Clin Kidney J (2014) 7: 513–517
doi: 10.1093/ckj/sfu092
Advance Access publication 12 September 2014

CKJ Review

Cocaine and kidney injury: a kaleidoscope of pathology

Narender Goel[1,2], James M. Pullman[3] and Maria Coco[2]

[1]Division of Nephrology and Hospital Medicine, Middletown Medical PC and Orange Regional Medical Center, Middletown, NY, USA, [2]Division of Nephrology, Montefiore Medical Center & Albert Einstein College of Medicine, Bronx, NY, USA and [3]Division of Pathology, Montefiore Medical Center & Albert Einstein College of Medicine, Bronx, NY, USA

Correspondence and offprint requests to: Narender Goel; E-mail: drnarendergoel@gmail.com

Abstract

Cocaine is abused worldwide as a recreational drug. It is a potent activator of the sympathetic nervous system leading to intense vasoconstriction, endothelial dysfunction, oxidative stress, platelet activation and decrease in prostaglandins E2 and prostacyclin. Cocaine can lead to widespread systemic adverse effects such as stroke, myocardial infarction, arterial dissection, vascular thrombosis and rhabdomyolysis. In human and rat kidneys, cocaine has been associated with glomerular, tubular, vascular and interstitial injury. It is not uncommon to diagnose cocaine-related acute kidney injury (AKI), malignant hypertension and chronic kidney disease. Cocaine abuse can lead to AKI by rhabdomyolysis, vasculitis, infarction, thrombotic microangiopathy and malignant hypertension. It is reported that 50–60% of people who use both cocaine and heroin are at increased risk of HIV, hepatitis and additional risk factors that can cause kidney diseases. While acute interstitial nephritis (AIN) is a known cause of AKI, an association of AIN with cocaine is unusual and seldom reported. We describe a patient with diabetes mellitus, hypertension and chronic hepatitis C, who presented with AKI. Urine toxicology was positive for cocaine and a kidney biopsy was consistent with AIN. Illicit drugs such as cocaine or contaminants may have caused AIN in this case and should be considered in the differential diagnosis of causes of AKI in a patient with substance abuse. We review the many ways that cocaine adversely impacts on kidney function.

Keywords: AIN; AKI; cocaine; vasoconstriction

Background

Cocaine, also known as benzoyl methyl ecgonine, is a tropane alkaloid found in erythroxylon coca leaves. Cocaine is widely abused worldwide despite being banned since early 19th century. As per the World Health Organization, the lifetime prevalence of cocaine abuse is 1% worldwide and 3% in developed countries, with higher rates in the USA [1]. Recent reports suggest that as of 2011, 17 million people across the world have used cocaine at least once in the last year [2]. Cocaine causes systemic adverse effects such as stroke, myocardial infarction, dissection, vascular thrombosis and rhabdomyolysis, and is associated with renal complications such as acute kidney injury (AKI), malignant hypertension and chronic kidney disease (CKD) [3, 4]. Cocaine abuse also poses challenges during pregnancy and kidney transplantation. Cocaine can cause a kaleidoscope of renal pathology. As illicit drugs are frequently contaminated with adulterants which can have additional mechanisms of kidney injury, acute interstitial nephritis (AIN), though unusual, should be included in the differential diagnosis of AKI.

Case report

A 49-year-old male with history of diabetes mellitus, hypertension, chronic hepatitis C and substance abuse presented with nausea, vomiting and decreased oral intake for 1 week. He was afebrile and normotensive. He had no rash, pericardial rub, edema or asterixis. His home medications included atorvastatin, gabapentin, metformin, insulin, metoclopramide and ibuprofen 800 mg four times a day for 2 weeks prior to admission. He later confirmed the ongoing use of intravenous cocaine as urine toxicology screen was positive for cocaine, methadone and opiates. Admission chemistries showed AKI [serum creatinine: 1080 μmol/L (12.2 mg/dL)], normal creatine phosphokinase [CPK] (45 U/L) and insignificant peripheral eosinophil count (3%). Urinalysis showed a specific gravity of 1.014, pH 7.0, a significant amount of blood but no protein and negative nitrite. Urine microscopy showed 9 RBC per high-power field, 70 WBC per high-power field and eosinophils but no casts. Urine culture was negative. Renal sonogram showed normal-sized kidneys without hydronephrosis or calculus. As the patient had refractory hyperkalemia, hemodialysis was initiated. Serologic workup

