26

Acute interstitial nephritis due to SGLT2 inhibitor empagliflozin; a case report

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SGLT2 inhibitors will likely become more widely used following the results of recent large randomised controlled trials which demonstrated improved cardiovascular outcomes and slower progression of chronic kidney disease (CKD), and therefore physicians should be cognisant of potential side-effects.

We report a patient with type 2 diabetes who presented with acute kidney injury (AKI) due to biopsy proven acute interstitial nephritis (AIN). A convincing timeline pinpointed empagliflozin as the causative agent. To the authors' knowledge this is the first published case of AIN due to an SGLT2 inhibitor

A 63 year old woman presented with a five-week history of gradually increasing lethargy, malaise and poor appetite. She was found to have stage 3 AKI by Acute Kidney Injury Network (AKIN) criteria, with a serum creatinine of 381umol/L (normal range 50-120umol/L), having been 60umol/L three months prior. Empagliflozin had been commenced six weeks before her presentation. On examination she was euvolaemic and hypertensive. Urinalysis showed erythrocytes + and glucose ++++, in keeping with SGLT2 inhibitor use. Urinary protein to creatinine ratio was 168mg/mmol (previously normal). Blood testing including 'renal immunology screen' was negative or normal. Despite supportive measures, her creatinine remained static and she therefore underwent a renal biopsy, which confirmed the diagnosis of florid AIN, superimposed on background diabetic changes (images available). Her creatinine rose to 466umol/L despite drug discontinuation, and she was started on intravenous methylprednisolone 500mg daily for three days, followed by oral prednisolone 60mg daily. Given the time course, a diagnosis of AKI due to empagliflozin-induced AIN was made, and the drug was permanently discontinued. She recovered without the need for dialysis with discontinuation of empagliflozin and corticosteroid treatment, though required insulin for steroid-induced hyperglycaemia.

Any drug has the potential to cause drug-induced acute interstitial nephritis (DI-AIN), and therefore it is vital to remain vigilant for AKI when initiating medications, especially given DI-AIN accounts for up to 20% of unexplained AKI. The novel clinical observation that SGLT2 inhibitors can cause AIN is likely to be seen more frequently as these drugs are increasingly prescribed.

The potential benefits of SGLT2 inhibitors still greatly outweigh the risks of side-effects. However, this case should prompt clinicians to obtain baseline renal function when starting empagliflozin, and though an initial small rise in serum creatinine due to haemodynamic effects should be expected and tolerated, one should contemplate the diagnosis of DI-AIN if a significant or progressive AKI occurs after SGLT2 inhibitor initiation.