Dexmedetomidine-induced atrial premature complex

The Editor,

Cardiac arrhythmia is a frequent and significant cause of morbidity and mortality in the perioperative setting[1] which can result from varied contributing factors.[2] Dexmedetomidine, a highly selective alpha 2 agonist, has gained importance because of its diversified role in anesthesia and Intensive Care Units (ICUs). Bradycardia and rarely atrioventricular blocks are some of the known electrocardiographic (ECG) abnormalities associated with dexmedetomidine use. Till date, there is no literature evidence of this drug triggering a premature atrial complex (PAC). Here, we report a rare clinical event of PAC associated with dexmedetomidine administration after obtaining permission from the patient herself. A 38-year-old woman of average built American Society of Anesthesiologists physical status Class I diagnosed to have fibroid uterus and was planned to undergo total abdominal hysterectomy. Her pulse rate was 90 beats/min, regular and blood pressure (BP) 130/80 mmHg. Laboratory workup did not reveal any abnormality. She was premedicated with tablet lorazepam 1 mg orally the night before and 2 h before the surgery.

In the operating room, ECG trace for lead II showed sinus rhythm with a heart rate (HR) of 92 beats/min. BP was 134/86 mmHg and SpO_2 was 97% on room air. After preloading with 20 ml/kg of lactated ringer's solution, subarachnoid block was performed instilling 3.0 ml of 0.5% hyperbaric bupivacaine with 26-gauge Quincke's spinal needle at L3–L4 interspace. After achieving sensory blockade till T6, surgery was started. The lowest BP recorded was 110/72 mmHg after subarachnoid block and HR remained around 74/min. A 10 cm subumbilical skin incision was given and subsequent layers were dissected. While the surgeons were manipulating the uterus, patient complained of discomfort and pain following a dragging sensation. She was supplemented with dexmedetomidine 1 mcg/kg, intravenous (IV) over 10 hour followed by 0.2–0.7 mcg/kg/min continuous infusion. Hemodynamic parameters and hemoglobin saturation remained within normal limits.

Surgery restarted after 10 min of loading dose and the patient remained pain-free throughout. HR dropped down to 65 beats/min and BP to 100/66 mmHg during this time. After 5 min of recommencing the surgery, we noticed atrial premature complex (APC) every sixth beat in lead II [Figure 1]. Within few seconds, frequency of APCs increased to every second to third beat with HR of 45 beats/min and BP 84/48 mmHg [Figure 2]. After confirming APCs in lead I and III, dexmedetomidine infusion was stopped and injection atropine 0.6 mg IV was given. HR gone up to 94 beats/min and BP to 106/69 mmHg with APCs every 5–6 beats [Figure 3]. Meanwhile, serum electrolytes and blood gas were checked and found to be in normal range. Surgery was continued with injection fentanyl 50 mcg intravenously as and when required. Surgery lasted for 2 h. The APCs persisted for 60 min after stopping the dexmedetomidine infusion. On completion, patient was shifted to Postanesthesia Care Unit where 12 lead ECG and transthoracic echocardiography were performed and failed to reveal any abnormality. Throughout the entire 5 days postoperative course of the patient in the hospital, HR and rhythm remained normal.

DISCUSSION

Dexmedetomidine is a highly selective alpha (α) 2 – adrenergic receptor agonist with a relatively high ratio for $\alpha 2/\alpha 1$ activity (1620:1) as compared to clonidine (220:1). In 1999, the

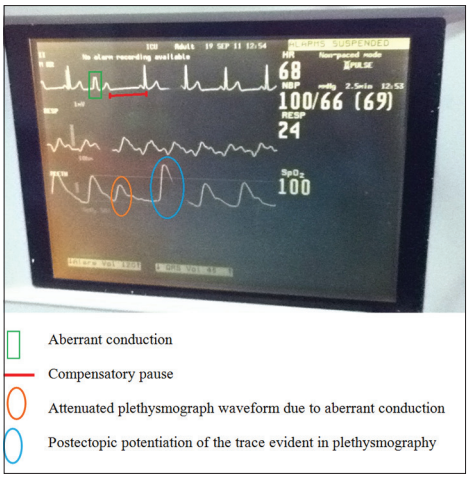

Figure 1: Lead II electrocardiographic showing atrial premature complex

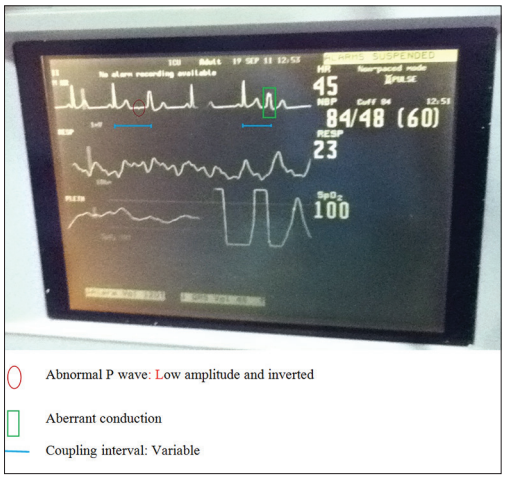

Figure 2: Lead II electrocardiographic showing increased frequency of atrial premature complexes

