

## Chronic heart failure in a long-standing methamphetamine abuser

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### Abstract

**Background:** Amphetamine-type stimulant (ATS) often damages cardiomyocytes through its sympathomimetic properties. Here, we present an autopsy case report describing ATS-associated cardiomyopathy (ATSAC) in an individual with a history of methamphetamine abuse of over 30 years.

**Case report:** A 50-year-old man was found deceased at his home. Just 3 days before his death, he had been released from prison after serving a 3-year sentence, during which period he had stopped drug use. Although the hearts of patients with ATSAC are generally hypertrophic or dilated, his heart showed a normal appearance. Histologically, heart failure cells were evident in the lungs. The myocardium consisted of a mixture of hypertrophic and atrophic cardiomyocytes. Contraction band necrosis and lipofuscin accumulation were

evident. Immunostaining for tenascin C was negative. These findings indicated extensive damage to the cardiomyocytes. We diagnosed the cause of his death as pulmonary edema due to chronic heart failure, despite the normal appearance of the heart. ATSAC is generally reversible after cessation of drug use. However, in this case, extreme long-standing abuse of methamphetamines resulted in severe damage to cardiomyocytes and consequent loss of recovery capacity.

**Conclusion:** To the best of our knowledge, this is the first case report describing atrophic cardiomyocytes in a long-standing ATS abuser. The present findings highlight the importance of histopathological examination in such cases, regardless of external tissue appearance.

**Key Words:** methamphetamine, long-standing abuse, cardiomyopathy, chronic heart failure

## INTRODUCTION

Amphetamine-type stimulants (ATS) cause various medical complications. ATS are sympathomimetic because their administration increases intra-synaptic levels of monoamines with effects on the cardiovascular system. Medicolegally problematic complications by ATS include coronary artery disease, malignant hypertension, and cardiomyopathy.

ATS-associated cardiomyopathy (ATSAC) is common and should be considered as a cause of death. An epidemiological study demonstrated that methamphetamine users had hypertrophic and heavier hearts compared with those of the control group (1). A recent review reported that most patients with ATSAC exhibit severe dilated cardiomyopathy (2). According to these studies, hearts with ATSAC tend to have increased volume and weight.

Here, we report a rare autopsy case of a methamphetamine abuser without apparent macroscopic findings, such as hypertrophy or dilation, in the heart. Notably, the deceased patient had an extremely long history of ATS abuse (more than 30 years). According to past clinical reports, to the best of our knowledge, the longest reported duration of drug use in a patient with ATSAC was 17 years (3). The present case report describes unique morphological and pathological changes in a long-standing ATS abuser.

## Case report

A 50-year-old man was found dead at his home. Although paramedics were called, resuscitation was not performed. The day before his death, the deceased had experienced a brief loss of consciousness when he talked with his son and friend but recovered quickly. The deceased had a history of methamphetamine abuse for more than 30 years, and had been arrested 19 times for violations of the Stimulants Control Act. According to the police log, he only used methamphetamine by intravenous injection. Just 3 days before his death, he had been released from prison after serving a 3-year sentence, during which period he had stopped drug use. Medico-legal autopsy was performed approximately 30 h after death owing to suspicion of recidivism.

## Autopsy findings

The deceased was 157 cm tall and weighed 62.0 kg. There were no signs of trauma, including needle marks, on his body. Alcohol was not detected in the blood and urine. No drugs, including ATS, were detected in the blood or urine by comprehensive toxicological screening using high-performance liquid chromatography equipped with a photodiode array detector (PDA-HPLC; Class-VP system, Shimadzu, Kyoto, Japan).

No intracranial hemorrhage was observed. The heart, which contained 100 mL of fluid blood, weighed 287 g. There were no atherosclerotic lesions or stenosis in the coronary arteries. The

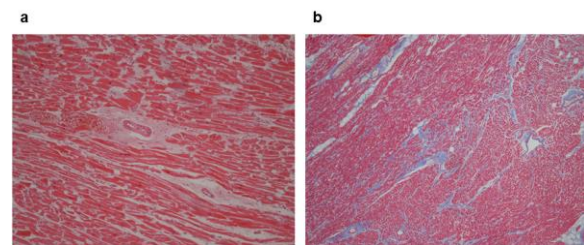
thickness of the myocardial wall was 0.8 cm, left ventricle; 0.8 cm, septum; and 0.3 cm, right ventricle. The mitral and aortic ring did not show dilatation. Hence, no remarkable findings of hypertrophy and dilatation were observed in the heart (Figure 1). The volumes of pleural fluid were 20 mL, left side; and 15 mL, right side. The left and right lungs weighed 534 g and 663 g, respectively, and showed remarkable congestion. No other macroscopic lesions, other than congestion, were observed in the vital organs.



