest, and the second group demonstrated only bradycardia, with no other signs of circulatory depression immediately before the event (Table 1). The findings for the latter group with the cardiac conduction abnormality are more specific properties of a dexmedetomidine-induced cardiac arrest. In these cases, an escape rhythm generated by the atrioventricular junction or Purkinje fibers was not observed. Shepard et al. [9] introduced a case in which atrial standstill developed and loss of

Table 1 Reported cases of suspected dexmedetomidine-induced cardiac arrest

Case number	Age (year)	Sex	Weight (kg)	Co-morbidity	Location	Dose of dexmedetomidine		Findings of ECG	Simulated concentration (ng/ml)	References
						Loading	Maintenance			
1	52	Female	60	Myasthenia gravis	Operating room	1 μg/kg over 10 min	0.2 μg/kg/h for 2 h[a]	Bradycardia to asystole	0.32	Ingersoll-Weng et al. [4]
2	NA	Female[a]	NA		Operating room	4 μg/kg/h for 15 min	0.3 μg/kg/h for 2 h[a]	Bradycardia to asystole	0.39	Videira and Ferreira [10]
3	76	Female	95[a]	Symptomatic bradycardia	Operating room	1 μg/kg over 15 min (3 μg/kg/h[b])		Pacing spikes without capture	1.7	Shah et al. [1]
4	50	Male	NA	Paroxysmal atrial fibrillation	Electrophysiology laboratory	200 μg/h over 45 min	50 μg/h for 1 h	Hypotension and bradycardia to asystole	0.93	Sichrovsky et al. [6]
5	74	Male	NA	Postoperative myocardial infarction		None	0.11–0.7 μg/kg/h for 6 h	Pulseless electrical activity	0.92	Gerlach et al. [11]
6	64	Female	90	First-degree atrioventricular block	Intensive care unit	None	0.17 μg/kg/h for 45 min followed by 0.3 μg/kg/h for 75 min	Complete atrioventricular block to asystole	0.31	Nagasaka et al. [2]
7	0.8	Male	7.25	Bone at 26 weeks gestation	Operating room	4 μg in two doses with propofol 30 mg		Bradycardia to asystole	NA	Shukry et al. [12]
8	18	Female	NA	Cystic fibrosis (transplant recipient)	Intensive care unit	1 μg/kg over 10 min	0.4–0.8 μg/kg/h for 8 h	Bradycardia to 10-s systolic pause	0.77	Zhang et al. [13]
9	62	Male	60		Operating room	1 μg/kg over 5 min (6 μg/kg/h[b])		Hypotension to pulseless electrical activity	1.4	Bharati et al. [3]
10	51	Male	70	Hypertension	Operating room	1 μg/kg over 10 min		Bradycardia to asystole	1.8	Bharati et al. [3]
11	15	Male	46		Operating room	1 μg/kg over 7 min (6 μg/kg/h[b])		Hypotension to cardiac arrest	1.6	Bharati et al. [3]
12	70	Male	58	Postcoronary artery bypass graft surgery, ischemic heart disease, hypertension	Operating room	1 μg/kg over 10 min		Hypotension to pulseless electrical activity	1.8	Bharati et al. [3]
13	76	Male	56		Operating room	1 μg/kg over 10 min	0.5 μg/kg/h for 10 min	Arrest	0.62	Bharati et al. [3]
14	66	Male	55		Operating room	1 μg/kg over 10 min	0.5 μg/kg/h for 20 min	Arrest	0.50	Bharati et al. [3]
15	55	Female	NA	After a bilateral orthotropic lung transplantation	Intensive care unit	None	0.5 μg/kg/h for 2 h	Arrest	0.37	Webb et al. [14]
16	56	Male	53	After a Bentall procedure	Intensive care unit	None	0.3 μg/kg/h for 5.5 h	Complete atrioventricular block to asystole	0.32	The present case

The simulated concentration was calculated using RUGLOOP©, version 3.14 (DeSmet and Struys, Department of Anesthesia, University Hospital Ghent)

NA not available from the data presented in the case report

[a] Data hypothesized based on the content of the report

[b] Infusion rate until the cardiac arrest event

capture occurred with a pacemaker in a pediatric patient after the initiation of dexmedetomidine. Shah's patient [1] had a history of symptomatic bradycardia and pacemaker implantation. The patient reported by Nagasaka et al. [2] showed first-degree atrioventricular block at preoperative examinations. Dexmedetomidine may not only disturb atrioventricular conduction; it may also have a severe inhibitory effect on cardiac pacing autoregulation, especially in patients with potentially disturbed conducting pathways. Severe bradycardia and asystole cannot be prevented by atrial pacing [1, 9].

