CASE REPORT

Alveolar hemorrhage observed in a case of amphetamine intoxication

Osamu Ogawa*, Yutaka Tsubata**, Junya Ajiro*, Takashi Ishida*, Kyuma Ota*, Takashi Kon*

Abstract: A 50-year-old man with acute amphetamine intoxication was admitted to the ICU. Fourteen days following admission, the patient showed respiratory distress with diffuse pulmonary infiltration. A diagnosis of alveolar hemorrhage was made from bloody fluid collected by bronchoalveolar lavage. He recovered fully following 5-day administration of methylprednisolone. Although there are many reports about vascular complications associated with amphetamine abuse, this may be the first case report about acute amphetamine intoxication complicated with alveolar hemorrhage. This report contains several discussions about possible vasculopathy associated with amphetamine intoxication.

Key words: 1) amphetamine, 2) alveolar hemorrhage, 3) cerebral hemorrhage

Introduction

Several reports have revealed acute amphetamine intoxication can cause some vascular complications such as stroke and ischemic heart attack1,2. Here, amphetamine intoxication complicated with alveolar hemorrhage will be discussed.

Case report

A 50-year-old man was transferred to our emergency department due to general convulsions and stupor lasting for more than thirty minutes. On arrival, his symptoms included hyperhidrosis, hypotension (84/62 mmHg), tachycardia (154 /min), tachypnea (34 /min), hypoxemia (oxygen saturation was around 80% on pulse oximeter even while administration of oxygen of 10 l/min) and pyrexia (41.6 ℃). His Glasgow Coma scale was five. Following the administration of sedatives, his convulsions subsided. The chest radiograph and computed tomography of both brain and body were normal. Gradually, blood pressure recovered to 112/75 mmHg after hydration without vasopressor, and his body temperature normalized by active external cooling. Drug testing of his urine (Triage® DOA, Biosite Diagnostics Inc. USA) qualitatively detected the presence of amphetamines3. Eventually, he confessed to amphetamine abuse and suggested that he took the substance intravenously the same day (prior to his admission that day). Although the police informed us of the quantitative detection of amphetamines in his urine, the exact chemical name of the substance remains undisclosed.

Fig. 1 is the clinical course of this case. Disseminated intravascular coagulation (DIC) and acute kidney injury due to rhabdomyolysis came up a few days after admission. We were compelled to perform extracorporeal hemodiafiltration and administer some coagulation factors for these complications. His DIC improved and the platelet count recovered to a normal range on the tenth day.

Two weeks after his admission, symptoms of both hypoxemia and tachypnea were demonstrated. His oxygenation index fell to around 100 mmHg. The chest radiograph showed a bilateral diffuse interstitial shadow on the lung. His chest computed tomography showed bilateral diffuse reticular opacity in the lung (Fig. 2). Bloody fluid was collected by bronchoalveolar lavage. Such findings indicated a diagnosis of pulmonary alveolar hemorrhage. Several tests for both immunological disease and hemorrhagic diathesis, however, were not able to reveal specific primary disease of pulmonary alveolar hemorrhage (Table 1). Although heparin sodium was administered for hemodiafiltration, activated partial thromboplastin time (APTT) was 40.0 seconds (compared to a normal range of 22.6 to 34.6 seconds), and his

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Fig. 1 Clinical course in ICU
Clinical events and therapeutic management are shown in the upper panel. Changes of urine volume (UV; black square) and body temperature (BT; solid line) are displayed in the middle panel. Change of numerical values of serum creatinine phosphokinase (CPK; fine dot panel), platelet counts (PLT; coarse dot line) and serum creatinine (Cre; solid line) are demonstrated in the lower panel.

Fig. 2 A plain chest computed tomography image obtained on the sixteenth day after admission

platelet count was 281,000 /μl at that time. Other coagulation, immunological and infectious tests did not reveal any primary cause for the alveolar hemorrhage (Table 1). After performing steroid pulse therapy in the same way as standard therapy for idiopathic pulmonary hemorrhage (methylprednisolone 1 g/day for first three days and 250 mg/day for following two days), his respiration (oxygenation) improved rapidly. The abnormal reticular shadows almost completely disappeared after about 7 days of treatment. The alveolar hemorrhage failed to reappear even after discontinuation of steroid administration.

