Case Report

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Cardiovascular crisis after small dose local infiltration of epinephrine in patient with asymptomatic subarachnoid hemorrhage
-A case report-

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The infiltration of dilute epinephrine solution has been used for many years to provide hemostasis. However, epinephrine has adverse cardiovascular effects, such as arrhythmia, pulmonary edema, and even cardiac arrest. We have experienced epinephrine-induced cardiovascular crisis, with severe hypertension, tachycardia, and cardiac arrest after subcutaneous infiltration of a 2% lidocaine and 1 : 200,000 epinephrine solution in a patient with an asymptomatic subarachnoid hemorrhage. We provided successfully advanced cardiac life support in the operating room and cardioverted the patient back into a sinus rhythm with no untoward effects. The patient recovered without any apparent sequelae after intensive care. (Korean J Anesthesiol 2010; 59: S53-S57)

Key Words: Asymptomatic subarachnoid hemorrhage, Cardiovascular crisis, Epinephrine.

Intracranial diseases such as acute ischemic or hemorrhagic stroke, subarachnoid hemorrhage, head trauma, tumor, or encephalomeningitis can cause various disorders in the cardiovascular system. Among these, subarachnoid hemorrhage has been known to be related to electrocardiographic disorder, arrhythmia, arrhythmia damage, and neurogenic pulmonary edema [1,2]. Epinephrine is widely used in various operations to reduce hemorrhaging by constricting the local blood vessels and diminishing the systemic toxic effect of local anesthetics. However, epinephrine can cause cardiopalmus, headache, pallor, and anxiety. Accidental intravenous injection of epinephrine or absorption of an excessive amount of it, though it has to be locally infiltrated, can cause cerebral hemorrhage, ventricular arrhythmia, pulmonary edema, or even cardiac arrest. It was reported that even local infiltration of a safe dose of epinephrine can cause severe hypertension, ventricular arrhythmia, acute pulmonary edema, or cardiac arrest [3,4]. The authors have experienced a case of cardiovascular crisis immediately followed by cardiovascular collapse after injection of locally infiltrated epinephrine into a patient with

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an asymptomatic subarachnoid hemorrhage for facial nerve decompression, and we herein report the case with a related literature survey.

Case Report

A 167 cm, 65 kg, male patient at the age of 27 was observed in the neurosurgery department for a linear fracture at the temporal bone caused by a motorcycle accident that had taken place 11 days before the operation and a tiny amount of subarachnoid hemorrhage corresponding to Grade 1 of the Hunt and Hess grading system (Fig. 1). During the observation, facial nerve paralysis, a complication of the fracture, was found and a facial nerve decompression operation was planned. Though he had cerebral hemorrhage in the history from the traffic accident 3 years before, he was provided with no particular treatment and there was no specific cerebral hemorrhage finding. The encephalomalacia by the previous trauma and subarachnoid hemorrhage by the recent accident were found in the neuroimaging. All the findings were normal in all the preoperative tests that were carried out in the laboratory, including the electrocardiography and the chest radiography.

Thirty minutes before the patient's arrival in the operation room, an intravenous injection of glycopyrrolate 0.2 mg and midazolam 3.0 mg was performed. After arriving at the operation room, an electrocardiograph, an automated noninvasive blood pressure device, and a pulse oximeter were attached to the patient. Before the induction, the blood pressure was 115/67 mmHg, the heart rate was 75/min, and the oxygen saturation was 99%. The induction was performed by an intravenous injection of propofol 120 mg, rocuronium 50 mg, and fentanyl 50 μg, and endotracheal intubation was carried out after sufficient muscular relaxation. After checking the continuous positive-end carbon dioxide expiration and the uniform breath sound from both sides of the chest, the tube was fixed at the proper endotracheal location and the mechanical ventilation was initiated with O_2 1.5 L/min, N_2O 1.5 L/min and sevoflurane 2 vol%. After the initiation, the positive end expiratory pressure was kept at 33−37 mmHg. When preparing the operation, the systolic blood pressure was maintained at 100−120 mmHg, the heart rate at 80−90/min, and the peripheral oxygen saturation at 100%.

