# Fatal Subarachnoid Hemorrhage due to Intravascular Adrenaline Absorption

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## Abstract

Vasoconstrictors are commonly administered with local anesthetics (LAs) to decrease intraoperative bleeding. However, inadvertent systemic absorption of adrenaline is not uncommon and is associated with significant hemodynamic consequences and arrhythmias, which are usually inconsequential. We report a case of suspected intravascular adrenaline absorption in a 1-year-old girl with craniosynostosis, which led to subarachnoid hemorrhage, herniation, and death.

## Introduction

The use of combined vasoconstrictor and local anesthetic (LA) infiltration to decrease intraoperative bleeding is common. Accidental intravascular adrenaline absorption can have significant hemodynamic adverse effects. There are reports of malignant arrhythmias, cardiac failure, and even cardiac arrest in patients with and without neurological diagnosis who have recovered without sequelae.[1-3] We report a case where systemic adrenaline absorption resulted in critical intracerebral insult which proved fatal.

## Case Report

A 7-month-old female child presented with an abnormal head (tower) shape since birth with no other complaints. She had hypertelorism and her head circumference was 85th percentile with mild motor delay. The child had a premature fusion of sagittal, coronal, and lambdoid sutures, resulting in turricephaly. Magnetic resonance imaging (MRI) showed platybasia, prominent lateral ventricles with small posterior fossa, and tonsillar herniation 13 mm below foramen magnum. She underwent a foramen magnum decompression, $C_1$ arch excision, and posterior fossa remodeling uneventfully and was planned for anterior cranial fossa remodeling later.

At 1 year of age (weight 8 kg), she came for bilateral orbitofrontal advancement. Her preoperative computed tomography (CT) scan was normal (►**Fig. 1A**). Anesthesia was induced with fentanyl, thiopentone, and atracurium, and her trachea was intubated with a 5-mm uncuffed endotracheal tube. Anesthesia was maintained with $O_2$, air, and sevoflurane. Invasive blood pressure monitoring was conducted. Prior to making a surgical incision, lignocaine with adrenaline (40 mg of lignocaine and 10 µg of adrenaline [2 mL of 1:200,000 diluted to 8 ml, i.e., 1:800,000]) was infiltrated into the incision site. Within 15 seconds of infiltration, blood pressure (BP) increased to 180/110 mm Hg and heart rate (HR) decreased from 110 to 70 beats/min. This was followed by tachycardia (HR > 140–150 beats/min). Supplemental fentanyl 15 µg and propofol 20 mg were administered to deepen the plane of anesthesia. However, tachycardia continued and there was a drop in EtCO2 and BP (54/38 mm Hg) and increase in airway pressure from 18 mm Hg to 27 mm Hg. On auscultation, coarse crepitations were heard and patient had pink frothy secretions. Arterial blood gas analysis revealed a $PaO_2$/$FiO_2$ ratio of 100. A diagnosis of pulmonary edema was made. $FiO_2$ was increased to 1.0, 5 cm $H_2O$ PEEP was added, and 5 mg furosemide, 1.5 mg of morphine, and 3.0 mg mephentermine were administered. With these measures, oxygen saturation was maintained > 95%. However, an ST depression was seen on ECG. In view of refractory hypotension, noradrenaline infusion was started. Airway pressures slowly improved and BP increased to 95/50 mm Hg with noradrenaline infusion. Surgery was abandoned and the patient was shifted to ICU for further management.
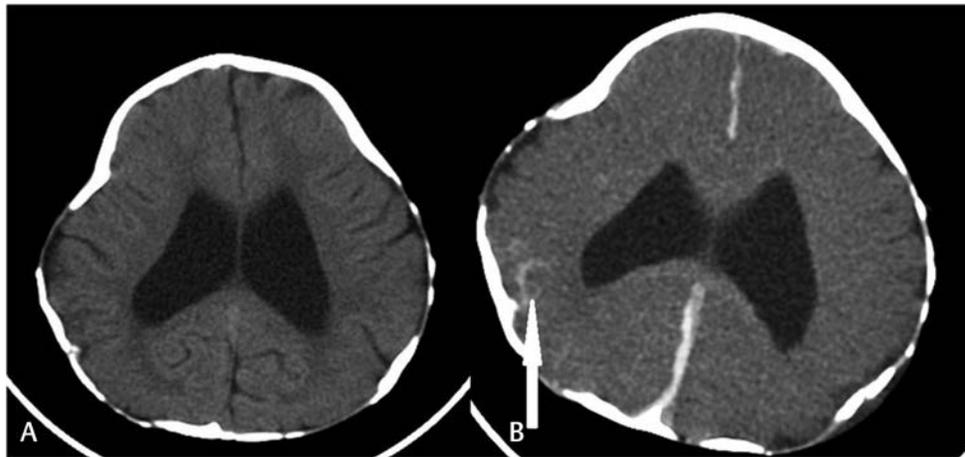
**Fig. 1** (**A**) Preoperative CT scan of the brain. (**B**) CT scan of the brain showing diffuse brain edema, effacement of sulci, subdural hemorrhages along the falx and tent along with subarachnoid hemorrhage in the left parietal area. CT, computed tomography.

