Postmortem Findings in Two Cases of Chronic Methamphetamine Abuse

Sohyung Park, Byung-Ha Choi

Department of Forensic Investigation, National Forensic Service, Wonju, Korea

Received: July 12, 2021
Revised: August 2, 2021
Accepted: August 19, 2021

Correspondence to

Sohyung Park
Department of Forensic Medicine,
National Forensic Service, 10
Ipchun-ro, Wonju 26460, Korea
Tel: +82-2-2600-4614
Fax: +82-2-2600-4828
E-mail: zzeva@korea.kr

We present two cases of death associated with chronic methamphetamine abuse. Several findings were observed in chronic methamphetamine abuse; pathologic changes in the heart and coronary artery, pulmonary embolism by foreign materials (drug materials), small scars on the subcutaneous vein on the arms with skin infection and sepsis, and so on. These complications can be fatal pathological findings that explain sudden death. The toxicological test results should be carefully interpreted; the presence of methamphetamine in the toxicological results should not automatically be interpreted as acute intoxication. A meticulous postmortem examination with review of the scene, circumstances and past history is crucial in identifying these findings and interpreting them appropriately.

Key Words: Methamphetamine; Cardiotoxicity; Pathology; Autopsy

Introduction

Methamphetamine is a sympathomimetic amine that is widely and illegally used as a stimulant in the world. According to the World Drug Report 2021 published by the United Nations, a growing trend in the use of methamphetamine has been reported in Korea [1]. This implies that the morbidity and mortality associated with methamphetamine abuse will also increase soon, which will have an impact on the public health, as well as acute intoxication. Therefore, it is important to review findings that can be observed in chronic methamphetamine abuse in Korea, so that

those findings will be helpful in the clinical practice for clinicians as well as forensic pathologists. Here, we present two cases of chronic methamphetamine abuse.

Case Report

1. Case 1

The deceased was a 67-years-old man, who was staying with a woman at a hotel for several days. They injected methamphetamine with mineral water into their arms and buttocks one day prior to his death. The next day, the deceased felt unwell and rested in the room all day. At night, he complained of abdominal pain,

difficulty in breathing, and was observed to suddenly collapse. The deceased was immediately transferred to a hospital, however, he died. According to the affidavit, methamphetamine was injected into each other in the past. It was understood that the family of the deceased also suspected methamphetamine abuse by him for decades. The deceased had a past history of chronic hepatitis C, somatoform autonomic dysfunction, acute streptococcal gingivostomatitis, chronic complex periodontitis, and panic disorder.

On external examination, edentulous mouth was observed. Several linear scars were identified on the abdomen and the right lower arm. Tattoos were observed on the left side of the chest, left shoulder and left arm, and on the right arm. Needle puncture marks were identified on the right side of the neck, anterior aspect of the left wrist, dorsum of the left hand, anterior aspect of the right lower arm, dorsum of the right hand, left inguinal area, and the medial side of the left and right ankles. Some of the marks were assumed to be related to the emergency treatment and resuscitation. No injuries were identified.

Upon internal examination, the heart weighed 478 g. The myocardium of the left ventricle showed patch fibrosis and both ventricles revealed mild dilatation; the circumference of tricuspid and mitral valves, and pulmonary and aortic valves were 14.5 cm, 11.8 cm, 9.8 cm, and 8.0 cm, respectively. The thickness of the right ventricle, interventricular septum, and left ventricular free wall were 0.4 cm, 1.2 cm, and 1.2 cm, respectively. The coronary arteries revealed asymmetric intimal fibrosis with mild luminal stenosis (approximately 30%–40%) (Fig. 1A, B). Patchy myocardial fibrosis and interstitial fibrosis (replacement fibrosis) were observed in the myocardium and papillary muscles (Fig. 1C). Myocyte hypertrophy with atypical nuclei, and an increased interstitium were identified (Fig. 1D). Foreign materials were observed in the pulmonary capillaries, which were also visualized as birefringent materials (Fig. 1E, F). The liver showed chronic hepatitis including lobular necrosis, acute and chronic inflammation of the portal tracts, and mild macrovesicular steatosis, which was consistent with history of chronic hepatitis C.