Twenty-five minutes after the induction, the doctor performing the operation injected 2% lidocaine 4 ml including 1 : 200,000 epinephrine at the retroauricular temporal lobe parts for incision after checking the negative blood aspiration. Between 20−30 seconds after the local infiltration, the heart rate suddenly increased to 160/min and the measured blood pressure was 204/135 mmHg. Then, since ventricular arrhythmia was found by the electrocardiograph, injection of all the anesthetics and the operation were stopped, providing 100% oxygen. Though an intravenous injection of lidocaine 100 mg was immediately carried out, the ventricular arrhythmia continued. Even after the second intravenous injection of lidocaine 100 mg, the arrhythmia continued. The peripheral pulse was not enhanced, and the blood pressure was not measured. Thus, cardiopulmonary resuscitation was immediately performed. Following the defibrillation at monophasic 200-300-360 J, the heart rate was turned to the sinus tachycardia of 110−120/min and the measured systolic blood pressure was 100−110 mmHg. However, pulseless ventricular arrhythmia was found again after 2 minutes, and defibrillation was performed at monophasic 360 J. After that, the heart rate was turned to the sinus tachycardia of 110−120/min again, and the measured systolic blood pressure was 100−110 mmHg. Again, a supraventricular tachycardia unresponsive to vagal maneuver took place and adenosine 6 mg was injected rapidly through the external jugular vein. Though the heart rate was turned to the sinus tachycardia, defibrillation at monophasic 360 J was conducted since the pulseless ventricular arrhythmia was found again after 3 minutes. After that, sinus rhythm was recovered and the blood pressure and the heart

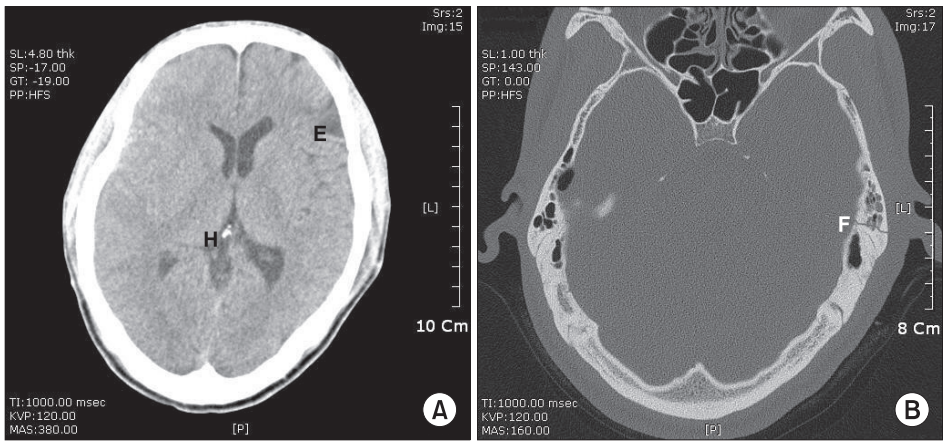

Fig. 1. Brain CT shows subarachnoid hemorrhage, right fronto-temporal convexity and multi-focal encephalomalacia of the left frontal and temporal lobes due to old brain contusion (A). Also, Linear skull fracture of the left temporal bone was detected (B). E: encephalomalacia, F: linear skull fracture, H: subarachnoid hemorrhage.

rate were stabilized at 133/81 mmHg and 98/min, respectively. The total duration of the cardiopulmonary resuscitation was 12 minutes. The arterial blood gas test performed at that time showed pH 7.435, $PaCO_2$ 33.3 mmHg, PaO_2 369 mmHg, Bicarbonate 23.1 mmol/L, and SaO_2 100%. According to cardiac enzyme test, creatine kinase-MB (CK-MB) was increased to 4.2 ng/ml, and Troponin-I to 1.23 ng/ml.

After the cardiac rhythm of the patient became normal, the assisted respiration was continuously carried out in the operation room until the spontaneous respiration was recovered. The consciousness and the spontaneous respiration were restored about 2 and 1/2 hours after the induction, and then, the patient was transported to the intensive care unit after extubation of the tracheal tube. The fluid injected in the operation room was crystalloid solution 500 ml and colloid solution 500 ml, and the urination was 300 ml.

