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S. D'Errico, S. Niballi, D. Bonuccelli

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**Aortic dissection in cocaine abuse: a fatal case**

D'Errico S.\* PhD, Niballi S.\* MD, Bonuccelli D.\* MD

*\*Department of Legal Medicine, Azienda USL Toscana Nordovest Lucca, Italy*

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## Introduction

Cocaine is a naturally occurring alkaloid extracted from the leaves of *Erythroxylum coca*, first isolated by the chemists Dr Gaedcke and Dr Nieman in 1860. Cocaine is cleared through tissue uptake and is metabolized by liver and plasma esterases into active and inactive metabolites that are eventually excreted in the urine. The onset and duration of cocaine's effects depend on its route of use, consequently varying its cardiovascular and hemodynamic effects. In general the intravenous and inhaled routes have a very rapid onset of action (seconds) and short-lived (30 min) duration compared with the mucosally absorbed (e.g. oral, nasal, rectal, vaginal) routes. The excretion of cocaine and its metabolites is not affected by cocaine's route of ingestion; the half-life of cocaine is usually 60 to 120 min and that of its metabolites is approximately 4 to 7 h. These half-lives can be considerably prolonged however, with repeated dosing [1]. Cocaine abuse represents a considerable threat to the integrity of the cardiovascular system. In contrast to other addictive drugs that exert their harmful effects through a limited mechanism, cocaine has a multitude of pathophysiological pathways by which it affects the cardiovascular system. Although cocaine-induced acute myocardial infarction remains a better-described entity, there is growing evidence that aortic dissecting is also an important cardiovascular complication of cocaine abuse [2]. It has been suggested that cocaine associated aortic dissection occurs in predominantly male patients with illicit drug abuse who were younger than patients with aortic dissection without cocaine use [3-5].

## Case report

We present the case of a 50 yo man found lifeless in his car. He was known as cocaine abuser and he spent all the night with his boyfriend sniffing cocaine. In the early morning rescues were alerted when he was found lifeless. He was a known heavy smoker affected by hypertension controlled with drugs. A complete post mortem examination was performed the day after death. Gross examination was unremarkable for external injuries. Pericardial tamponade was recorded with 300 cc of blood and a 210 gr clot in the pericardial sac. Wide haemorrhagic infiltration of ascending aorta with rupture of ascending aortic wall were recorded. Descending aorta was unremarkable. Cervico-thoracic organs were removed en bloc (Ghon): heart was normal in size (cm 12x10.5x5.5) with mild left ventricular overall concentric hypertrophy (gr 550 weighed); coronary study according to Baroldi and Fineschi method was unremarkable for lumen obstruction [6]. White foam on the main bronchi and pulmonary oedema were recorded. Gross examination of abdominal organs and brain were unremarkable. Stanford type A (DeBakey type II) aortic dissection with intimal flap entrance 1.5 cm above the aortic valve and medial mild hematoma extending to the aortic arch was detected exploring aortic lumen, where adventitial rupture site was observed 3.5 above leaflets, approximately (Fig. 1A-C). Samples of organs were collected for a complete histopathological study. Netlike myocardial fibrosis, compensatory interstitial hypertrophic cardiomyocytes with enlarged hyperchromatic nuclei and multiple foci of contraction band necrosis were observed. Samples of dissecting aorta were collected and stained with E&O, elastic van gieson and alcian blue (Fig 4A-D). Finally, toxicological examination was performed with GC/MS confirming acute cocaine intoxication (table 1).

## Discussion

The sympathomimetic action of cocaine is attributable to both peripheral and central mechanisms [7]. Cocaine prevents re-uptake of norepinephrine and other monoamines at the synaptic cleft by inhibiting the monoamine re-uptake protein in the presynaptic neuronal membrane. In addition, cocaine may act centrally to increase sympathetic nerve activity which results in increased norepinephrine release in the synaptic cleft. This induces super sensitivity of the adrenoceptors to catecholamines, resulting in amplification of the overall sympathetic tone [8-12]. Cocaine's