such as ANA, ANCA, anti-GBM antibody, hepatitis B and HIV were negative. Complement levels [C3 (1.4 g/L) and C4 (0.33 g/L)] were normal. A kidney biopsy performed on Day 14 showed 11 glomeruli with mild mesangial expansion but no crescents. Podocytes were normal. Tubules were 95% intact without acute injury, and arteries were normal. The interstitium showed edema, scattered clusters of eosinophils with a few neutrophils, largely confined to the medulla, and no fibrosis, all consistent with a diagnosis of AIN, likely drug related, with illicit drug or adulterants as possible etiology. The patient was started on oral prednisone 60 mg daily. With gradual renal recovery, hemodialysis was discontinued and he was discharged home 9 days after kidney biopsy on oral prednisone with a serum creatinine of 310 µmol/L (3.5 mg/dL). The patient presented a week later with a history of anuria for 1 day after repeated intravenous cocaine use. Laboratory data again showed AKI [serum creatinine 1060 µmol/L (12 mg/dL), hyperkalemia (potassium 7 mmol/L), normal CPK (37 U/L) but high WBC count of 35×10^9/L. Hemodialysis was again required, now for 21 days after readmission. Steroids were tapered off as the hospital course was complicated by acute bacterial endocarditis requiring aortic valve replacement. He was again discharged with renal recovery [creatinine 265 µmol/L (3 mg/dL)]. The patient returned several weeks later, again following a cocaine binge, with AKI. He was returned to dialysis. He eventually succumbed to multi-organ failure.

Discussion

In this case, the kidney biopsy was consistent with AIN with interstitial edema and scattered clusters of eosinophils. Serologic evaluation did not suggest acute glomerulonephritis, while urinalysis showed sterile pyuria and eosinophiluria. As described by Perazella *et al.*, AIN induced by NSAIDs occurs after prolonged exposure (several months) and interstitial infiltrates are usually not eosinophilic [5]; hence ibuprofen use as the cause for AIN, though not definitively excluded, was less likely. It is unclear whether cocaine itself or the adulterant could have caused AIN. Nevertheless, regardless of the agent involved, AIN should be considered in the differential diagnosis of kidney injury in a patient with substance abuse. His second and third presentations of AKI followed further cocaine exposure, which favored cocaine as the likely trigger, although the clinical course was greatly complicated by infective endocarditis and multi-system organ failure which could have had additional mechanisms for causing AKI independent for cocaine. This case illustrates the complexities involved in the diagnosis of kidney injury in the setting of cocaine abuse due to various possibilities of underlying pathology.

Cocaine can be abused via the oral, intravenous, inhalation or intranasal route. Currently available forms of cocaine are water soluble cocaine hydrochloride (powdered form) which can be snorted or used intravenously and water insoluble cocaine base (freebase) or crack cocaine which is used via the inhalation route [6].

Pathophysiology of cocaine effects

Cocaine is a sympathomimetic and acts by blocking the uptake of serotonin, norepinephrine and dopamine in presynaptic nerve terminals [7]. It blocks voltage-specific sodium channels which impart a local anesthetic property [7]. Cocaine can cause endothelial dysfunction and promote oxidative stress and platelet aggregation, all of which can lead to kidney injury.