In the postmortem toxicological test, methamphetamine and amphetamine were found to be positive in the blood,

gastric contents, urine, skin and subcutaneous tissue around the needle mark on the right hand, and hair. The concentrations of methamphetamine in the heart and peripheral bloods were 1.26 mg/L, and 0.81 mg/L, respectively. In addition, escitalopram, trazodone, amitriptyline and nortriptyline were also found to be positive and their concentrations were within the therapeutic levels. The blood alcohol concentration was less than 0.010%. The postmortem biochemistry results were unremarkable.

The cause of death was determined to be a sudden cardiac death associated with chronic methamphetamine use, based on the findings of postmortem examination and studies, and the historical and circumstantial information.

2. Case 2

The deceased was a 48 years old man who was found dead and, naked in a motel room. He stayed in the motel and changed the rooms several times for a week. On the last night, an acquaintance visited him with food because the deceased told him that his condition was not good. The deceased did not go out but stayed all day in the room. The deceased had a criminal record of illegal drug abuse and it was assumed that it might be methamphetamine-related, according to the investigator's explanation. Small wrapped pouches containing an unknown powder were found with cigarettes in the cigarette packet.

On external examination, a small oval ulcer was observed in the mucosa of the lower lip. Small ill-defined localized scars that appeared to be old needle puncture marks, were identified on the anterior aspect of the left elbow, posterior aspect of the left lower arm, anterior aspect of the right elbow, and lateral aspect of the right lower arm. There were no significant injuries except for small contusions on the back and extremities.

Upon internal examination and microscopic examination, the lower lobe of the left lung showed acute lobar pneumonia with purulent pleuritis and pyothorax (approximately 190 mL). The heart weight was 365 g. The left and right coronary arteries showed mild stenosis of atherosclerosis (30%). Myocyte hypertrophy and, perivascular and interstitial fibrosis were observed in the myocardium (Fig. 2A). Septic

Fig. 1. In case 1, intimal thickening is observed in the coronary artery (H&E, $\times 10$) (A), and asymmetric intimal fibrosis is observed (Masson's trichrome, $\times 10$) (B). The myocardium shows patchy fibrosis (H&E, $\times 40$) (C), and myocyte hypertrophy (H&E, $\times 200$) (D). Foreign materials are observed in pulmonary capillaries (H&E, $\times 100$) (E), which are also visualized as birefringent materials (F).

emboli were identified in a few microvessels of the myocardium with interstitial hemorrhage and mild inflammation around them (Fig. 2B). A focal

microscopic ulcer with intradermal microabscesses was observed in the epidermis of the scars of the left arm. Acute inflammation with small clusters of bacteria,

hemorrhage, and fibrosis were also observed in the dermis and subcutaneous fibroadipose tissue of the scars (Fig. 2C, D). The subcutaneous vein under the scars revealed septic emboli.

In the postmortem toxicological tests, methamphetamine, and amphetamine were found to be positive in the blood, urine and hair. The concentrations of methamphetamine in the heart and peripheral blood were 0.87 mg/L, and 0.78 mg/L, respectively. In addition, topiramate was positive in the blood and the concentration was within the therapeutic range. The blood alcohol concentration was less than 0.010%. The postmortem biochemistry on the vitreous humor revealed high urea nitrogen (80.8 mg/dL; reference range, 4–23 mg/dL) and creatinine (3.06 mg/dL; reference range, 0.5–1.2 mg/dL). The procalcitonin

level on the postmortem blood was also high (19.31 ng/mL; reference range <0.50 mg/dL). A postmortem microbiology culture of the abscess of the left pleura revealed *Staphylococcus aureus*, and *Morganella morganii*.

The cause of death was determined as sepsis in a man with methamphetamine toxicity.