hemodynamic effect is dose-dependent; early stages of toxicity induce heart rate and blood pressure elevation (10% to 25% of baseline); advanced stages show further elevations in heart rate and blood pressure (although blood pressure drop might be seen as a result of sustained tachyarrhythmias). In late stages, a significant depressive effect is found, with severe bradycardia and circulatory failure. Importantly, because some cocaine metabolites continue to be active, they might exert cardiovascular effects similar to those of the drug itself [13,14]. Cardiovascular complications of cocaine use have been evermore widely recognized and include acceleration of atherosclerosis, coronary artery spasm, acute myocardial infarction, myocarditis, dilated cardiomyopathies, and cardiac arrhythmias [15,16]. In recent years, it has become increasingly evident that cocaine also serves as a predisposing factor for aortic dissection [17-21]. The association of aortic dissection and cocaine use was first reported by Edwards and Rubin in 1987; since then an increasing body of evidence has emerged concerning the relation of aortic dissection with cocaine use. In the large International Registry for Aortic Dissection (IRAD), which collected data on acute aortic dissection from 17 international centres, the prevalence of cocaine abusers among acute aortic dissection cases was only 0.5% [22]. In another study Hsue et al reported their 20-year experience with acute aortic dissection at an inner city hospital; remarkably their findings indicate that 37% treated for acute aortic dissection reported having used cocaine in the minutes or hours preceding their presentation [23-26]. Because of low incidence of aortic dissection in cocaine abusers (approximately 1% of patients), it has been suggested that the presence of pre-existent aortic disease allows a cocaine induced intimal injury to precipitate the aortic dissection process. The pathophysiology behind cocaine induced acute aortic dissection is multifactorial. Presumably the mechanism relates first to an underlying process that has weakened the elastic media of the aorta and, second, to the severe shear forces that result from the sudden and profound hypertension and tachycardia that accompany cocaine (particularly crack) use [27]. Cocaine by inhibiting the re-uptake of both epinephrine and norepinephrine at the neural synapses, leads to profound sympathetic stimulation that presumably causes such shear stress on the aorta's intima that a small tear occurs [28]. In the setting of cocaine use, such tears may occur most often at the ligamentum arteriosum because this region of the aorta is relatively fixed anatomically and is less able to withstand the accelerating aortic pressure wave that speeds down the aorta after ventricular contraction. Once such an intimal tear has occurred, the weakened aortic wall allows entry of luminal blood, followed by propagation of the dissecting hematoma down (and/or up) the aorta. This physiology is particularly acute with use of crack cocaine, after which the onset of systemic effects is almost immediate. It has been demonstrated that 13 of 14 patients with cocaine-related acute aortic dissection smoked crack cocaine. The rapid onset of action of smoked crack triggers an abrupt hemodynamic response and its short duration of action induces frequent use in short intervals, consequently exposing the patients to repeated bouts of hemodynamic stress [29,30]. Cocaine was shown to induce vascular smooth muscle cell apoptosis and cystic medial necrosis, with consequent vessel wall weakening; a pathological finding that might also serve to explain cocaine-related coronary and carotid artery dissections [31-36]. An echocardiographic study conducted in chronic cocaine abusers (average 10 years) showed a reduction in aortic compliance and an increase in thoracic aortic dimensions and stiffness compared with normal controls [37]. Another possible mechanism is that chronic cocaine use itself may lead to premature atherosclerosis. It has been postulated that recurrent cocaine exposure makes the endothelium more permeable to atherogenic low density lipoprotein and may accelerate the migration of leukocytes to the aortic wall. Thus, predisposition to aortic dissection could include not only the impact of hypertension but chronic cocaine's effects on the aorta as well [38]. Clinical manifestations of aortic dissection may occur within minutes after cocaine exposure or up to 24 hours later [39]. Pain is the most common symptom. Pain has also been described in the neck, jaw, lumbar region, flank, abdomen and extremities depending on the location and extent of dissection. In patients with cocaine-related aortic dissection, hypertension occurs at

presentation in 75-80% of cases compared with approximately 50% of cases unrelated to cocaine use. However hypotension may occur [40,41]. Anyway, few fatal cases are reported, probably because of lack of post mortem investigation at the moment of death [42-44]. Because of large use of cocaine in young patients due to its high addiction potential and its ready availability, in case of acute onset chest pain, cocaine-related aortic dissection should be always suspected and investigated. In fatal cases, cocaine abuse should be highly suspected and a complete post mortem investigation should be performed. This case want to be a strong reminder of the association between a major public health problem and a life-threatening disease.