1. *Sympathetic activation:* Cocaine induces intense activation of the sympathetic nervous system by blocking the uptake of norepinephrine and stimulating central sympathetic outflow [8] and causing vasoconstriction by impairing nitric oxide-mediated vasodilation [9].
2. *Endothelium:* Cocaine has been shown to increase plasma and urinary endothelin-1 [10], a potent vasoconstrictor produced by endothelial cells. Cocaine impairs endothelium-dependent vasorelaxation [11]. Both of these actions can result in altered vascular homeostasis. Cocaine stimulates transforming growth factor-β production by inhibiting interleukin-8 expression, resulting in further endothelial cell dysfunction [12].
3. *Platelet activation:* In a randomized, double-blind crossover trial, healthy humans were exposed to intranasal cocaine versus placebo. An over-expression of platelet factor 4 and β-thromboglobulin, and stimulated formation of platelet-containing microaggregates were noted with cocaine exposure [13]. Rinder *et al.* showed that some cocaine users had higher levels of activated platelets by promoting platelet α-granule release via an unclear mechanism [14]. Activated platelets can activate leukocytes by binding and forming a platelet-leukocyte complex which produces chemokines, further facilitating leukocyte recruitment, monocyte adhesion, inflammation and endothelial dysfunction [15]. In rats, inhibition of platelet-activating factor was shown to be protective against ischemic-reperfusion injury [16].
4. *Prostaglandin pathways:* Prostaglandin pathways play a crucial role in maintaining stable systemic and renal vascular homeostasis. Some members of the pathway such as prostaglandin E2, a direct vasodilator, and prostacyclin (prostaglandin I2), a platelet aggregation inhibitor in addition to being a direct vasodilator, were decreased in a dose-dependent manner in cultures of first-passaged endothelial cells from human umbilical cord, when these cells were incubated with various doses of cocaine [17].
5. *Oxidative stress:* When metabolized, cocaine forms reactive oxygen species and contributes to oxidative stress leading to mitochondrial respiration inhibition, intracellular glutathione depletion and cell death [18]. Cocaine metabolizes into benzoylecgonine, ecgonine methyl ester and norcocaine [19]. Norcocaine metabolites, which include nitroxide, nitrosonium and iminium [20], play a crucial role in oxidative stress and reactive oxygen species (ROS) generation and lipid peroxidation. In the primary cultured proximal tubular epithelial cell, norcocaine induced nephrotoxicity and apoptosis [19]. Cocaine also increases superoxide dismutase activity in various tissues and lipid peroxidation in rat kidneys, as measured by malondialdehyde levels [21].

Nephropathology of cocaine

Rats exposed to intraperitoneal cocaine developed significant glomerular, vascular, tubular and interstitial damage encompassing glomerular atrophy, glomerular sclerosis, mesangial cell proliferation, capillary loop thrombosis and rupture, capillary basement membrane thickening, tubular

epithelial cell swelling and necrosis, interstitium with foci of necrosis and hemorrhage [22]. Cocaine interacts with macrophages and modulates mesangial cell proliferation via interleukin-6 and transforming growth factor-β [23]. It also may stimulate immunoglobulin G (IgG) aggregation in the mesangium and glomeruli [24].

In a series of 40 autopsies, it was noted that glomerular hyalinosis and periglomerular fibrosis was significantly higher in cocaine addicts when compared with controls. There was also a higher degree of arteriolar sclerosis, intimal and medial thickness and circumference [25], suggesting chronic adverse effects of cocaine on glomerulus and vasculature. In a postmortem analysis of 129 deceased illicit drug abusers, cocaine exposure was significantly associated with glomerular ischemia, arteriosclerosis and hypertensive-ischemic nephropathy [26].

Cocaine accelerates atherogenesis [27] and activates the renin-angiotensin-aldosterone system. It enhances the renal cortical mRNA expression of tissue inhibitors of metalloproteinase-2 and leads to increased matrix accumulation [28].

Cocaine is mainly associated with AKI which can require renal replacement therapy. It is important for clinicians to be aware of the mechanisms of cocaine-induced AKI as these can be highly variable as illustrated in multiple case reports (Table 1). Evidence linking cocaine, CKD and end-stage renal disease (ESRD) is limited. It is reported that 50–60% of people who use both cocaine and heroin [29] are at increased risk of HIV, hepatitis, additional risk factors that cause kidney disease.