In the intensive care unit, 100% oxygen 5 L/min was provided through a mask. The measured blood pressure was 123/72 mmHg; the heart rate was 97/min; and the peripheral oxygen saturation was 100%. The arterial blood gas test results were pH 7.379, $PaCO_2$ 43.3 mmHg, PaO_2 111 mmHg, Bicarbonate 24.5 mmol/L, and SaO_2 98%. Electrocardiography was performed due to the finding of a heart enzyme level increase, and the left ventricular ejection fraction was 35%, indicating dysfunction at the left ventricular which was regarded as the sequel of the defibrillation and cardiopulmonary resuscitation. There was no abnormal finding in the movement of the myocardium wall. On the day of entering the intensive care unit, the blood pressure was maintained with dopamine 5 μg/kg/min, but the dopamine injection was stopped on the second day in the intensive care unit. Since the heart enzyme and electrocardiography findings were normal and there was no specific finding in the patient's symptom or the physical examinations from the sixth day forward in the intensive care unit, the patient was moved to the general ward and was discharged after 2 days without any sequel.

Discussion

For the purpose of improving operative vision, a local infiltration of epinephrine is often carried out by mixing it with physiological saline or local anesthetic, and a side effect rarely takes place with the clinical dose. However, as in this case report, there are a few cases where cardiovascular collapse takes place by a little amount of epinephrine local infiltration.

Wanamaker et al. [3] reported the case where severe hypertension and tachycardia took place after the hypodermic injection of 1% lidocaine 3 ml mixed with 1 : 100,000 epinephrine for tympanoplasty, followed by ventricular tachycardia and ventricular fibrillation, and thus cardioversion was required. Woldorf and Pastore [4] also reported the case where pulmonary edema, as well as severe low blood pressure with the systolic blood pressure lower than 30 mmHg and tachycardia, took place after the infiltration of 1% lidocaine 5 ml mixed with 1 : 200,000 epinephrine to the gingivobuccal fold mucosa. In our case report, a hypodermic injection of 2% lidocaine 4 ml mixed with 1 : 200,000 epinephrine was carried out, dividing the total amount into several times, into the part around the retroauricular mastoid, as in the case of the first example. The total amount of epinephrine used in the quoted cases was 30 μg and 25 μg, respectively, and the amount in our case was 20 μg. The maximum allowable dose for adults is the maximum therapeutic dose of 0.5−1 mg and the minimum lethal dose of 4 mg for hypodermic injection, which are a little amount compared to the maximum allowed dose of 7−8 mg [5]. In addition, considering that the maximum safe dose of epinephrine can be increased due to the endogenous vasoconstriction and the protective effect of lidocaine that is jointly used [6], the amount in this case was insufficient to cause cardiovascular collapse, even though it is assumed that all the injected epinephrine was immediately absorbed in the linear fracture at the temporal bone or the vein.

A few factors were presumed as the causes of the electrocardiographic disorder by the tiny amount of epinephrine in this case report.

First, subarachnoid hemorrhage may be one of the factors, though there was no abnormal finding in the physical examination or other tests except the pain at the fractured part in the temporal region. In the acute phase of subarachnoid hemorrhage, cardiovascular crisis can take place due to an imbalance in neurovegetative control, an increase of catecholamine in the circulatory system, and local myocardial tissue or hypopituitarism [1,7]. Long QT, P-pulmonale, ST segment-elevation and ST segment-depression, inversion of T wave, prominent U wave, and temporary pathologic Q wave are generated [8], and the generation rate is almost 50−90%. Such changes are frequently found in the acute phase (0−72 hours) and turn to the normal states after a few days. However, clinically significant arrhythmias, such as ventricular tachycardia and atrial tachyarrhythmia, are also found in 1−4% of the patients [7].

The possibility that epinephrine caused hypersensitization in the body cannot be ruled out. Carter et al. [9] measured the discharged epinephrine and the metabolites after an epinephrine hypodermic injection and reported that the detected amount was 2 times more than the expected value. They mentioned the possibility of endogenous catecholamine hypersensitization by the externally injected catecholamine. However, this explanation might be valid only for the clinical pattern when hundreds of small quantity epinephrine units are

injected.

