Forensic Science International 212 (2011) e1–e4

Contents lists available at ScienceDirect

Forensic Science International

journal homepage: www.elsevier.com/locate/forsciint

Case report

The unique histology of methamphetamine cardiomyopathy: A case report

Steven B. Karch

P.O. Box 5139, Berkeley, CA, USA

ARTICLE INFO

Article history:
Received 8 December 2010
Received in revised form 29 April 2011
Accepted 30 April 2011
Available online 12 June 2011

Keywords:
Methamphetamine
Heart failure
Cardiomyopathy
Myocardial infarction
Scar-reentry
Myocardial remodeling

ABSTRACT

This report describes the histological changes observed in the heart a young methamphetamine abuser who died of heart failure. Most of the microscopic changes in the heart have previously been described in experimental animals, but never clearly illustrated in man. Gross examination of the heart revealed concentric myocardial hypertrophy (heart weight 470 g versus median predicted weight of 312 g). Areas of old myocardial infarction were also evident, along with enzymatic evidence indicating that a new infarct had occurred. Myocardial remodeling was extensive with perivascular and interstitial fibrosis, cellular vacuolization, and ongoing myocyte destruction with proliferation of fibromyocytes in the intestitum. Of note were the widespread, bizarre looking, distorted, cell nuclei. They were reminiscent of those seen in viral-induced dilated congestive cardiomyopathy. Clinical chemical measurements also showed unequivocal evidence of both evolving infarction and profound heart failure, with a BNP $>$ 5000. This pattern has not previously been reported in humans, probably because forensic pathologists rarely examine the hearts of methamphetamine abusers microscopically. If the pattern observed here is typical for methamphetamine-induced cardiotoxicity, it could well explain increasing reports of heart failure in methamphetamine abusers. It might also be diagnostic for the disorder.

1. Introduction

Epidemic methamphetamine abuse in the United States, particularly in Hawaii [1,2], began in the early 1990s and somewhat earlier in Japan [3]. Since this drug was first introduced, the prevalence of methamphetamine toxicity has increased dramatically around the world. Three different retrospective autopsy series have been published on methamphetamine-related deaths [3,4], but only one included histology [5].

Methamphetamine abuse accounts for 40% of all patients under the age of 45 years admitted to hospitals with cardiomyopathy [7]. Recently, a United States registry containing information on more than 11,000 patients with decompensated heart failure reported that more than 5% were stimulant abusers [6]. In Hawaii, more than 20% of young people with heart failure were found to be former or active methamphetamine abusers. Published histological studies have involved mainly (with the exception of some un-translated work) been of experimental animals, mainly rats or mice [8–11]. Whether the results of these studies accurately reflect the underlying process in man is open to question. For example, in some of the animal studies, methamphetamine treatment has resulted in eccentric left ventricular hypertrophy [12], while in others, the pattern of left ventricular hypertrophy appears to be exclusively concentric [10], reflecting the pattern normally observed in humans [5].

In the animal studies, hypertrophy, cellular dissolution, contraction band necrosis (also referred to as colliquative myocytolysis) which may be present to a variable degree, fiber disarray, vacuolization, and fibrosis are always apparent with light microscopy. With electron microscopy, additional changes such as mitochondrial translocation and swelling of the sarcoplasmic reticulum are evident. The most recent studies suggest that these alterations are induced by oxidative stress [11,12].

In our 1999 study of 413 methamphetamine-related deaths, interstitial fibrosis was the fifth most common histological finding and, compared to age-matched controls, nearly one quarter suffered from moderate to severe multiple coronary artery disease [5]. There are many manifestations of methamphetamine cardiotoxicity, but the three most discussed are myocardial infarction, dissecting aneurysm, and cardiomyopathy. The case reported here demonstrates most of the same changes seen in animal models of cardiomyopathy but, in addition, also present was striking nuclear atypism, of the type normally seen in non-methamphetamine associated dilated congestive cardiomyopathy.

2. Case report

The decedent, a 23-year-old man, had been paraplegic for 5 years following a T2 transsection. He was bed bound and suffered from massive decubitus ulcers of the sacrum and buttocks. He had been treated for all the usual sequalae of paraplegia, including

0379-0738/$ – see front matter © 2011 Elsevier Ireland Ltd. All rights reserved.
doi:10.1016/j.forsciint.2011.04.028

recurrent urinary tract infections. He was known to have been a chronic methamphetamine and marijuana smoker prior to his injury, and he continued to use both drugs afterwards. One week prior to his death he had presented at a local hospital complaining of chest pain and shortness of breath. A Pulmonary Ventilation/Perfusion Scan (V/Q scan) revealed no emboli, but it did show an enlarged heart. The following week the man was found at home, in bed, pulseless. Paramedics transported him to the hospital where he was converted from assystole to sinus tachycardia, albeit remaining hypotensive, requiring vasopressor support at all times.

Blood and urine cultures, and a screening urine toxicology test were collected at the hospital; the urine screening tests indicated the presence of both THC metabolite and amphetamines. The patient was intubated and sent to the Intensive Care Unit where he died 12 h later. EKG in the Emergency Room showed only sinus tachycardia. Initial blood tests, including screening tests for myocardial infarction were negative; Troponin I was 0.01 while the CK was 65 U/l (range 30–200). However, 5 h after admission there was a profound rise in the cardiac enzymes. The CPK, CK and Troponin I had risen to 2400, 1800 and 600 ng/ml (normal $<$ 0.29 ng/ml) respectively. The concentration of plasma ß-naturetic peptide was 8119.5 pg/ml (normal $<$ 99).

