# A Rare Case of Intracerebral Hemorrhage in Anaphylactic Shock Following Administration of Intramuscular Adrenaline: A Case Report

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**Abstract**

Intracerebral hemorrhage should be considered as a possible adverse event in patients with anaphylactic shock who are treated with adrenaline administration, especially those on dialysis.

**Introduction:**

Anaphylaxis with rapidly life-threatening systemic hypersensitivity reactions occurring after being triggered by inflammatory mediators can lead to fatal airway obstruction and shock[1][2]. Approximate acute management of anaphylactic shock remains prompt intramuscular injection of adrenaline, which has a significant impact on favorable outcomes[3][4]. However, previous published reports have rarely shown the incidence of intracranial hemorrhage following anaphylactic shock treated with adrenaline injection[5][6]. Furthermore, intracerebral hemorrhage can occur after adrenaline administration via any route, including in patients undergoing therapeutic upper-gastrointestinal endoscopy and those with asthma[7][8]. Although a definitive pathology has not been completely established, these serious adverse events can be fatal and require further intervention. In addition, the number of elderly people with multiple comorbidities and taking many medications who are at high risk for hemorrhage may increase every year[9].

Sharing our experience may help clinicians recognize cerebrovascular complications after injection of adrenaline in elderly dialysis patients with anaphylactic shock; adrenaline injection is the first-line management for these patients.

**Clinical Case:**

A 75-year-old-female who had been on hemodialysis for chronic kidney disease for over four years visited her family physician's clinic complaining of fever. She denied any personal history of drug allergy or anaphylaxis and no allergic reactions had previously occurred. She had a history of hypertension and arteriosclerosis obliterans treated with axillary-femoral bypass, for which she was prescribed aspirin 100mg per day.

Empirically, she was given intravenous antibiotics (1g cefoperazone-sulbactam) for a suspected bacterial infection three hours after initiation of hemodialysis. A few minutes later, she proceeded to develop periorbital edema, dyspnea, and altered consciousness, and her blood pressure fell to 54/30 mmHg. Her family physician diagnosed her with anaphylactic shock caused by the antibiotic and intramuscularly administered 0.3 mg of

adrenaline (1:1000 dilution) twice every five minutes, as well as 5 mg of chlorpheniramine maleic acid, 20 mg of famotidine, and 125 mg of methylprednisolone. A few minutes after receiving adrenaline, the patient developed tachycardia with a pulse rate of 140 beats/min and hypertension with a blood pressure of 208/88 mmHg. Thirty minutes after onset upon arrival of emergency medical services personnel at the scene, her blood pressure fell to 94/44 mmHg. She was admitted to our institution for further treatment one hour after the incident.

En route to the emergency department, she appeared pale. She had a Glasgow Coma Scale (GCS) score of 12 (E2V4M6), respiratory rate of 20 breaths/min, arterial oxygen saturation of 100% with oxygen delivered through a face mask (3 L/min), pulse rate of 110 beats/min, blood pressure of 104/78 mmHg, and body temperature of 37.1°C. Findings from her physical neurological exam were unremarkable.

Laboratory test results demonstrated chronic kidney disease as indicated by urea nitrogen levels of 17 mg/dL, elevated creatinine levels of 4.86 mg/dL, thrombocytopenia (blood platelets cell count of 9.0 x $10^4$ cells/L), normal prolonged prothrombin time, and activated partial thromboplastin time. Blood culture test did not identify any bacteria. A computed tomography (CT) scan was conducted to screen for causes of altered consciousness and acute shock other than anaphylaxis. The CT scan revealed a hemorrhagic lesion measuring 9x9x5 mm in the right basal ganglia (Figure 1-A). We conducted conservative treatment using nicardipine hydrochloride to promptly stabilize her systolic blood pressure to under 140 mmHg, as well as tranexamic acid. Neurological examination showed the patient failed to achieve complete clarity of consciousness; she had a GCS score of 11 (E2V3M6) and her left upper and lower limbs were paralyzed without sensory neuropathy four hours after onset. We performed a follow-up head CT scan, which showed that the intracerebral hemorrhage had increased in size to 52x35x30 mm (Figure 1-B). During the first few days, the patient presented no additional neurological deterioration without further expansion of the intracerebral hemorrhage.

