

Clinical Report

Contrast-induced acute kidney injury following iodine opacification other than by intravascular injection

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Abstract

Contrast-induced acute kidney injury (CI-AKI) classically occurs following the intravascular administration of iodinated contrast medium (CM). However, some cases of iodine-induced nephrotoxicity have been reported in patients who did not receive intravascular CM, as a consequence of iodine absorption through mucosae, burned skin or interstitial tissues. Recently, we observed the first case of CI-AKI occurring after an enteroclysis without any direct intravascular injection of CM. Here, we report this case, and review other clinical situations in which renal toxicity has been reported following the non-intravascular use of iodinated compounds.

Keywords: acute kidney injury; acute renal failure; contrast-induced acute kidney injury; enteroclysis; iodine toxicity

Introduction

Contrast-induced acute kidney injury (CI-AKI) remains a common cause of in-hospital acute renal failure. Its pathophysiology is multifactorial and has not yet been understood completely, involving iodine-induced renal ischaemia and tubular toxicity. Risk factors for CI-AKI include pre-existing renal failure, hypotension, heart failure, older age, anaemia, diabetes mellitus and concomitant nephrotoxic medications [1, 2].

In clinical practice, CI-AKI is defined as a relative ($\geq 25\%$) or absolute (≥ 0.5 mg/dL = 44 $\mu\text{mol/L}$) rise in serum creatinine level over baseline within 3 days of the administration of an iodinated compound, in the absence of any other explanation for the acute kidney injury. In the case of CI-AKI, serum creatinine typically reaches a peak value on Day 3–7 but usually returns to, or close to, baseline within 1–3 weeks [1, 2].

Classically, CI-AKI complicates the intravascular injection of iodinated contrast medium (CM), but we report here a case of CI-AKI that occurred after an intraenteric radiocontrast administration without any direct intravascular injection of CM. To our knowledge, this is the first reported case of CI-AKI after enteroclysis, but in the literature some other cases of iodine-induced nephrotoxicity following non-intravascular use of iodinated compounds have been reported. In the following, the different clinical situations in which this complication occurred as well as the mechanisms involved will be discussed.

Case report

A 57-year-old woman having two stomies due to a long history of intestinal resections was admitted to the intensive care unit (ICU) because of an acute rise in serum creatinine level (from 67 to 134 $\mu\text{mol/L}$ in 24 h) with oliguria and drowsiness. Three days before, she developed fever with C-reactive protein elevation attributed to a digestive bacterial translocation and was treated by Imipenem 500 mg t.i.d without any other change in her current medication. On the same day, looking for a peritoneal fistula, a trans-jejunostomy enteroclysis was performed with 300 mL of Iopamiro 300 (low-osmolar CM; 90 g iodine load), which showed no intestinal leak. Since ICU admission, the patient remained haemodynamically stable and after rehydration a normal diuresis resumed. To note, the urine sediment was normal, in particular without leukocyturia nor eosinophiluria, while the urinary βNAG and lysozyme were markedly increased. Thereafter, the serum creatinine level continued to increase rapidly up to 481 $\mu\text{mol/L}$ on Day 6 after enteroclysis and then slowly returned to baseline within a month (Figure 1).

In the attempt to find the reason for this acute renal failure, it turned out that the radiologist had noticed the presence of CM in the urinary tracts already during the enteroclysis. For this reason, he had performed a native abdominal computed tomography (CT)-scan 1 h later, which confirmed the unexpected presence of CM in both renal pelvis and ureters, without evidence for any peritoneal resorption of CM (Figure 2). Therefore, although no

intravascular-iodinated CM had been administered to this patient, we considered the diagnosis of CI-AKI on the basis of the presence of CM in both urinary tracts associated with a typical clinical evolution. As no leak of CM into the peritoneal space was detected on the CT-scan, we assumed that the rapid absorption of CM occurred through the intestinal mucosa, the permeability of which was apparently increased by the local inflammatory

state. Moreover, in our patient, the transmucosal resorption of CM could have been sustained, as suggested by the persistence of CM in the caecum on a native CT-scan made 7 days after the enteroclysis.

Discussion

To our knowledge, this is the first case of CI-AKI after enteroclysis reported in the literature. However, on review of the PubMed database, we found other cases of CI-AKI in patients who did not receive any intravascular injection of CM. In fact, these patients either underwent diagnostic hepatobiliary [3–8] and gynaecological [9–11] procedures with iodinated CM, or had topical treatments using iodinated antimicrobials [12–18]. Some clinical data of the 33 cases reported in the literature, including the one here presented, are summarized in Table 1. In most of them, the diagnosis of CI-AKI was suggested either by the detection of CM in urinary tracts on radiological exams, or by highly supra-physiological serum iodine concentrations. The assumed mechanism for toxicity was to be iodine absorption through mucosae or burned skin or interstitial tissues.