On the other hand, the studies that compared the vasoconstriction effect depending on the ratio of local anesthetic revealed that there was no significant clinical difference, although a wide range of concentrations were tested from 1 : 50,000 to 1 : 400,000 [10,11]. If so, the use of a lower concentration of epinephrine for the vasoconstriction effect can be helpful in reducing various complications.

Inhalation anesthetics can also affect the occurrence of arrhythmia by a little amount of epinephrine injected from outside. However, this can hardly be the cause of the ventricular arrhythmia since sevoflurane, which was used in this case report, shows a low epinephrine-induced arrhythmia incidence rate, although it has a negative myocardial inotropic effect similar to that of isoflurane and desflurane [12].

The patient in this case report undertook the operation on the 11th day after the injury, after the acute phase, and did not show any abnormality in the electrolyte test and electrocardiography in the preoperative tests without any past history of heart disease. Even though the patient did not have any specific symptoms like those, a little amount of subcutaneous infiltration caused the arrhythmia 11 days after the injury. In conclusion, it can be assumed that the asymptomatic, but definitely existing, subarachnoid hemorrhage might have caused the increase of catecholamine and hypopituitarism that were not clinically revealed as well. Under such conditions, the externally-injected catecholamine caused an overresponse by the endogenous catecholamine hypersensitization.

To prevent the epinephrine-induced cardiovascular crisis, a patient's family and personal history regarding cardiovascular diseases, cryptorrhea, and medication should be thoroughly investigated before the operation and attention should be paid to the ventilation, blood pressure, heart rate, and the heart rhythm during the operation.

The therapy for epinephrine-induced cardiovascular crisis is symptomatic and similar to the therapy for pheochromocytoma. For the treatment of severe hypertension, α-adrenergic blockers such as phentolamine are recommended, and β-adrenergic blockers are recommended for the treatment of tachycardia. Esmolol, the short acting β1-selective blocker, is preferred because it has a short half-life; it can be used by volume titration depending on the heart rate; and it can reduce the risk of hypertension and coronary spasm due to the excessive α-stimulation that is found in nonspecific β-blockers [13]. Calcium-channel blockers, such as verapamil and diltiazem, are also used for hypertension, tachycardia, and arrhythmia. The cardiopulmonary resuscitation algorithm is practiced for the treatment of arrhythmia and cardiac arrest. In this case, since ventricular arrhythmia was found a few seconds after tachycardia and hypertension, lidocaine, which has been used for a long time with a less immediate adverse reaction, was used, but there was no response. Since the pulseless ventricular arrhythmia was found, the defibrillator was prepared and cardioversion was tried. For the defibrillation, monophasic 200-300-360 J, the conventional 3-successive-shock, was used, but intravenous injection of amiodarone and biphasic 1 shock are recommended in the present cardiopulmonary resuscitation guidelines [14]. Amiodarone affects the sodium channel, potassium channel, and calcium channel, and it has a blocking effect on α and β sympathetic nerve receptors. It is injected in ventricular fibrillation or ventricular tachycardia patients who are not responsive to cardiopulmonary resuscitation, electroshock, or vasoconstrictor by an initial intravenous injection of 150 mg for 10 minutes, and the daily maximum allowance is 2.2 g. Because the 3 successive shocks can interrupt the thoracic compression and inhibit the perfusion pressure to the coronary artery, biphasic 1 shock 200 J is recommended at present. It should be corrected that we did not follow the treatment guidelines revised in 2005, but applied the drugs and procedures that were recommended before the revision in this case.

In conclusion, this case shows that cardiovascular crisis, such as arrhythmia and cardiac arrest, took place after a small amount, clinical volume of epinephrine was injected in a healthy patient without any heart disease. As in this case report, for the patients who have the potential of hypersensitization to externally injected epinephrine due to an intracranial lesion, positive monitoring and preparation are required in case of cardiovascular crisis, even if there is no abnormal finding in the physical examination or the laboratory tests for the operation after the acute phase.

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