Contrast-induced nephropathy in a patient with type 2 diabetes and coronary artery disease: a case report

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Abstract

Contrast-induced nephropathy (CIN) is the impairment of kidney function defined as a serum creatinine increase of 25% or 44 μmol/L compared with baseline, usually occurring 24 to 48 hours after the use of intravenous contrast. Important risk factors for CIN include female sex, advanced age (>65 years), type 2 diabetes (T2D), kidney disease, advanced heart failure, and intravascular volume depletion. We herein present a male patient with T2D, moderately reduced renal function, no albuminuria, and a positive echocardiography stress test. He underwent percutaneous coronary intervention (PCI), and two drug-eluting stents (in the left anterior descending coronary artery) and three bare-metal stents (in the right coronary artery) were implanted. Despite adequate rehydration (0.9% intravenous NaCl with 8.4% sodium bicarbonate) before and after the procedures, he developed irreversible kidney injury after coronary angiography and PCI. This case report demonstrates the unpredictable clinical course of CIN. Patients with T2D are at high risk for the occurrence of CIN, so careful clinical assessment is recommended with global renal functional reserve evaluation.

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Background

Contrast-induced nephropathy (CIN) is the third leading cause of acute kidney injury in hospitalized patients. It represents the impairment of kidney function, measured as a creatinine increase of 25% or 44 µmol/L compared with baseline. It usually occurs 24 to 48 hours, or even up to 5 days, after intravenous contrast administration.[1] In patients with multiple co-morbidities undergoing coronary angiography and intervention, the incidence of CIN can even be up to 50%,[1,2] and is associated with substantial mortality.[3] The most important risk factors for the development of CIN are female sex, advanced age (>65 years), type 2 diabetes (T2D), kidney disease, advanced heart failure, and intravascular volume depletion.[4,5]

T2D is also a major risk factor for the development of coronary artery disease (CAD),[6] which often presents as silent myocardial ischemia. Investigating the existence of CAD in T2D begins with non-invasive physical or pharmacological tests,[7,8] followed by coronary angiography, if required.[9] Patients with T2D often have kidney disease, so it is not surprising that CIN occurs three times more frequently in patients with T2D and CAD.[10]

Case presentation

A 67-year old male patient presented with arterial hypertension (120–130/80–90 mmHg) that had been well-controlled for 7 years by 5 mg ramipril and 2.5 mg bisoprolol. He also had T2D for 10 years, with adequate glucose control (glycated hemoglobin 7.1%) using oral agents 2000 mg metformin and 2 mg glimepiride. His medical history included dyslipidemia that was well-controlled with 10 mg simvastatin. He was diagnosed with chronic kidney disease (CKD) stage 3A about 1 year previously, with an estimated glomerular filtration rate (eGFR; MDRD equation) of 52.6 mL/minute/1.73 m^2, serum creatinine up to 126 µmol, proteinuria 0.18 g/24 hours, urine albumin-to-creatinine ratio up to 2.77 mg/mmol, and C-reactive protein (CRP) 1.2 mg/L (normal). He had no other diagnosed microvascular or macrovascular complications of T2D.

During the past 4 months, he had complained of fatigue and shortness of breath during mild to moderate physical activity. Considering the long duration of his T2D, a cardiology assessment was indicated. The physical examination was normal, although echocardiography found a preserved left ventricular (LV) ejection fraction (55%), normal LV dimensions, enlarged left atrium, and significant LV diastolic dysfunction (E/E′=17). An echocardiography stress test using the Bruce protocol was terminated because of fatigue in the first minute of the third stage, at a heart rate of 115 beats/minutes. The patient did not experience chest pain, but there was a 0.5- to 1.0-mm ST-segment depression in inferior-lateral leads on the electrocardiogram. At peak exercise, echocardiography detected LV apical hypokinesis. Selective coronary angiography was indicated; because he was considered a high-risk patient (with a long duration of T2D, CKD stage 3A, and hypertension) with serum creatinine levels of 126 µmol, adequate rehydration was initiated 4 hours before the intervention (300 mL intravenous [i.v.] 0.9% NaCl with 8.4% sodium bicarbonate) and continued for 6 hours following the procedure (700 mL i.v. 0.9% NaCl with 8.4% sodium bicarbonate).