The patient was transferred to the local rehabilitation hospital 28 days after admission with weakness of the left upper and lower limbs, which affected her daily life, and a modified Rankin Scale score of 5.

**Discussion:**

We herein report a 75-year-old female patient on dialysis with serious sequelae caused by intracranial hemorrhage following anaphylactic shock treated with intramuscular administration of adrenaline.

Leukopenia, non-occlusive mesenteric ischemia, ischemic stroke, and intracerebral hemorrhage are adverse events after anaphylactic shock that have previously been reported in the medical literature [5][10][11][12][13].

Although other etiologies cannot be excluded, we assume that acute hypertensive attack induced by adrenaline and dialysis with a high risk of hemorrhage may be associated with the pathogenesis of intracerebral hemorrhage, in our case at least partially. Indeed, during anaphylactic shock, our patient's cerebral blood flow decreased more than what could be anticipated based on the blood pressure observed in animal experiments[14]. Therefore, the pathogenesis of intracerebral hemorrhage may have etiologies other than anaphylaxis. Similar to our case, previous reports have hypothesized that intracerebral hemorrhage after anaphylactic shock can result from elevated blood pressure induced by adrenaline administration when there is no evidence of vascular abnormality or intracerebral tumor[5][6].

Adrenaline is one of the most commonly used medications to manage conditions such as cardiac arrest, asthma, septic shock, and anaphylactic shock, but serious adverse events can occur, including arrhythmias, lactic acidosis, pulmonary edema, and cerebrovascular disease[6][15][16][17]. Intracerebral hemorrhage after administration of adrenaline via different routes, including intravenous and intramuscular administration and inhalation, has previously been described[5][8][18]. Adrenaline can lead to stimulation of all $\alpha$ and $\beta$ adrenergic receptors, eliciting short-term systolic hypertension, and suppress inflammatory mediators released from mast cells and basophils[19]. Adrenaline influences a significant dysfunction of cerebral autoregulation and the blood brain barrier in animal experiments[20]. These pharmacological mechanisms may have contributed to intracerebral hemorrhage.

A second hypothesis for the cause of the intracerebral hemorrhage is dialysis. Intracerebral hemorrhage

is a common and potential risk for dialysis patients due to altered platelet-vessel wall interactions and platelet dysfunction, as well as factors that impair normal platelet aggregation and adhesion [21]. Moreover, hemodialysis patients have received anticoagulants during dialysis. The number of elderly people with multiple comorbidities who require dialysis tends to increase every year[9]. Therefore, clinicians must consider the risk of intracerebral hemorrhage in dialysis patients.

**Conclusion:**

Intracranial hemorrhage following anaphylactic shock treated with intramuscular administration of adrenaline should be recognized as an adverse event, especially in patients on dialysis.

**Author Contributions:**

Conceptualization: Shunki Yamamoto, Takashi Hongo, Atsunori Nakao.

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**Conflict of Interests:**

The authors declare that they have no competing interests.

**Data Availability Statement:**

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

**Ethical approval:**

Written informed consent for participation was obtained.

**Consent:**

Written informed consent was obtained from the patient for the publication of this case report and the accompanying images. A copy of the consent form is available for review by the Editor-in-Chief of this journal.

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**Figure Legends**

**Fig. 1.** Computed tomography scan of the patient's head.**A:** An intracranial hemorrhage measuring 9x9x5 mm was revealed in the right basal ganglia on admission. **B:** The intracranial hemorrhage increased to 52x35x30 mm three hours after admission.