Discussion

These two cases illustrate the various postmortem findings related to chronic methamphetamine abuse. The scene and circumstances gave an impression of chronic methamphetamine abuse, such as the past history of methamphetamine injection and abuse for a long time, the criminal record of illegal drugs (assumed

Fig. 2. In case 2, perivascular and interstitial fibrosis are observed in the myocardium (H&E, ×40) (A). A septic emboli is identified in a small vessel in the myocardium (H&E, ×200) (B). A small ulcer with infection is observed in the epidermis (H&E, ×100) (C), and small abscesses with bacteria are observed in the subcutaneous tissue (H&E, ×200) (D).

to be methamphetamine-related) and unknown white powder found in the personal effects. On postmortem examination, recent needle puncture marks, irregular linear scars, and skin infections were identified on the arms or legs which can be easily accessed for injection. Systemically, pathologic changes in the heart that can cause susceptibility to cardiac arrhythmias with an increased risk of sudden death, pulmonary embolism of foreign materials, and systemic infection were observed. The results of the toxicological tests supported chronic methamphetamine abuse within the presence of methamphetamine in the hair.

It is very important to recognize the morbidity associated with chronic methamphetamine abuse. This is because it is critical to determine the manner of death as well as the cause of death, and to interpret as the results of the toxicological tests. As the manner of death can be determined as natural when a deceased died of the morbidity associated with chronic alcoholism, the manner of death can be considered as natural if a deceased died of complications associated with chronic methamphetamine abuse. The interpretation of the postmortem blood level of methamphetamine should be done carefully, because it is impossible to assess drug tolerance in toxicology tests, and because postmortem redistribution should be also considered due to the release from the heart after death where methamphetamine is concentrated [1]. In a study comparing a group in which methamphetamine toxicity was ruled as the cause of death, and a group that the cause of death other than methamphetamine toxicity, such as trauma, the mean blood levels of methamphetamine were not statistically different between the two groups [2]. Therefore, the presence of methamphetamine in postmortem blood, cannot be ruled automatically as acute methamphetamine intoxication. It is necessary to review the scene, circumstances, postmortem findings and the results of ancillary testing in context.

The pathologic changes in the heart is well known in chronic methamphetamine abuse, including hypertrophy, interstitial fibrosis and microvascular disease [2–5]. Coronary artery disease and myocardial infarction, pulmonary hypertension, cardiomyopathy, or aortic dissection can occur in methamphetamine

abusers, which can be fatal pathological findings to explain the cause of death. The pathophysiology is that catecholamine toxicity indirectly mediated by methamphetamine would cause endothelial and smooth muscle injuries, resulting in intimal hyperplasia of the coronary artery and myocardial injury as well as a direct effect on the cardiomyocytes [2,5]. These effects of methamphetamine also accelerate heart disease [2]. In case 1, the deceased had a hypertrophied heart with remodeling and coronary intimal fibrosis, a potentially fatal pathologic substrate that can lead to sudden death [2–4]. In case 2, focal interstitial and perivascular fibrosis was also observed in the myocardium, which could not be explained by other findings of the heart, including the normal heart weight and only mild stenosis of the coronary artery without any other medical history. This suggests that chronic methamphetamine abuse can promote or aggravate cardiovascular diseases. If necessary, the reviewing of the toxicological results would be also helpful in cases of fatal cardiovascular diseases.

Pathologic findings related to methamphetamine abuse can be observed in other organs; pulmonary embolism, pneumonia, acquired immune deficiency syndrome, and emphysema [2]. When drug tablets are crushed and intravenously injected, pulmonary embolism due to the insoluble fillers of the drug, such as microcrystalline cellulose, corn starch, or cotton fibers, can be observed in the pulmonary vessels, which can be seen as birefringent crystals. In case 1, some amorphous foreign materials were observed in the pulmonary capillaries, which were also visualized as birefringent materials. This finding could be explained by the fact that the deceased dissolved methamphetamine into mineral water and injected it into the arm and buttock. Chronic hepatitis consistent with history of chronic hepatitis C, edentulous mouth, and other past histories including somatoform autonomic dysfunction, acute streptococcal gingivostomatitis, chronic complex periodontitis, and panic disorder, could be also complications associated with chronic methamphetamine abuse.