Two days before the intervention, treatment with metformin was discontinued, while the ramipril dose was reduced by half to 2.5 mg. Coronary angiography was performed using 40 mL of low osmolar iodine contrast (Iopromide), and two-vessel coronary artery disease was found.

In the left anterior descending artery (LAD), 90% to 99% calcified stenosis was detected in the medial segment, 90% stenosis in the distal segment, and 90% to 99% stenosis in the first diagonal branch. Two major stenoses were seen in the right coronary artery (RCA): 70% to 90% in the proximal segment and 90% to 99% in the medial segment. The patient did not agree to the indicated surgical revascularization, so percutaneous coronary intervention (PCI) was planned. Four days later, PCI was performed following appropriate rehydration, with two drug-eluting stents implanted in the LAD with balloon angioplasty of the first diagonal branch (Figure 1). Additionally, three bare-metal stents were implanted in the RCA (Figure 2). Given the complexity of the procedure, 225 mL of low osmolar iodine contrast was used, followed by adequate rehydration. However, despite taking these precautionary measures, the kidney function worsened 36 hours after the
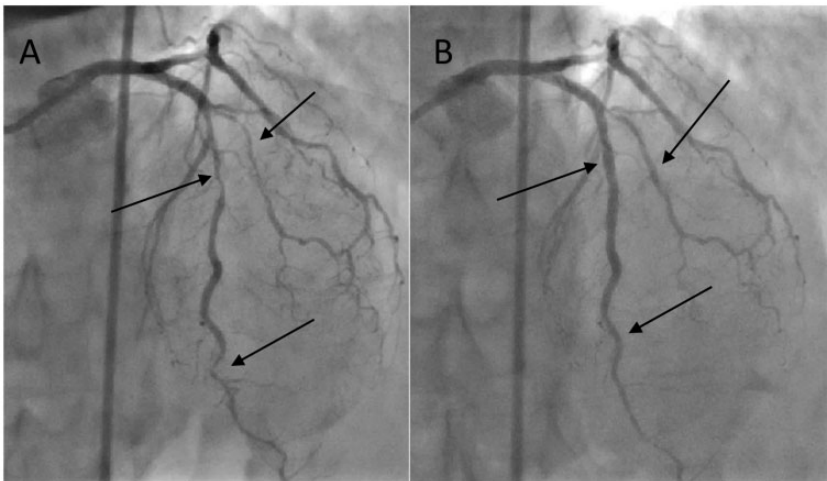

Figure 1. Baseline angiogram before (a) and after percutaneous coronary intervention of the left anterior descending artery (b).
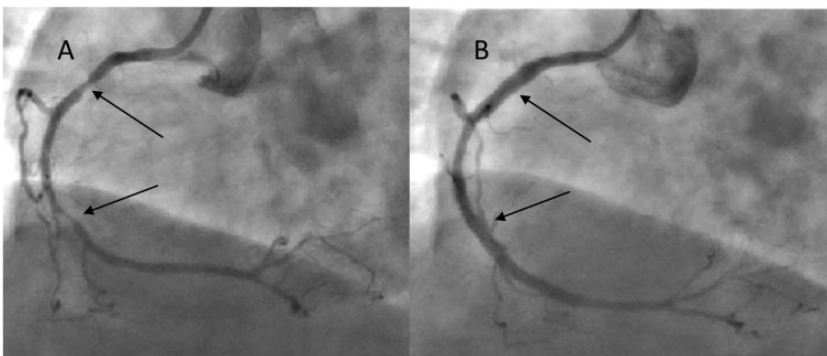

Figure 2. Baseline angiogram before (a) and after percutaneous coronary intervention of the right coronary artery (b).

intervention, with elevated blood urea nitrogen (15.7 mmol/L) and serum creatinine (from 150 to 227 μmol/L), but sustained diuresis.

The further clinical course was complicated by prolonged diarrhea and bilateral bronchopneumonia on the 10th day after the procedure, with a high CRP (72 mg/L). Despite intensive treatment with antibiotics and antidiarrheal agents as well as appropriate hydration and symptomatic therapy, kidney failure progressed to end-stage, with serum creatinine levels of 600 μmol and potassium 6 mmol/L. Hemodialysis was required, but an arteriovenous fistula could not be created, likely because of extensive atherosclerosis, so a permanent dual-lumen tunnel catheter for hemodialysis was implanted in the jugular vein. The patient was discharged in a stable condition, with planned hemodialysis three times per week.