Autopsy was performed 5 days after death. The decedent was 170 cm tall, and weighed 170.6 kg (BMI = 26.3). Straw colored effusions, approximately 200 cm^3 each, were present in both pleural cavities. Another 10 cm^3 of straw colored fluid was present in the pericardium. The right lung weighed 1000 g and the left 700 g; both were severely edematous. No emboli were found. The heart weighed 470 g (predicted mean weight 312 g) and the left ventricle was thickened, measuring 1.7 cm. The ventricles were said to appear dilated. Histochemical staining for apoptosis was not performed nor was this change apparent to the naked eye. There were multiple areas of old infarction, but the actual number was not specified in the original report. No coronary thrombi were identified and there was no significant coronary artery disease was apparent. The liver weighed 1900 g and was said to have the appearance of "cardiac cirrhosis." The left kidney weighed 200 g and the right weighed 190 g. The right kidney contained brown calculi. There was no urine in the bladder. No abscesses were seen anywhere in the body and there was no evidence of sepsis.

Analysis of the plasma specimen obtained in the hospital disclosed a methamphetamine concentration of 260 ng/ml and a carboxy-THC of 59 ng/ml. Amphetamine (the principle methamphetamine metabolite) was not measured and no other drugs were detected on a limited drug screen. Autopsy blood was collected for culture but never tested, while the hospital cultures (both blood and urine) were discarded at time of death. Tissues were collected for histological examination and stored in formalin, but were never processed. The cause of death was attributed to urosepsis secondary to long-standing paraplegia. Contributing factors were said to be "cardiomegaly, cardiac cirrhosis of the liver," and pulmonary edema.

Several years later the case was reassessed and tissue from four blocks of preserved heart were processed. Multiple abnormalities were evident. These included generalized myocyte vacuolization, enlarged, bizarre shaped nuclei (see Fig. 1), and generalized myocyte hypertrophy with some "box car" nuclei. There was also marked perivascular fibrosis and ongoing interstitial fibrosis (see Figs. 2–5).

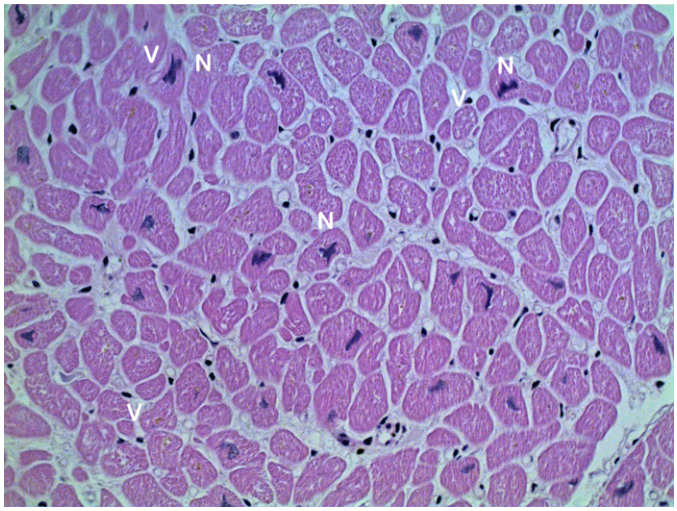

Fig. 1. H&E stain, 40× original magnification: the micrograph illustrates both myocyte vacuolization and large, abnormal, myocyte nuclei. Vacuoles are a relatively non-specific finding, commonly seen when there is chronic ischemia and also seen in dilated cardiomyopathy.

3. Discussion

The decedent had acute, enzymatically proven, myocardial infarction and heart failure as evidenced by markedly elevated BNP concentrations. Concentrations of BNP are also elevated in patients with myocardial ischemia, though the levels associated with ischemia are far lower (in the 100s) than were observed here. BNP concentrations are known to correlate with both the severity of symptoms and outcome in heart failure [13] and the BNP concentration of 8119 pg/l, drawn while the decedent was being resuscitated, is consistent with NYHA (New York Heart Association) class IV heart failure [13,14]. BNP concentrations greater than 700 pg/ml predict high mortality.

Save for the presence of bizarre, atypical cell nuclei, the histological picture seen here overlaps with the pattern described in experimental animals: myocardial remodeling manifested by concentric hypertrophy, interstitial and perivascular fibrosis and myocyte vacuolization [16,17]. However, in this case, medial hypertrophy of intra-cardiac arterioles was also evident, and none of the animal studies reported to date have displayed evidence of either small vessel medial hypertrophy or nuclear abnormalities.

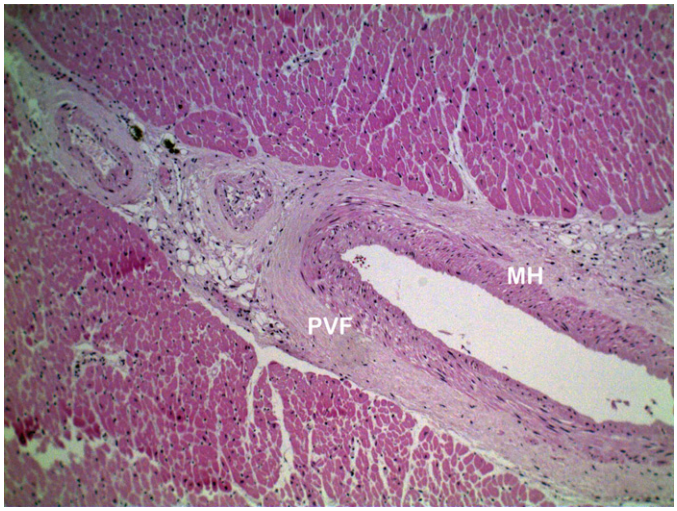

Fig. 2. H&E stain, 10× original magnification: region of dense perivascular fibrosis surrounding arteriols, but also showing evidence of intense vacuolization. Compression of the vessels is evident and may well have contributed to the decedent's final episodes of infarction.