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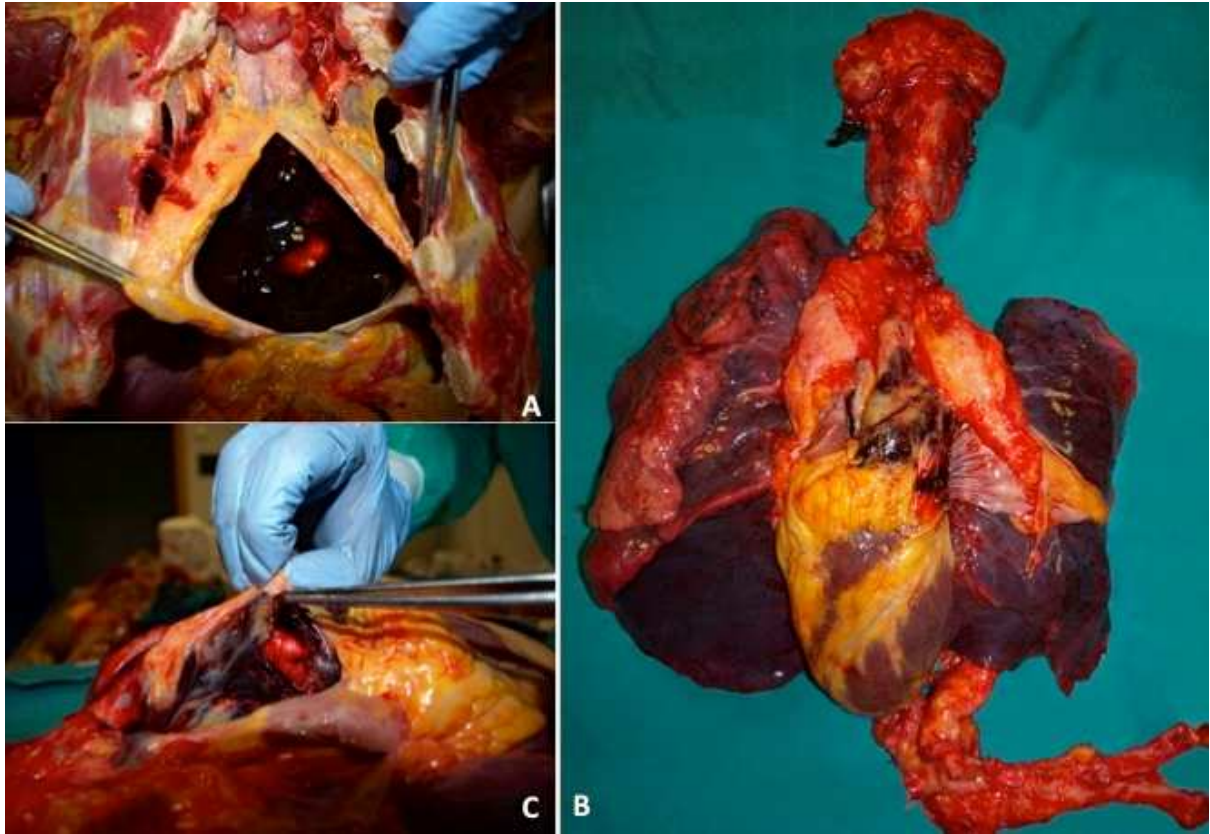
Table 1. Toxicological analysis (GC/MS).