Discussion

The pathogenesis of CIN is complex and poorly understood. Several mechanisms contribute to its development, including: 1) contrast-induced vasoconstriction reducing blood flow into the renal medulla and having a direct toxic influence[11]; 2) decreased compensatory mechanisms which maintain the filtration function in CKD, including diabetic nephropathy[12]; 3) the amount and type of angiographic contrast used[13,14]; and 4) pre-renal causes of acute kidney injury, including acute hypovolemia and volume depletion, and other nephrotoxic agents.

The presence of T2D is one of the most important risk factors for CIN.[15] This is largely because cardiovascular complications are common in T2D and often require diagnostic and interventional procedures that could potentially cause CIN. Additionally, almost 7% of patients already have albuminuria and some degree of kidney impairment at the time of T2D

diagnosis.[16] Although not all patients with reduced eGFR will develop CIN,[17] CIN Consensus Working Panel recommendations suggest that patients with baseline eGFR $< 60 \, \text{mL/min}/1.73 \, \text{m}^2$ undergo careful clinical assessment and that intensive caution be exercised in those with eGFR $< 45 \, \text{mL/min}/1.73 \, \text{m}^2$.[18] The amount of iodine contrast used during the procedure ($>350 \, \text{mL}$ in total or $>4 \, \text{mL/kg}$ body weight) represents an important risk factor *per se*, even when low and iso-osmolar contrasts are used.[13,14] Thus, it is necessary to vigilantly assess the risk of CIN when procedures using i.v. contrast are planned.

A simple scoring system, using baseline characteristics and procedural factors, has been advantageous in predicting the risks of CIN, dialysis, and long-term mortality in patients undergoing PCI.[4,15] Using this tool, the estimated risk of CIN for the current patient was 5 (7.5%) for the first and 7 (14%) for the second procedure. In comparison, the risk of acute kidney injury requiring dialysis was 0.04% and 0.12%, respectively.[18] Thus, our patient had a moderate risk for CIN at baseline, and received 265 mL of contrast in total (40 mL during the first and 225 mL during the second procedure) which is not considered to be large.[13,14]

A decreased glomerular filtration rate and reduced functional kidney "reserve" often seen in older patients, along with T2D, [19] most likely contributed to the development of CIN in this patient. Additionally, the presence of multiple infections (acute diarrhea and bilateral bronchopneumonia), and antibiotic treatment led to the deterioration of his kidney function.

Additional information regarding the risk of CIN in patients undergoing i.v. contrast administration could be offered alongside a global functional reserve measurement, which was not done in this patient.[20] An increase of creatinine occurring within 3 days after the procedure usually returns to baseline after 10 to 14 days.

In our patient, serum creatinine levels increased from 126 μmol/L to 150 μmol/L after the first procedure, to 227 μmol/L after the second application of iodine contrast, and finally to 600 μmol/L following the development of bilateral bronchopneumonia and prolonged diarrhea. Recent data suggest that 30% to 50% of patients that initiate dialysis because of CIN remain on it permanently,[1] and it has been proposed that a major factor of kidney injury reversibility is the ability of tubular cells to recover after exposure to the direct nephrotoxic effect of the contrast.

The deterioration of kidney function in our patient was assessed using the traditional biomarkers serum creatinine and urine output. These biomarkers change at a late stage in the clinical course of acute kidney injury, and have low diagnostic sensitivity and specificity. More specific biomarkers, such as neutrophil gelatinase-associated lipocalin, kidney injury molecule-1, and cystatin C are not routinely used in clinical practice, but rather for research purposes, as in many institutions worldwide.[21]

In summary, we present a patient with T2D and CAD who, despite appropriate prophylaxis, developed irreversible kidney injury following coronary angiography and PCI. The combination of several risk factors influenced the unfavorable course of CIN in this patient, including advanced age (>65 years), multiple comorbidities (T2D, hypertension, and dyslipidemia), a decreased glomerular filtration rate at baseline, the use of contrast, multiple infections, and a more extensive atherosclerosis than initially anticipated. This case highlights the insidious nature and clinical course of CIN, especially in patients with diabetes, and could be used for educational purposes.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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