When needle puncture marks or scars are observed along the subcutaneous vein on the arm or legs, a microscopic examination of these sites may provide

helpful information. In case 2, small, ill-defined scars were identified along the subcutaneous vein on both lower arms. Skin infection and inflammation with bacterial clusters were observed microscopically, which could explain systemic inflammation with septic emboli. Acute lobar pneumonia with purulent pleuritis and pyothorax was also observed, however, the possibility of hematogenous spread from the skin and subcutaneous infection cannot be excluded [6], based on the histologic findings and the circumstance of death. Occasionally, tattoos may be observed at the common sites of injection, making it difficult to identify injection marks. When cardiopulmonary resuscitation and emergency treatments are performed, it may be impossible to distinguish true needle puncture marks related to drug abuse from those of medical intervention during resuscitation. In case 1, it was impossible to find any other needle puncture marks or scars on the left arm, because a large tattoo covered most of the left arm.

These various findings associated with chronic methamphetamine use illustrated in our cases would be also helpful for clinicians as well as forensic pathologists. When they see a patient with cardiovascular disease that can be potentially fatal, clinical assessment, including the past history and physical findings related to drug abuse is necessary. Fournier gangrene after penile methamphetamine injection, aortic dissection and intracerebral hemorrhage due to vasculitis related to methamphetamine use have been previously reported in Korea [7-10]. However, to the best of our knowledge, the various findings which may be observed in chronic methamphetamine abuse in Korea, are not well known. We were able to present various systemic findings from our cases through postmortem examination. We hope that these findings will be helpful in diagnosing chronic methamphetamine abuse.

In summary, we present two cases of chronic methamphetamine abuse. To determine the cause of death and the manner of death in methamphetamine abusers, forensic pathologists should be aware of the complications associated with chronic abuse as well as acute intoxication. A meticulous postmortem examination with a careful review of the scene, circumstances and history is necessary and caution

should be exercised when interpreting the results of toxicological tests. If necessary, the possibility of chronic methamphetamine abuse should be also considered in fatal cardiovascular diseases.

ORCID: Sohyung Park: <https://orcid.org/0000-0002-1987-7908>; Byung-Ha Choi: <https://orcid.org/0000-0002-9401-1725>

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Acknowledgments

This study was supported by the National Forensic Service Clinical Research Fund (NFS2021CLI11), and was approved by the National Forensic Service Institutional Review Board (906-210118-BR-014-05).

References

1. United Nations Office on Drugs and Crime. World drug report 2021, booklet 4 - Drug market trends: cocaine, amphetamine-type stimulant [Internet]. Vienna: United Nations Office on Drugs and Crime Available; 2021 [cited 2021 Aug 10]. Available from: https://www.unodc.org/unodc/en/data-and-analysis/wdr-2021_booklet-4.html.
2. Karch SB, Drummer OH. Karch's pathology of drug abuse. 5th ed. Boca Raton, FL: CRC Press; 2016. p. 273-318.
3. Kaye S, McKetin R, Dufou J, et al. Methamphetamine and cardiovascular pathology: a review of the evidence. *Addiction* 2007;102:1204-11.
4. Schwarzbach V, Lenk K, Laufs U. Methamphetamine-related cardiovascular diseases. *ESC Heart Fail* 2020;7:407-14.
5. Cohle SD. Fatal coronary artery intimal hyperplasia due to amphetamine use. *Cardiovasc Pathol* 2013;22:e1-4.
6. Naraqi S, McDonnell G. Hematogenous staphylococcal pneumonia secondary to soft tissue infection. *Chest* 1981;79:173-5.
7. Yang DW, Kang JK, Lee SA, et al. Cerebral vasculitis and intracranial hemorrhage associated with methamphetamine abuse. *J Korean Neurol Assoc* 1996;14:1055-9.
8. Moon HS, Lee JH, Choi HY, et al. A case of Fournier gangrene after penile methamphetamine injection. *Korean J Androl* 2010;28:223-5.
9. Na JY, Kim JJ, Park JT. A fatal intracerebral hemorrhage due to chronic methamphetamine use. *Korean J Leg Med* 2018;42:98-101.
10. Han SW, Kim KS, Kim MJ, et al. A case of acute dissection of the aorta associated with methamphetamine abuse. *J Korean Soc Echocardiogr* 1999;7:75-9.