It is important to note that since the first cases of nephrotoxicity reported after oral cholecystography in the 1960s [3, 8], it appeared that Iopanoic acid was a common cause of AKI, causing even irreversible renal damage. Accordingly, this extremely hazardous workup examination has been replaced by more accurate and safe diagnostic tests [19]. Similarly, because of several reported cases of systemic toxicity, it is clear that the use of povidone-iodine as CM for gynaecological diagnostic procedures should also be avoided [9, 11].

In patients with cutaneous burns, one previous study showed that the iodine absorption through the burned skin is proportional to the surface of the injury [20], and therefore, repeated topical antimicrobial treatment of large-area burns with povidone-iodine should be discouraged [17]. Similarly, a rapid interstitial absorption of iodine during experimental mediastinal irrigation with povidone-iodine has been documented in dogs [21]. According to the results of this latter study and to the cases of CI-AKI reported in patients with mediastinitis treated by mediastinal irrigation with povidone-iodine, this anti-septic treatment should obviously be undertaken only with great caution [14, 21].

In summary, the present case report as well as the aforementioned data highlight that CI-AKI sometimes

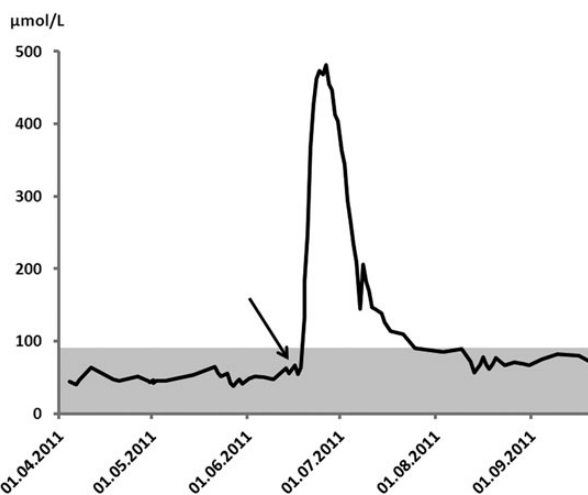


Fig. 1. Evolution of blood creatinine level after enteroclysis (arrow).

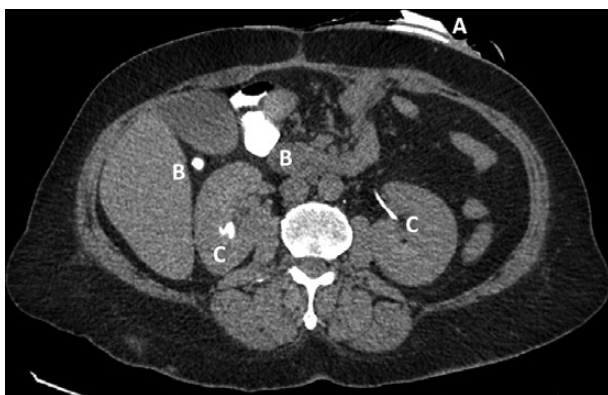


Fig. 2. Abdominal native CT-scan made 1 h after enteroclysis showing contrast media in the enterostomy (A), intestine (B) and renal pelvis bilaterally (C).

Table 1. Reported cases of CI-AKI following non-intravascular iodinated compounds use

Use of iodinated product	Procedure	Type of iodinated product	Suspected mechanism of resorption	Number of patients with CI-AKI
Contrast agent	Percutaneous cholangiography	Diatrizoate meglumine sodium [4, 6]	Transmucosal	7
	Oral cholecystography	Unknown [5, 7]	Local trauma	6
		Iopanoic acid [3]	Transmucosal	
Antimicrobial	Gynaecological tract opacification	Bunamiodyl sodium [8]	Transmucosal	3
	Enteroclysis	Povidone-iodine [9–11]	Transmucosal	1
	Topical disinfection of large burned areas	Iopamidol (presented case)	Transmucosal	1
	Continuous mediastinal irrigation (mediastinitis)	Povidone-iodine [12, 17]	Transcutaneous (burned skin)	11
	Local repetitive irrigation (cellulitis)	Povidone-iodine [13–15, 18]	Interstitial	4
		Povidone-iodine [16]	Interstitial	1

occurs in patients who did not receive intravascular injection of iodinated CM and in whom iodine causes systemic toxicity after absorption through mucosae, burned skin or interstitial tissues. Therefore, the diagnosis of CI-AKI should not be excluded solely by the absence of intravascular injection of CM, and clinicians should always consider the diagnosis of CI-AKI when an acute kidney injury develops soon after the use of iodine-based products.

Conflict of interest statement. None declared.

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