In the third week, transient convulsion followed by hemiparesis and dysarthria occurred. His brain computed tomography demonstrated right occipital cerebral hemorrhage. Blood pressure was around 160/95 mmHg, platelet count was 275,000 /μl and APTT was 37.8 seconds at that time. The patient’s neurological capabilities partially recovered with time.

Hemodiafiltration was finally discontinued on twenty-sixth day after admission. The patient was discharged from ICU one week later. Finally, he was discharged from the hospital after 8 week hospital stay.

Discussion
There are many reports about cerebral stroke, mostly cerebral hemorrhage, as a complication of amphetamine intoxication. There are also some reports about methamphetamine-induced angiopathy, in which vasospasm, coagulopathy (thrombosis) and vasculitis may cause vascular complications such as cerebral stroke5). Acute noncardiogenic pulmonary edema and pulmonary hypertension has been reported in amphetamine abuse, although its mechanism remains unclear5).

Although pulmonary alveolar hemorrhage is characterized by several clinical symptoms and signs, recognition of alveolar hemorrhage often requires bronchoalveolar lavage6). The pulmonary capillaritis is the most common histology of alveolar hemorrhage7). Although alveolar hemorrhages are often associated with various systemic disorders, infectious or toxic exposures may also associate with this condition. The most common drugs that can cause alveolar hemorrhage are
Alveolar hemorrhage in amphetamine intoxication

There is a report about cocaine abuse complicated with diffuse alveolar hemorrhage \(^6\), \(^7\). Possible mechanisms of alveolar hemorrhage are: 1) direct damage to both the alveolar epithelium and endothelium of pulmonary capillaries; 2) vasoconstriction of the pulmonary vascular bed; 3) injury of the pulmonary capillaries via immunopathological reaction to cocaine.

There are no previously known reports about complication of alveolar hemorrhage with amphetamine intoxication in both acute and chronic toxic conditions. Although heparin usage may be related to alveolar hemorrhage in this case, it was possible that this hemorrhagic complication was caused by pulmonary vascular abnormalities (vasculitis and/or capillaritis) caused from amphetamine intoxication rather than anticoagulant therapies and hypertension. This case occurred without severe hypertension, overdose of anticoagulation drugs or other bleeding tendencies such as DIC (refer to Fig. 1 and Table 1). Steroid therapy proved to be very effective for the alveolar hemorrhage in this case. These findings may indicate that this alveolar hemorrhage was caused via immunological and/or inflammatory mechanisms, instead of the mechanism of bleeding tendencies (anticoagulation therapy and DIC).

Given that amphetamine usage by patients may be rarely disclosed in Japan, medical professionals must be vigilant in such cases. When confronting unexplained abnormalities in patients such as unconsciousness, hyperthermia, rhabdomyolysis and hemorrhagic disorders, differential diagnosis concerning illicit drug intoxication may be required.

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References


<table>
<thead>
<tr>
<th>Table 1</th>
<th>Laboratory data on fourteenth day after admission (when the pulmonary alveolar hemorrhage occurred)</th>
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</thead>
<tbody>
<tr>
<td>WBC</td>
<td>25,100 /μl</td>
</tr>
<tr>
<td>RBC</td>
<td>275 × 10^4 /μl</td>
</tr>
<tr>
<td>Hb</td>
<td>8.3 g/dl</td>
</tr>
<tr>
<td>Ht</td>
<td>23.9 %</td>
</tr>
<tr>
<td>PLT</td>
<td>28.1 × 10^4 /μl</td>
</tr>
<tr>
<td>APTT</td>
<td>40.0 seconds</td>
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<tr>
<td>PT</td>
<td>69 %</td>
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<tr>
<td>Fibrinogen</td>
<td>411 mg/dl</td>
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<tr>
<td>FDP</td>
<td>29.3 μg/ml</td>
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<tr>
<td>AT</td>
<td>56.1 %</td>
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</tbody>
</table>

Anti-GBS antibody, anti-glomerular basement antibody; APTT, activated partial thromboplastin time; AT, antithrombin; Hb, hemoglobin; Ht, hematocrit; MPO-ANCA, myeloperoxidase-anti-neutrophil cytoplasmic antibody; PLT, platelet count; PR3-ANCA, proteinase-3-anti-neutrophil cytoplasmic antibody; PT, prothrombin time; RBC, red blood cell count; WBC, white blood cell count.