If we had applied not only atrial pacing but also ventricular pacing during the perioperative period using dexmedetomidine, the devastating event that occurred in our case could have been prevented. Synchronous pacing of both atrium and ventricle is ideal, but the traditional pacemaker we used had only one channel for output. The cardiovascular surgeon preferred atrial pacing because it allows much more cardiac output to be obtained with the atrial kick. Thus, ventricular pacing was not applied in this case. Intensivists should discuss the risk before using dexmedetomidine.

In summary, we have reported a case of cardiac arrest in a postoperative patient. Although sedation using dexmedetomidine is considered safe and effective, there may be room for discussion concerning cardiac conduction system abnormalities. Intensive monitoring and caution are required even when this drug is administered at a low infusion rate.

Conflict of interest None of the authors of this report has any conflict of interest.

References

1. Shah AN, Koneru J, Nicoara A, Goldfeder LB, Thomas K, Ehlert FA. Dexmedetomidine related cardiac arrest in a patient with permanent pacemaker; a cautionary tale. Pacing Clin Electrophysiol. 2007;30:1158–60.
2. Nagasaka Y, Machino A, Fujikake K, Kwamoto E, Wakamatsu M. Cardiac arrest induced by dexmedetomidine. Masui. 2009;58:987–9 (Japanese with English abstract).
3. Bharati S, Pal A, Biswas C, Biswas R. Incidence of cardiac arrest increases with the indiscriminate use of dexmedetomidine: a case series and review of published case reports. Acta Anaesthesiol Taiwan. 2011;49:165–7.
4. Ingersoll-Weng E, Manecke Thistlethwaite GR Jr. Dexmedetomidine and cardiac arrest. Anesthesiology. 2004;100:738–9.
5. Muntazar M, Kumar FC. Cardiac arrest, a preventable yet a possible risk of dexmedetomidine: fact or fiction? Anesthesiology. 2004;101:1478–9.
6. Sichrovsky TC, Mittal S, Steinberg JS. Dexmedetomidine sedation leading to refractory cardiogenic shock. Anesth Analg. 2008;106:1784–6.
7. Ebert TJ, Hall JE, Bamey JA, Uhrich TD, Colinco MD. The effects of increasing plasma concentrations of dexmedetomidine in humans. Anesthesiology. 2000;93:382–94.
8. Hendrickx JFA, Eger EI II, Sonner JM, Shafer SL. Is synergy the rule? A review of anesthetic interactions producing hypnosis and immobility. Anesth Analg. 2008;107:494–506.
9. Shepard SM, Tejman-Yarden S, Khanna S, Davis CK, Batra AS. Dexmedetomidine-related atrial standstill and loss of capture in a pediatric patient after congenital heart surgery. Crit Care Med. 2011;39:187–9.
10. Videira RLR, Ferreira RMV. Dexmedetomidine and asystole. Anesthesiology. 2004;101:1479.
11. Gerlach AT, Dasta JF. Dexmedetomidine: an updated review. Ann Pharmacother. 2007;41:245–52.
12. Shukry M, de Armendi AJ, Cure JA. Angiotensin-converting enzyme inhibitor and cardiac arrest following induction of anesthesia. Ann Card Anesth. 2010;13:72–3.
13. Zhang X, Schmidt U, Wain JC, Bigatello L. Bradycardia leading to asystole during dexmedetomidine infusion in an 18 year-old double-lung transplant recipient. J Clin Anesth. 2010;22:45–9.
14. Webb CA, Weyker PD, Flynn BC. Asystole after orthotopic lung transplantation: examining the interaction of cardiac denervation and dexmedetomidine. Case Rep Anesthesiol. 2012;2012:203240.