(a) *Acute kidney injury (AKI)*

1. *Rhabdomyolysis:* There are several cases reports suggesting cocaine-induced rhabdomyolysis and resultant renal failure [30, 31]. Proposed mechanisms of cocaine-induced rhabdomyolysis include non-traumatic injury due to direct toxicity of cocaine leading to acute skeletal myofibrillar degeneration and vasoconstriction leading to muscle ischemia and necrosis, or traumatic due to seizure or hyperpyrexia [32]. Once myoglobin is released it has the potential to cause AKI by renal vasoconstriction, free radical generation, direct cytotoxicity, intraluminal cast formation, acute tubular necrosis, activation of endothelin receptor and negating the effect of vasodilatory nitric oxide [32, 33]. It is interesting to note that several of these rhabdomyolysis-related renal injury mechanisms are shared by the direct effects of cocaine as well. Thus cocaine and rhabdomyolysis are the double jeopardy for AKI.
2. *Vasculitis:* It is estimated that 69% of cocaine is adulterated with levamisole [34], an immunomodulatory drug used as an anti-helminthic drug in animals but withdrawn from the markets due to severe side effects such as agranulocytosis [34, 35] and leukoclastic vasculitis. Levamisole is being used as a cutting and bulking agent and thought to potentiate the effect of cocaine by stimulating the sympathetic nervous system as an agonist for nicotinic acetylcholine receptor. Additionally, it potentiates the effect of increased release of dopamine due to cocaine [36]. Levamisole is proposed to be the mediator of cocaine-induced vasculitis [36]. A case series of 30 patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) in relation with cocaine and likely levamisole [37] has been reported. These patients with AAV were all positive for a characteristic several fold higher titer of myeloperoxidase (MPO) ANCA titer and 50% also had co-existent anti-proteinase 3 ANCA (PR-3 ANCA). Additionally, many patients also had antinuclear antibody positivity and low complements. A case report has also speculated that anti-glomerular basement membrane disease could be associated with cocaine [38].
3. *Infarction:* Renal infarction (Figure 1) in association with cocaine has been well described [27, 39–41]. Its pathophysiology includes vasoconstriction and thrombosis mediated by cocaine-induced stimulation of platelet aggregation and thromboxane synthesis [27]. Acute aortic thrombosis [40], renal artery thrombosis [41] and even dissection [41] in association with cocaine have been described.
4. *Acute Interstitial Nephritis (AIN):* Recently, a few case reports have been published suggesting a link between AIN and cocaine exposure in patients presenting with AKI and cocaine abuse [42–44, 45].

Table 1. Spectrum of renal injury related to cocaine

Clinical presentation	Established causes	Pathophysiology	Nephropathology
Acute kidney injury [25, 28, 35–44]	Rhabdomyolysis [30, 31]	Skeletal myofibrillar degeneration, muscle ischemia. Necrosis, seizure, hyperpyrexia [32]	Renal vasoconstriction [9, 11], free radical generation [18–21], endothelin receptor activation, direct cytotoxicity, intraluminal cast formation [32, 33]
	Vasculitis [34, 35, 36]	Adulterant as levamisole [34], leukoclastic vasculitis [34, 35]	Myeloperoxidase and anti-proteinase 3 ANCA vasculitis [37], anti-GBM vasculitis [38]
	Thrombotic microangiopathy and malignant HTN [46]	Sympathetic activation [7, 8], platelet activation [13–15, 47], endothelial injury [15]	Aortic thrombosis [38], renal arterial thrombosis [40], dissection [41], microangiopathy
	Infarction [27, 39–41]	Platelet aggregation [27], thromboxane synthesis stimulation [27]	Renal vasoconstriction [9, 11], thrombosis [40, 41], dissection [36]
Chronic kidney disease [26, 29]		Mesangial and glomerular IgG aggregation [24], atherogenesis [27], RAAS activation [27], increased matrix accumulation [28]	Glomerular atrophy, sclerosis [22], periglomerular fibrosis [25], mesangial cell proliferation [23], basement membrane thickening [22], tubular epithelial swelling and necrosis [22]
Hypertension [48, 49]		Sympathetic activation [7, 8], increased endothelin [10], endothelial injury [15], activation of RAAS [27]	Arterial sclerosis, intimal and medial thickness and circumference [25]

ANCA, anti-neutrophilic cytoplasmic antibody; GBM, glomerular basement membrane; RAAS, renin-angiotensin aldosterone system; HTN, hypertension.

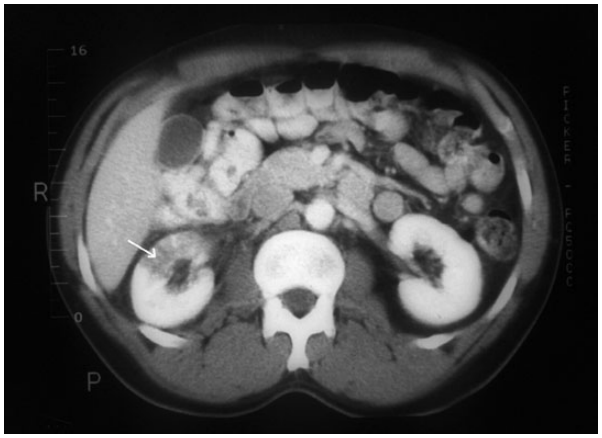

Fig. 1. Computerized tomography showing areas of focal decreased enhancement of the anterior lower poles (white arrow) of the right kidney suggesting renal infarction (Figure taken from reference [27] with permission).

