Case Report

Amphetamine-indeced Myoglobinuric Acute Renal Failure

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A 36-year-old man was admitted because of sopor and dark urine after intravenous amphetamine injection. He subsequently developed myoglobinuria and acute renal failure. Serum myoglobin value was remarkably elevated to 83,000 ng/ml, and urine myoglobin was 400,000 ng/ml. Renal biopsy revealed tubular degeneration and tubular obstruction with myoglobin casts by immunofluorescence examination. Amphtamine-induced rhabdomyolysis was suspected to cause myoglobinuric acute renal failure.

Key Words: Amphetamine, Myoglobinuria, Acute renal failure, Rhabdomyolysis

Abuse of amphetamine may cause sweating, mydriasis, tachycardia, hyperactivity and confusion[1]. Severe over-dosage may be followed by delirium, circulatory collapse, convulsion and coma. Rhabdomyolysis and acute renal failure associated with amphetamine have been reported in several cases[2-8]. Presence of myoglobin have not been clearly demonstrated histologically in these cases.

In this report, we performed histological examination with immunofluorescence study and considered the pathogenesis of acute renal failure induced by amphetamine.

CASE REPORT

A 36-year-old Japanese man was admitted to the emergency room of Tuchiura Kyodo Hospital December 1986 in delirious state. He had abused amphetamine intravenously since 1970 to 1978. He had been in good health until one month before admission, and began amphetamine injection again since November 1986. He injected unknown dose of amphetamine intravenously in December 9. Within several hours after the injection, he became confused and excited. Sopor and dark urine were observed twelve hours after the injection.

On admission, his blood pressure was 142/70 mmHg; pulse, 72/min; body temperature, 36.2°C. Examination of the eyes, heart, lungs, abdomen and extremities was unremarkable. The hematocrit value was 42.8% and the WBC was 24100/cu mm with a normal differentiation. The platelet count was 124000/cu mm. The erythrocyte sedimentation rate, 15mm/hour; fibrinogen level, 169mg/dl; fibrinogen degeneration product level, above 40 μg/ml. The urine was dark brown with a pH of 6.5 and specific gravity of 1.030. Proteinuria 3+, urine occult blood 3+, granular casts were present. The urine volume was 200 ml per day. Serum electrolyte values were sodium 132 mEq/L, chloride 95 mEq/L, bicarbonate 19.7 mEq/L, and potassium 5.2 mEq/L. Other laboratory values were BUN 58 mg/dl, creatinine 5.1 mg/dl, glucose 161 mg/dl, albumin 4.5 g/dl, calcium 6.4 mg/dl, inorganic phosphate 11.8 mg/dl, uric acid 23.8 mg/dl, CPK 50348 U/L, SGOT 4840 U/L, and SGPT 3597 U/L. Serum myoglobin value was remarkably elevated to 83,000 ng/ml (normal range less than 60 ng/dl) and urine myoglobin was 400,000 ng/ml (normal negative). Renal ultrasonography revealed slightly enlarged kidneys without

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evidence of ureteral dilatation. The following tests were negative: ASO titer, rheumatoid factor, antinucleotid antigen, hepatitis antigen.

Although fluid replacement and furosemide were started intravenously, urine output remained low. On the third hospital day, the BUN level was 72 mg/dl and the serum creatinine level was 9.1 mg/dl. After one treatment of hemodialysis, hemofiltration was performed from the next day for five successive days. On the tenth hospital day, the urine volume gradually increased and hemodialysis was done once every two or three days. Consciousness level recovered in these days. Three weeks after the admission, BUN and creatinine values were 32 mg/dl and 2.5 mg/dl, when hemodialysis was discontinued.

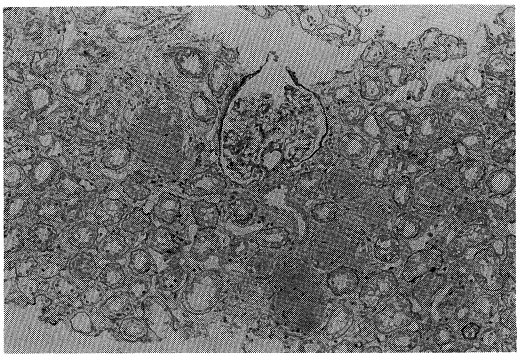

Fig. 1. Gromeruli showed no remarkable abnormalities. Interstitial edema and cell infiltrations were noted. Focal tubular necrosis and degeneration of tubular epithelial cells were observed. Eosinophilic substances occluded some tubular lumen. (hematoxylin and eosin stain; x 250).

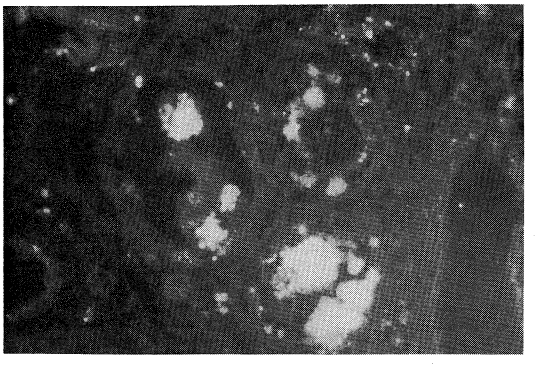

Fig. 2. On immunofluorescence examination, massive myoglobin casts were observed diffusely in tubular lumen. (x 400).