**Figure 1.** External appearance of the heart: hypertrophy and enlargement were not observed.

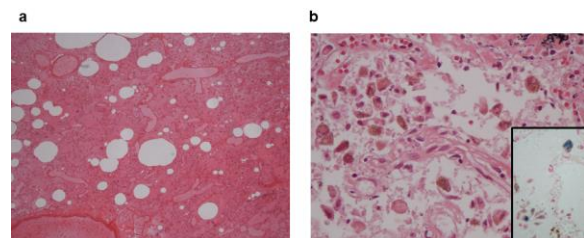
Microscopic examination revealed a mixture of cardiomyocytes of various sizes; an irregular arrangement of hypertrophic and atrophic myocardial fibers was diffusely observed (Figure 2a). Lipofuscin, a wear-and-tear

pigment, was detected in cardiomyocytes (data not shown). Evident perivascular fibrosis was observed on Azan staining (Figure 2b). Immunostaining for tenascin C was negative (data not shown).



**Figure 2.** A: Myocardium consisting of hypertrophic and atrophic cardiomyocytes (H&E staining, 100 $\times$ ). B: Evident perivascular fibrosis (Azan staining, 100 $\times$ ).

The lungs showed severe congestion and edema (Figure 3a). Hemosiderin-containing macrophages, i.e., heart failure cells, were observed in the lungs (Figure 3b). The existence of hemosiderin was confirmed by Berlin blue staining (Figure 3b, inset). No other pathological lesion was apparent.



**Figure 3.** A: Severe congestion and edema in the lung (H&E staining, 40  $\times$ ). B: Presence of numerous heart failure cells in the lung (H&E staining, 400  $\times$ ); inset: Berlin blue staining confirmed the presence of phagocytized hemosiderin (400  $\times$ ).

## Discussion

Methamphetamine may be detected in the blood and urine for approximately 2 and 3 days after drug use, respectively (4). We did not detect methamphetamine in the blood or urine samples obtained 30 h after death by comprehensive toxicological screening. Furthermore, because the deceased had been released from prison just 3 days before his death and needle marks were not seen on his body, we concluded that methamphetamine use was unlikely before his death. The cardiomyocytes demonstrated characteristic pathological changes. Obvious edema and the emergence of hemosiderin-containing macrophages in the lungs suggested congestive heart failure. Other lesions were not detected. Toxicological analysis excluded death by intoxication. We, thus, identified the cause of death as pulmonary edema due to chronic heart failure. We could not present direct evidence implicating ATS abuse as the cause of cardiomyopathy. However, as it was obvious that the deceased had abused ATS over a long period, the potential role of ATS abuse in the observed cardiomyopathy and eventual death could not be ignored.

Several clinical reports have demonstrated that ATSAC is reversible (3, 5). Even patients who have abused ATS for over a decade have recovered from ATSAC after the cessation of drug use. Similar recovery has been observed in animal models (6). However, in the present case, ATSAC-induced chronic heart failure led to death, despite an apparent lack of drug use for at

least 3 years. This indicates that the long-standing use of ATS damaged the individual's cardiomyocytes. This inference was confirmed by immunostaining for tenascin C, a sensitive marker for myocardial remodeling (7). Negative tenascin C staining and the accumulation of lipofuscin suggested extensive damage to cardiomyocytes, resulting in a loss of recovery capacity.

Damage to cardiomyocytes influences the external appearance of the heart. The most striking macroscopic feature of ATSAC is an increase in heart weight; methamphetamine users typically suffer from hypertrophic or dilated cardiomyopathy (1, 2). However, the deceased had a normal appearance of the heart. Although an increase in hypertrophic myocardial fibers is the most common pathological change in ATSAC (8), the myocardium of this individual contained a significant portion of atrophic cardiomyocytes. Thus, increase in the number of damaged and atrophic cardiomyocytes was considered to offset the hypertrophic changes, explaining the normal-looking heart.

Fibrosis, especially in the perivascular area, is a common finding in ATSAC, even in the absence of coronary occlusion (8). Because fibrotic lesions are a risk factor for arrhythmia, the brief unconsciousness on the day before his death may have been caused by arrhythmia. Arrhythmia may have been associated with the direct cause of death.

## Conclusion

The histological findings in this case suggest that the observed severe atrophy of cardiomyocytes resulted in heart failure, despite the normal appearance of the heart. The interruption in drug use owing to imprisonment may have restored normal cardiac condition. However, repeated and long-term ATS administration results in irreversible damage to the heart. ATS increased intra-synaptic levels of catecholamines via release from vesicles and inhibition of reuptake. Catecholamine directly induces disseminated focal myocardial degeneration and necrosis, and it indirectly injures cardiomyocytes by vasospasm-related shortage of oxygen. Animal studies have shown that long-term administration of ATS causes histopathological changes in cardiomyocytes, such as atrophy and fibrosis, as observed in the present case (9, 10). However, as far as we know, this is the first case report describing atrophic cardiomyocytes in a long-standing abuser. The present findings highlight the importance of histopathological examination, regardless of external tissue appearance.

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**Author contribution:** SK performed the autopsy and drafted the manuscript. TK contributed to the pathological interpretation and edited the manuscript. RK, KY, and HK edited

the manuscript and contributed to the interpretation of autopsy findings.

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