It is unclear whether cocaine in itself or contaminants could be involved. However, this association of cocaine and AIN underlies an additional novel mechanism of AKI related to the drug.

5. *Thrombotic microangiopathy and malignant hypertension:* Cocaine use has been associated thrombotic microangiopathy with accelerated and malignant hypertension which has the potential to cause significant renal injury [46]. A prothrombotic effect of cocaine has been suggested by case reports of aortic, renal artery and renal venous thrombosis culminating in renal failure. Endothelial injury and platelet activation are proposed mechanisms [47].

(b) *Chronic kidney disease:* Evidence linking cocaine, CKD and ESRD is limited. It is reported that 50–60% of people who use both cocaine and heroin [29] are at increased risk of HIV, hepatitis, additional risk factors that cause kidney disease.

(c) *Hypertension:* In a review of 301 black male patients admitted for cocaine addiction treatment, the drug was associated with acute hypertension but not with chronic hypertension or albuminuria [48, 49], although, it was associated with hypertension in HIV patients [50].

(d) *Pregnancy and fetal kidney:* Cocaine abuse during pregnancy may have adverse effects on the fetal kidney. Studies have suggested a decrease in fetal arterial flow, urine output, bladder cycle, higher resistance index of the renal artery, thickening of the interlobular arterial wall of the fetal kidney and luminal narrowing [51, 52].

(e) *Kidney transplantation:* In an analysis of Scientific Registry of Transplant Recipients (SRTR) data on kidneys from deceased donors, the odds of rejection of extended donor kidney were significantly higher with donor cocaine abuse, although in the lower kidney donor risk index (1.4–1.6) category only [53]. Successful transplantation of a kidney from a patient who died from cocaine abuse has been reported [54]. Active substance abuse including cocaine is a relative contraindication for kidney transplantation, and kidney recipients are required to abstain from substance abuse for at least 6 months.

Conclusion

In conclusion, kidney injury associated with cocaine can have variable underlying causes and requires the physician to have knowledge of possible pathophysiological mechanisms to be able to define an appropriate diagnosis and make a decision regarding further treatment.

Conflict of interest statement. None declared.

References

1. Guide to Drug Abuse Epidemiology. World Health Organization. 2000. http://whqlibdoc.who.int/hq/2000/a58352_PartA.pdf (24 February 2014, date last accessed)
2. United Nation office on Drugs and Crime. World Drug Report, May 2013. http://www.unodc.org/unodc/secured/wdr/wdr2013/World_Drug_Report_2013.pdf (24 February 2014, date last accessed)
3. Riezzo I, Fiore C, De Carlo D *et al*. Side effects of cocaine abuse: multiorgan toxicity and pathological consequences. *Curr Med Chem* 2012; 19: 5624–5646
4. Nzerue CM, Hewan-Lowe K, Riley LJ Jr. Cocaine and the kidney: a synthesis of pathophysiologic and clinical perspectives. *Am J Kidney Dis* 2000; 35: 783–795
5. Perazella MA, Markowitz GS. Drug-induced acute interstitial nephritis. *Nat Rev Nephrol* 2010; 6: 461–470
6. Jaffe JA, Kimmel PL. Chronic nephropathies of cocaine and heroin abuse: a critical review. *Clin J Am Soc Nephrol* 2006; 1: 655–667
7. Schwartz BG, Rezkalla S, Kloner RA. Cardiovascular effects of cocaine. *Circulation* 2010; 122: 2558–2569
8. Vongpatanasin W, Mansour Y, Chavoshan B *et al*. Cocaine stimulates the human cardiovascular system via a central mechanism of action. *Circulation* 1999; 100: 497–502
9. Mo W, Singh AK, Arruda JA *et al*. Role of nitric oxide in cocaine-induced acute hypertension. *Am J Hypertens* 1998; 11 (6 Pt 1): 708–714
10. Wilbert-Lampen U, Seliger C, Zilker T *et al*. Cocaine increases the endothelial release of immunoreactive endothelin and its concentrations in human plasma and urine: reversal by coincubation with sigma-receptor antagonists. *Circulation* 1998; 98: 385–390
11. Havranek EP, Nademanee K, Grayburn PA *et al*. Endothelium-dependent vasorelaxation is impaired in cocaine arteriopathy. *J Am Coll Cardiol* 1996; 28: 1168–1174
12. Mao JT, Zhu LX, Sharma S *et al*. Cocaine inhibits human endothelial cell IL-8 production: the role of transforming growth factor-β. *Cell Immunol* 1997; 181: 38–43
13. Heesch CM, Wilhelm CR, Ristich J *et al*. Cocaine activates platelets and increases the formation of circulating platelet containing microaggregates in humans. *Heart* 2000; 83: 688–695
14. Rinder HM, Ault KA, Jatlow PI *et al*. Platelet alpha-granule release in cocaine users. *Circulation* 1994; 90: 1162–1167
15. Wagner DD, Frenette PS. The vessel wall and its interactions. *Blood* 2008; 111: 5271–5281
16. Kelly KJ, Tolkoff-Rubin NE, Rubin RH *et al*. An oral platelet-activating factor antagonist, Ro-24-4736, protects the rat kidney from ischemic injury. *Am J Physiol* 1996; 271 (5 Pt 2): F1061–7
17. Mastrogiannis DS, O'Brien WF. Cocaine affects prostaglandin production in human umbilical cord cell cultures. *J Matern Fetal Neonatal Med* 2003; 14: 261–266
18. Valente MJ, Carvalho F, Bastos Md *et al*. Contribution of oxidative metabolism to cocaine-induced liver and kidney damage. *Curr Med Chem* 2012; 19: 5601–5606
19. Valente MJ, Henrique R, Vilas-Boas V *et al*. Cocaine-induced kidney toxicity: an *in vitro* study using primary cultured human proximal tubular epithelial cells. *Arch Toxicol* 2012; 86: 249–261