Renal biopsy was performed four weeks after the admission. On light microscopy, twenty-eight glomeruli showed no remarkable abnormalities, such as cell proliferation or crescent formation. There were interstitial edema and focal infiltration of lymphocytes, plasma cells and polymorphonuclear leukocytes. Focal tubular necrosis and degeneration of proxymal tubular epithelial cells were noted focally and eosinophilic substances occluded some tubular lumens (Figure 1). On immunofluorescence study, massive myoglobin casts were observed diffusely in tubular lumen. No significant myoglobin was detected in the glomeruli by immunofluorescence examination. (Figure 2).

DISCUSSION

In recent years, nontraumatic rhabdomyolysis and myoglobinuria have been reported as a cause of acute renal failure[5]. Many harmful effects caused by intravenous use of amphetamine have been described in humans[6] and in experimental animals[9]. In our knowledge, twelve cases of acute renal failure induced by amphetamine have been reported[2-8]. But in no case reports, presence of myoglobin in tubular lumen was demonstrated histologically by immunofluorescence examination. Reports of acute renal failure associated with amphetamine usage are listed in the Table 1.

The first case which was reported by Ginsberg et al.[2] demonstrated hyperpyrexia, coagulopathy and reversible renal failure after ingesting amphetamine. Penn et al.[3] suspected the possibility that amphetamine induced prolonged coma, immobility and these condition led low perfusion of muscle and myoglobinuric renal failure. Kendrick et al.[6] reported five patients who had injected phenmetrazine or methamphetamine developed septic shock, disseminated intravascular coagulation, rhabdomyolysis with myoglobinuria and azotemia. Scandling et al.[7] described a case of myoglobinuric renal failure after the ingestion of amphetamine in absence of prolonged coma or major myotonic factors. A case of acute interstitial nephritis associated with amphetamine was reported by Foley et al.[8], and they suggested that amphetamine alone, without hyperpyrexia or

Table 1. Reported cases of acute renal failure associated with amphetamine.

Case	Age	Sex	Drug	Myogrobinuria	Complication	Authors
1	21	M	amphetamine	+	fever, shock, DIC	Ginsberg et al[2]
2	?	?	methamphetamine	+	hypotension, coma	Penn et al[3]
3	19	M	dextroamphetamine	+	muscular exertion	Hamilton et al[4]
4	18	M	amphetamine	+	coma, dehydration	Grossman et al[5]
5	27	M	methamphetamine	+	fever, hypotension, DIC	Kendrick et al[6]
6	28	F	phenmetrazine	+	fever, hypotension, DIC	Kendrick et al[6]
7	27	F	phenmetrazine	+	fever, hypotension, DIC	Kendrick et al[6]
8	23	M	phenmetrazine	+	fever, hypotension, DIC	Kendrick et al[6]
9	23	M	phenmetrazine	+	coma, hypotension, DIC	Kendrick et al[6]
10	30	M	amphetamine	+	coma	Scandling et al[7]
11	32	M	amphetamine	−	interstitial nephritis	Foley et al[8]
12	36	M	amphetamine	+	coma	present case

muscle damage, may cause acute renal failure.

In our case, the patient injected unknown dose of amphetamine intravenously, and became confused and sopor. Dark urine and renal dysfunction were observed half a day after the injection.

The pathogenesis of acute renal failure in our case was suspected due to myoglobinuria and acute tubular necrosis, because the histological examination revealed tubular degeneration and obstruction of tubular lumen by myoglobin in immunofluorescence study. But other mechanisms, such as direct toxicity of amphetamine and renal vasoconstriction could not be strictly ruled out. Citron et al.[10] described a number of amphetamine abusers who had a syndrome indistinguishable from periarteritis nodosa. Vasospasmus was observed in cerebral vessels of drug users[11] and experimental animals injected with intravenous amphetamines[12]. In our case, no vascular abnormalities like periarteritis nodosa were found in renal histological examination. Myoglobinuria was considered caused by rhabdomyolysis, because of the remarkable elevation of muscle enzymes and serum myoglobin.

The mechanisms of rhabdomyolysis was considered as follows: prolonged immobitity, decreased muscle perfusion, coagulopathy, systemic hypotension and hyperpyrexia. In our case, the patient became immobile state for about half a day. The weight of the body on a limb raised the pressure of the muscle compartment to a high level enough to obstruct blood flow[3]. The decreased perfusion led muscle to ischemic and edemateous state. These conditions might contribute to depression of muscle metabolism and lead to rhabdomyolysis[13]. Damaged muscle might have released a tissue thromboplastin, activated platelet aggregation, and fibrin deposition. The release of creatinine phosphokinase, creatine, and probably adenosine diphosphate were supposed to promote platelet aggregation[14]. Finally, extensive leakage of plasminogen activator from muscle might have caused excessive fibrinolysis[15]. In our case, decrease of fibrinogen value and platelet count were noted and the level of fibrinogen degeneration product was increased. These coagulopathy might have possibility to make damages to muscle perfusion and renal blood flow.

On admission, blood pressure and body temperature were within normal range in our case. Some reported cases[2,3,6] showed hyperpyrexia and hypotension after amphetamine injection. There was a possibility that these symptoms might be present before admission, and might have some roles in the pathogenesis of rhabdomyolysis and acute renal failure.

In summary, a 36-year-old man became acute renal failure after injection of amphetamine. The renal biopsy findings indicated tubular degeneration and myoglobin casts. Serum and urine myoglobin concentration elevated high values. The pathogenesis of acute renal failure was considered rhabdomyolysis and myoglobinuria.

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