Title: Severe contrast-induced nephropathy leading to dialysis occurring in a patient with near-normal baseline creatinine undergoing CT angiography using intravenous contrast only

Running title: IV contrast does cause Nephropathy

Keywords: Contrast-induced nephropathy; contrast media; dialysis, intravenous contrast, Acute kidney injury; coronary angiography; intra-arterial contrast exposure;

Abstract:

Contrast-induced nephropathy can be a major health issue in patients undergoing iodinated contrast exposure. Recently a published paper misleadingly suggested that intravenous administration of iodinated contrast is not a significant cause of contrast-induced nephropathy. This contrasts with previous studies and clinical observations of numerous contrast-induced nephropathy cases occurring in the setting of intravenous contrast exposure. We are presenting a severe cause of contrast-induced nephropathy occurring in a patient with near-normal creatinine receiving intravenous contrast only leading to dialysis and near death.

Background: Many non-randomized retrospective studies suggesting that intravenous (IV) contrast does cause contrast-induced nephropathy leading to increasing unjudicial use of iodinated contrast in the population. We are presenting a case that suggests even moderate IV contrast use in a patient with near-normal creatinine can lead to severe contrast-induced nephropathy and dialysis.

Case report:

The patient was an 86-year-old male with a past medical history of hypertension, hyperlipidemia, and hypothyroidism presented to the emergency room with an acute onset of severe back pain accompanied by shortness of breath (SOB) at rest. His sob occurred after a vigorous attempt to swallow his potassium tablet leading to upper airway obstruction. On initial evaluation, the patient was found to be hypoxic on the room air needing O2 supplementation. Laboratory studies revealed a BUN of 24 and a near-normal creatinine of 1.2 with normal hematocrit and white counts.

CT angiogram of his chest, abdomen, and pelvis were performed utilizing a total of 90 ml of IV Ipomidol contrast after his presentation in the emergency department. No pre-treatment with hydration was given in the emergency room before her CT angiography due to her normal baseline creatinine. It revealed normal aorta and visceral arteries with no evidence of pulmonary emboli and an atrophic left kidney. The next day, his creatinine increased to 2.1 and BUN to 33. His repeat creatinine the next day revealed almost doubling of his creatinine to 3.9 and despite receiving IV fluid, he suffered from severe oliguria and renal failure requiring emergent hemodialysis.

His acute renal failure was deemed to be from acute tubular necrosis due to IV iodinated contrast exposure. His GFR remained low needing hemodialysis for the next 3 weeks. His acute contrast-induced nephropathy course was complicated by bacteremia from Streptococcus salivarius and Klebsiella pneumonia as well as parapneumonic effusion requiring chest tube insertion.

His acute renal failure also led to fluid overload and respiratory failure requiring endotracheal intubation. Finally, after a very long prolonged hospital course, the patient gradually improved with his renal function and eventually was able to be weaned from his hemodialysis.

Discussion:

Iodine contrast media is very commonly utilized with an estimated 80 million doses used worldwide in 2003. (1) An estimated 1,790,000 cardiac catheterizations were performed in the year 2000 with more than 59,000 (3%) cases of contrast-induced nephropathy with a risk of dialysis of about 10%. (2,3). There is a recent discussion about differences between intra-arterial vs intravenous administration of contrast regarding causing contrast-induced nephropathy. (4) Many studies describing a higher occurrence of CIN in patients who underwent coronary angiography suggesting that intra-arterial contrast injection is more nephrotoxic than intravenous administration. However, the fact that coronary angiography is routinely combined with left ventriculography is not considered in these studies. (5) It is important to notice that intracoronary injection will not directly expose kidneys to contrast as most of the contrast will enter the coronary sinus and will be diluted before reaching the kidneys. However, left ventriculography which is routinely performed in the majority of patients undergoing coronary angiogram will expose the kidneys directly to the contrast without dilution that may be responsible for a higher occurrence of CIN in patients undergoing cardiac catheterization.

Furthermore, higher contrast exposure by adding left ventriculography to the coronary angiogram can be the main reason for the higher occurrence of CIN in this population. Retrospective studies using propensity score-adjusted models tried to reduce bias and have contemplated that intravenous contrast administration has very a low risk for CIN despite the fact that in the most retrospective studies, the authors studied a younger population and missed many confounding factors such as dehydration, hypoxia, lung disease, etc that could not be adjusted. (6-8) In a recent review discussing this issue, the authors have emphasized that without prospective randomized trials, bias cannot be eliminated, and the results of retrospective studies should be interpreted with caution. (9) For several reasons, the notion that intravenous contrast administration is benign is not valid and there is no conclusive evidence exists that intra-arterial injection is riskier. A randomized controlled trial for the above misconception does not exist. (9) The argument that intravenous contrast does not cause any harm (10) is very misleading. (8) In a controlled study, (11) 19% of critically ill patients undergoing contrast-enhanced CT with normal renal function, and creatinine of less than <1.5 mg/d, had a serum creatinine elevation of >25% from baseline, and two patients from 14 suffered contrast-induced nephropathy requiring hemodialysis. Another study evaluating very critically ill patients revealed renal replacement therapy utilization in 21% of the patients suffering from contrast-induced nephropathy after undergoing contrasted enhanced CT. (12)

It is important to realize that randomized and non-randomized CT studies evaluating the renal effect of contrast have excluded high-risk patients with significantly elevated creatinine, congestive heart failure, recent contrast exposure, severe diabetes, and abnormal hemodynamics. (13,14) These studies are not representative of a real-world situation as many unstable patients will undergo contrast-enhanced CT that were excluded in these trials. Based on the above discussion and lack of randomized trials, safety should be the priority particularly in high-risk patients (15) with multiple risk factors and recent contrast exposure. (16)

It is well known that CIN does not have any safe threshold and even very low doses can induce it. (17) Furthermore, the amount of contrast and severity of renal disease play an important role in the occurrence of nephropathy in addition to other risk factors. (18) The finding of no significant differences in the occurrence of CIN comparing intravenous contrast administration vs intra-arterial route substantiate the fact that IV contrast is as risky as intra-arterial contrast exposure. (19-21) Therefore, without randomized trials that should also include more women, elderly, and critically ill patients, indiscriminate use of intravenous contrast should be avoided.

Conclusion: This case is a classic example that even a moderate amount (90ml) of IV contrast in the setting of near-normal renal function can lead to severe contrast-induced nephropathy. Therefore, the recent notion that IV contrast use cannot lead to contrast-induced nephropathy is very misleading and should not lead to indiscriminate use of IV iodinated contrast.

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