20. Kovacic P. Role of oxidative metabolites of cocaine in toxicity and addiction: oxidative stress and electron transfer. *Med Hypotheses* 2005; 64: 350–356
21. Pomierny-Chamioło L, Moniczewski A, Wydra K *et al*. Oxidative stress biomarkers in some rat brain structures and peripheral organs underwent cocaine. *Neurotox Res* 2013; 23: 92–102
22. Barroso-Moguel R, Mendez-Armenta M, Villeda-Hernandez J. Experimental nephropathy by chronic administration of cocaine in rats. *Toxicology* 1995; 98: 41–46
23. Mattana J, Gibbons N, Singhal PC. Cocaine interacts with macrophages to modulate mesangial cell proliferation. *J Pharmacol Exp Ther* 1994; 271: 311–318
24. Pan CQ, Singhal PC. Coordinate and independent effects of cocaine, alcohol, and morphine on accumulation of IgG aggregates in the rat glomeruli. *Proc Soc Exp Biol Med* 1994; 205: 29–34
25. Di Paolo N, Fineschi V, Di Paolo M *et al*. Kidney vascular damage and cocaine. *Clin Nephrol* 1997; 47: 298–303
26. Buettner M, Toennes SW, Buettner S *et al*. Nephropathy in illicit drug abusers: a postmortem analysis. *Am J Kidney Dis* 2014; 63: 945–953
27. Bemanian S, Motallebi M, Nosrati SM. Cocaine-induced renal infarction: report of a case and review of the literature. *BMC Nephrol* 2005; 6: 10
28. Singh VP, Singh N, Jaggi AS. A review on renal toxicity profile of common abusive drugs. *Korean J Physiol Pharmacol* 2013; 17: 347–357
29. Leri F, Bruneau J, Stewart J. Understanding polydrug use: review of heroin and cocaine co-use. *Addiction* 2003; 98: 7–22
30. Turbat-Herrera EA. Myoglobinuric acute renal failure associated with cocaine use. *Ultrastruct Pathol* 1994; 18: 127–131
31. Singhal P, Rubin B, Peters A *et al*. Rhabdomyolysis and acute renal failure associated with cocaine abuse. *J Toxicol Clin Toxicol* 1990; 28: 321–330
32. Huerta-Alardín AL, Varon J, Marik PE. Bench-to-bedside review: rhabdomyolysis—an overview for clinicians. *Crit Care* 2005; 9: 158–169
33. Vanholder R, Sever MS, Erek E *et al*. Rhabdomyolysis. *J Am Soc Nephrol* 2000; 11: 1553–1561
34. Larocque A, Hoffman RS. Levamisole in cocaine: unexpected news from an old acquaintance. *Clin Toxicol (Phila)* 2012; 50: 231–241
35. Lee KC, Ladizinski B, Federman DG. Complications associated with use of levamisole-contaminated cocaine: an emerging public health challenge. *Mayo Clin Proc* 2012; 87: 581–586
36. Álvarez Díaz H, Mariño Callejo AI, García Rodríguez JF *et al*. ANCA-positive vasculitis induced by levamisole-adulterated cocaine and nephrotic syndrome: the kidney as an unusual target. *Am J Case Rep* 2013; 14: 557–561
37. McGrath MM, Isakova T, Rennke HG *et al*. Contaminated cocaine and antineutrophil cytoplasmic antibody-associated disease. *Clin J Am Soc Nephrol* 2011; 6: 2799–2805