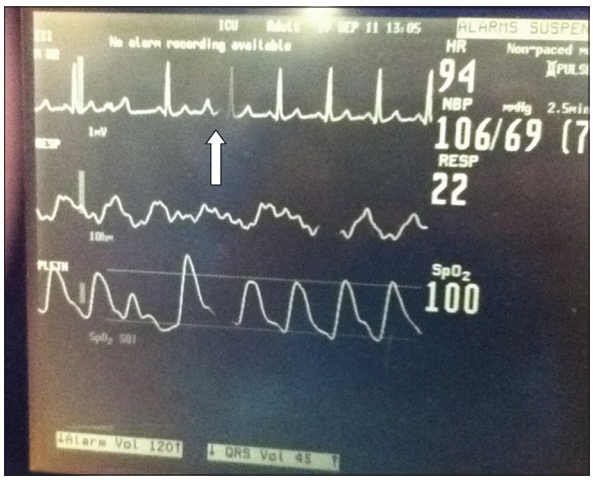

Figure 3: Lead II electrocardiographic showing changes in electrocardiographic after atropine injection and a fusion beat (arrow)

Food and Drug Administration approved this drug as a sedative agent for patients in ICUs requiring mechanical ventilation.[3] The shorter elimination half-life of 2 h and the availability of antagonist atipamizole[4] make it an ideal agent for IV continuous infusions in operating rooms, ICUs, and other areas as well. Apart from ICU sedation, it has got valuable role in procedural sedation, attenuation of pressor response to tracheal intubation/extubation, prevention of emergent delirium, parental separation, reducing minimum alveolar concentration of inhalational agents, opioid sparing, prolonging the duration of sensory block of local anesthetics during spinal anesthesia, and peripheral nerve blocks and the list continues to grow.[5]

It is noteworthy that dexmedetomidine is known to have therapeutic role in the setting of acute perioperative atrial and junctional tachyarrhythmias[6] for rate as well as rhythm control. This anti-arrhythmic action of the drug is explained to be due to its imidazoline structure which acts on nucleus reticularis lateralis in the ventrolateral medulla, thus modulating vagal activity.[7]

With these enormous clinical applications, side effects are shadowed. Apart from nausea, it poses potential adverse cardiovascular effects such as hypotension, hypertension, and bradycardia.[8] There are a few additional reports of conduction abnormalities with the use of dexmedetomidine. In 1992, Bloor *et al*.[9] reported two events of junctional escape rhythm with dexmedetomidine at an IV infusion dose of 2 mcg/kg over 2 min, which required no medical intervention. Gerlach and Murphy[10] in 2009 published a case report of dexmedetomidine associated pulseless electrical activity in a 74-year-old postmyocardial infarcted patient on ventilator who was on metoprolol. They also stressed on four similar high-risk cases that developed dexmedetomidine-induced sinus arrest.

While the above-reported conduction abnormalities in humans were all bradyarrhythmias, we encountered PAC in normal young adult patient at normal recommended dose and rate.

PAC represents 10% of intraoperative arrhythmias[2] which is characterized by abnormal P-wave morphology and compensatory pause. It is because of PAC which resets the sinus node. Pause is said to be incomplete if sum total of pre- and post-ectopic R–R interval is less

than twice of the interval between two sinus beats. QRS complex may be absent if PAC is totally blocked at AV node or can be narrow/normal if conduction to the ventricle is undisturbed or can be wide even if conduction through ventricles is aberrant (Ashman's phenomenon). The coupling interval which is the interval between an ectopic and preceding sinus beat is fixed when PAC is unifocal and variable if PAC is multifocal.[11] In our patient, we noticed a low amplitude inverted P-wave with a compensatory pause with varying coupling interval indicating multifocal origin [Figures 1 and 2].

PAC can occur in variety of situations such as infection, inflammation, myocardial ischemia, and usage of tobacco, alcohol, caffeine or by anxiety, and hypokalemia.[11] We failed to establish any of the above triggering factors for PAC in this case. PAC in this patient appeared at end of loading dose of dexmedetomidine and gradually disappeared after 60 min of stopping indicates clearly the culprit for PAC being dexmedetomidine itself. Yet, the reason why dexmedetomidine triggered PAC is not quite clear.

Although PACs generally do not require therapy,[12] Waktare *et al*. have demonstrated the significance of PAC in initiating paroxysmal atrial fibrillation.[13] Our patient developed PAC with sinus bradycardia associated with hemodynamic disturbance which was abolished using 0.6 mg of atropine intravenously. The possible role of the vagus nerves in facilitating the induction of atrial tachyarrhythmia was demonstrated, and it was suggested that atropine may have an added benefit of reducing the likelihood of development of atrial tachyarrhythmias.[14]

CONCLUSION

Dexmedetomidine has evolved as a panacea for various applications in anesthesia and intensive care for all age groups. Thus, clinicians should be vigilant and be aware of potential although rare complication like PAC as we reported.

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Conflicts of interest

There are no conflicts of interest.

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