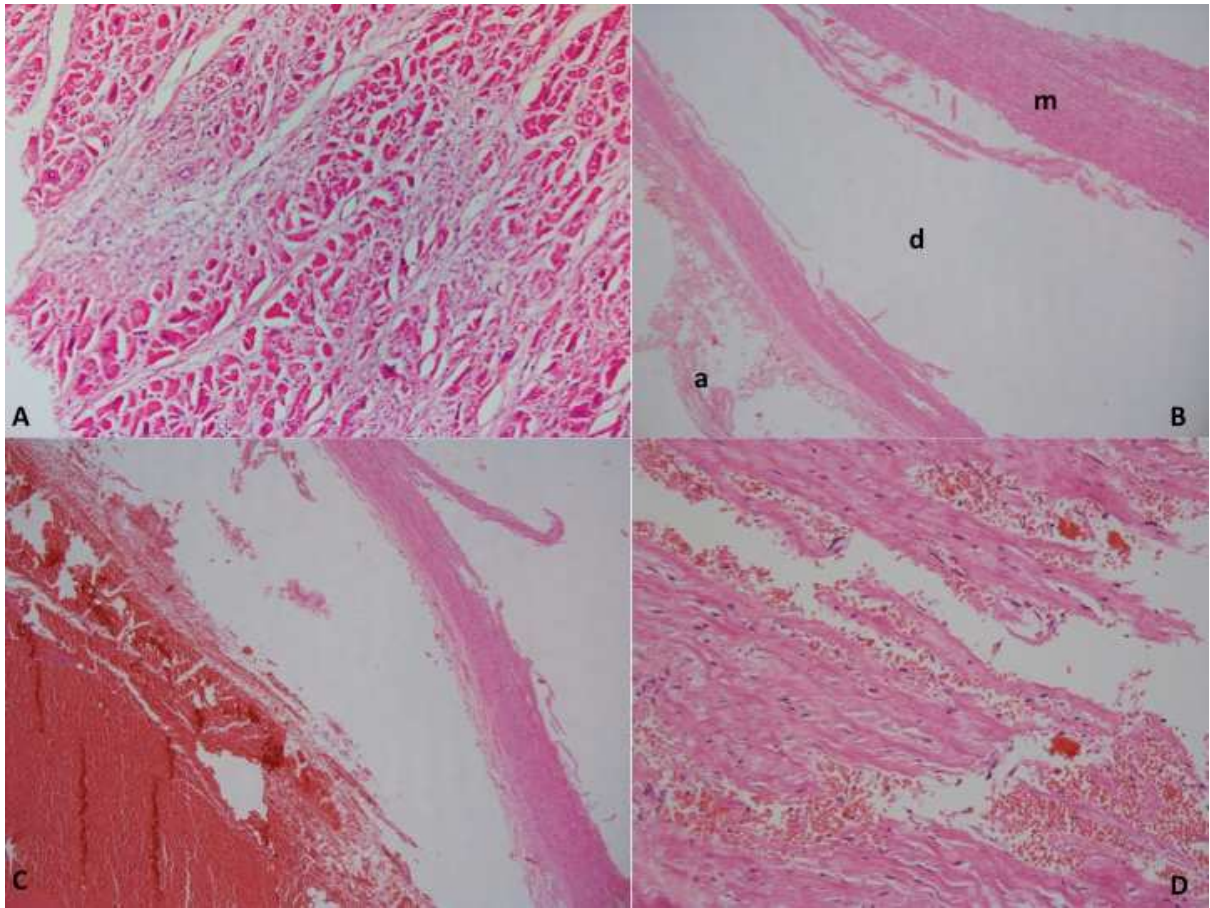
	<i>Cocaine and metabolites (µg/ml)</i>	<i>Benzoilecgonine (µg/ml)</i>	<i>Ecgonine_ME (µg/ml)</i>
<b>Blood</b>	0.527	2.335	
<b>Bile</b>	0.79	1.03	
<b>Liver</b>	0.03		
<b>Kidney</b>			21.24
<b>Urine</b>	0.02		

**Captions**

Figure 1. A. Blood clot in the pericardial sac. B. Cervicothoracic organs removed according to Ghon's technique. C. Dissection of aortic wall and rupture of adventitia.

Figure 2. A. Netlike myocardial fibrosis. B. Aortic dissection (a. adventitia. d. dissection. m tunica media). C. Erythrocytes in the adventitia and defect in the tunica media (muscle layer). D. Erythrocytes inside the muscle layer of the tunica media.





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Aortic dissection as a complication of cocaine abuse

Autopsy technique for aortic dissection

Complete histopathological panel for vascular diseases

Suspecting cocaine abuse in young patient with chest pain and aortic dissection

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