38. Peces R, Navascués RA, Baltar J *et al*. Antiglomerular basement membrane antibody-mediated glomerulonephritis after intranasal cocaine use. *Nephron* 1999; 81: 434–438
39. Hoefsloot W, de Vries RA, Bruijnen R *et al*. Renal infarction after cocaine abuse: a case report and review. *Clin Nephrol* 2009; 72: 234–236
40. Mochizuki Y, Zhang M, Golestaneh L *et al*. Acute aortic thrombosis and renal infarction in acute cocaine intoxication: a case report and review of literature. *Clin Nephrol* 2003; 60: 130–133
41. Edmondson DA, Towne JB, Foley DW *et al*. Cocaine-induced renal artery dissection and thrombosis leading to renal infarction. *WMJ* 2004; 103: 66–69
42. Alfaro R, Vasavada N, Paueksakon P *et al*. Cocaine-induced acute interstitial nephritis: a case report and review of the literature. *J Nephropathol* 2013; 2: 204–209
43. Decelle L, Cosyns JP, Georges B *et al*. Acute interstitial nephritis after cocaine sniffing. *Clin Nephrol* 2007; 67: 105–108
44. Wojciechowski D, Kallakury B, Nouri P. A case of cocaine-induced acute interstitial nephritis. *Am J Kidney Dis* 2008; 52: 792–795
45. Alvarez D, Nzerue CM, Daniel JF *et al*. Acute interstitial nephritis induced by crack cocaine binge. *Nephrol Dial Transplant* 1999; 14: 1260–1262
46. van der Woude FJ. Cocaine use and kidney damage. *Nephrol Dial Transplant* 2000; 15: 299–301
47. Gu X, Herrera GA. Thrombotic microangiopathy in cocaine abuse-associated malignant hypertension: report of 2 cases with review of the literature. *Arch Pathol Lab Med* 2007; 131: 1817–1820
48. Akkina SK, Ricardo AC, Patel A *et al*. Illicit drug use, hypertension, and chronic kidney disease in the US adult population. *Transl Res* 2012; 160: 391–398
49. Brecklin CS, Gopaniuk-Folga A, Kravetz T *et al*. Prevalence of hypertension in chronic cocaine users. *Am J Hypertens* 1998; 11 (11 Pt 1): 1279–1283
50. Fine DM, Garg N, Haas M *et al*. Cocaine use and hypertensive renal changes in HIV-infected individuals. *Clin J Am Soc Nephrol* 2007; 2: 1125–1130
51. Mitra SC, Seshan SV, Salcedo JR *et al*. Maternal cocaine abuse and fetal renal arteries: a morphometric study. *Pediatr Nephrol* 2000; 14: 315–318
52. Mitra SC. Effect of cocaine on fetal kidney and bladder function. *J Matern Fetal Med* 1999; 8: 262–269
53. Woodside KJ, Merion RM, Leichtman AB *et al*. Utilization of kidneys with similar kidney donor risk index values from standard versus expanded criteria donors. *Am J Transplant* 2012; 12: 2106–2114
54. Caballero F, López-Navidad A, Gómez M *et al*. Successful transplantation of organs from a donor who died from acute cocaine intoxication. *Clin Transplant* 2003; 17: 89–92

Received for publication: 25.6.14; Accepted in revised form: 13.8.14