In the ICU, after reversal of the neuromuscular blockade, the patient's Glasgow coma scale (GCS) was $E_1V_tM_1$ and pupils were dilated and did not react to light. An echocardiogram showed dilated left ventricle which was poorly contracting. Patient continued to be hypotensive, requiring additional dopamine, dobutamine, and adrenaline infusion. There were no crepitations and chest X-ray was clear. A CT scan of the brain showed diffuse brain edema and subarachnoid hemorrhage (SAH) (►Fig. 1B). An external ventricular drain (EVD) was inserted to drain the cerebrospinal fluid (CSF) and reduce the intracranial pressure. Ten mL of CSF could be drained from this EVD. There was no further neurological improvement and the patient finally succumbed on the fourth day.

## Discussion

The temporal sequence of events in this case suggest a high-probability of intravascular adrenaline absorption being responsible for severe hypertension (HTN) and tachycardia in the early phases. The initial brief bradycardia could be reflex consequent upon HTN. The other possible cause of bradycardia could be that sudden and severe HTN led to SAH which caused a sudden increase in intracranial pressure (ICP) and herniation. The sympathetic surge associated with SAH would have later led to tachycardia. The tachycardia and hypotension can also be due to direct effects of systemic intravascular adrenaline. Adrenaline is known to cause myocardial stunning and acute cardiac failure (as was seen in the echocardiogram of this patient). As this occurred very early during the complication, cardiac failure may be responsible for causing pulmonary edema. It is also possible that the pulmonary edema is neurogenic in origin as a consequence of SAH.

Vasoconstrictors such as adrenaline are usually administered with LA to decrease bleeding (especially in children) during surgery. Although subcutaneous epinephrine is safe, inadvertent intravascular absorption of epinephrine can cause severe HTN, tachycardia and even malignant arrhythmias such as ventricular tachycardia and

ventricular fibrillation, leading to cardiac arrest.[1] Therefore, the safe use of adrenaline warrants certain precautions. The dose of adrenaline for subcutaneous infiltration needs to be reduced with inhalational agents as they can sensitize the myocardium to adrenaline. Arrythmogenic potential is higher for halothane (dose of adrenaline is 1 μg/kg) than for isoflurane or desflurane.[4] Epinephrine less than 7 μg/kg has been found to be safe with desflurane and isoflurane as anesthetics. The smallest dose of epinephrine to elicit three or more premature ventricular contractions within 5 minutes of its administration has been reported to be 7 μg/kg for desflurane and 7.3 μg/kg for isoflurane.[5] Arrythmogenic potential is similar for isoflurane and sevoflurane.[6] Addition of LA increases the safe dose by 50%. Also, higher concentration of adrenaline (>1/100,000 or 1/200, 000) and using it alone (without combining it with LA) increases the likelihood of side effects.[2] Hypoxia and hypercarbia may enhance the possibility of arrhythmias with adrenaline.[7] In our case, the dose of adrenaline used was 1.25 μg/kg in a dilution of 1/800,000 and along with LA, which is well below the recommended dose. In the earlier reports with a similar complication, there was no mortality.[1-3] However, in this patient, the hemodynamic effects of epinephrine were poorly tolerated. This is because patients with multisutural complex craniosynostosis are likely to have intracranial hypertension (ICHT) due to multifactorial etiology. The causes for such ICHT are as follows: (1) Craniocephalic disproportion, (2) venous hypertension due to impedance to venous outflow and consequent hydrocephalus, (3) obstructive sleep apnea, and (4) Arnold Chiari malformation.[8] Although the current patient underwent foramen magnum decompression, the decrease in ICP would have been only partial and patient would still be having ICHT due to other contributing causes. In such a patient, SAH caused by a sudden increase in BP would have further increased the ICP. Moreover, in pediatric patients, the autoregulation may not have been fully developed and the latency for autoregulation may be increased.[9] In pediatric patients, autoregulation curve is steeper on both sides, below the lower limit, and also above the upper limit of autoregulation. Hence, they poorly

tolerate either hypotension or HTN. Even transient episodes of HTN can lead to ICHT in small children. At 1 year of age, as in this case, autoregulation is unlikely to be completely developed. This might be the reason for systemic HTN caused by adrenaline to increase the cerebral blood flow and rupture of the cerebral blood vessels, causing SAH.

Venous hypertension due to venous outflow impedance is also not uncommon in patients with craniosynostosis. Inadvertent intravascular injection of adrenaline might have raised the venous pressure and caused the venous bleed.

Keeping in mind the age of the patient combined with the presence of trans-osseous venous collaterals and perturbed venous drainage, there is an increased risk of massive intraoperative blood loss during skin dissection and bone removal, which justifies the need for adrenaline infiltration. However, one should be very cautious in using epinephrine in patients with an intracranial pathology, as it can lead to a devastating complication. Need for repeated aspirations and slow injection cannot be overemphasized.

### Conflict of Interest
None declared.

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