Late development of crystal nephropathy secondary to high dose intravenous aciclovir – a clinical case report

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Introduction

- Crystal-induced nephropathy is a recognised complication of several drugs including aciclovir. Incidence is approximately 12-48% [1].
- Aciclovir has low solubility in urine and is excreted to high concentrations in renal tubules.
- Rapid administration of high doses can cause intratubular crystal deposition and result in significant acute renal injury due to tubular obstruction, typically within 24-48 hours.
- Aciclovir can also cause toxic acute tubular necrosis [5] but this is felt to be less of a contributing factor than crystal deposition in most cases.
- Degree of renal impairment is usually proportional to the dose given.
- Urinalysis may reveal crystalluria.

Presentation

- On 06/04/2016, a 53 year old man with no significant comorbidity was admitted to his local DGH in the North of England via ambulance in status epilepticus.
- This followed two days of malaise, fevers, headache and visual hallucinations.
- He was admitted to ITU until his seizures were controlled (he required no organ support). He transferred the next day to the acute medical ward.

Initial investigations

- Admission blood tests showed normal inflammatory markers, glucose and baseline renal function.
- Lumbar puncture results: 235 white cells/mL, 100% lymphocytes, glucose 2.7, lactate 2.6, protein 0.86.

Initial management

- Treatment commenced on suspicion of bacterial meningitis/viral encephalitis: IV ceftriaxone 2g QDS and IV aciclovir 10mg/kg TDS (dose given 800mg). (Cephalosporin stopped following LP result.)

Imaging

- Day 1 - CT head: unremarkable.
- Day 3 - MRI brain: Right temporal lobe enhancement in keeping with acute encephalitis (see images and report below).

Clinical course

- No further generalised tonic-clonic seizures following admission. Several days of ongoing intermittent disorientation and periods of reduced responsiveness and fixed gaze in keeping with simple partial seizures. Observations stable. Due to complete 14 days of high-dose IV aciclovir and then for discharge planning.

Development of AKI

- On day 7, the patient developed a stage 3 AKI (see trend of creatinine below).
- At the time of developing AKI, the patient was euvoaemic and had been exposed to no new nephrotoxic drugs.
- A routine renal screen showed no other contributing factors for AKI.
- US5 kidneys, autoantibody screen, additional virology screen, immunoglobulins and complement all normal.
- Light chains raised in keeping with viral illness.
- Urine culture: no growth.
- Blood culture: coagulase-negative Staphylococcus (likely contaminant).
- Urinalysis result unfortunately unavailable.

Treatment of AKI

- Plan following review by consultant nephrologist:
  - Discontinue IV 0.9% saline 3L/24h to run continuously during aciclovir course.
  - Reduce aciclovir dose to 5mg/kg IV BD.
  - Cautiously re-increased to 5mg/kg IV TDS as renal function recovered.
  - Renal function rapidly improved and almost returned to baseline at end of treatment course.
  - Renal function back at baseline at 6 week follow-up appointment.

Discussion + recommendations

- Crystal nephropathy typically develops within 24h of commencing a causative drug but can present later[1].
- All clinicians involved in the prescription of IV aciclovir should be aware of this potential nephropathy.
- Patients should have regular monitoring of renal function and strict fluid balance (aiming for high urine output) throughout their treatment course.
- Concomitant intravascular depletion significantly increases risk and worsens kidney injury [2].
- Dose adjustment and IV crystalloid is usually sufficient to reverse kidney injury; occasionally patients may need dialysis.
- Boluses of aciclovir seem to be an independent risk factor[2], consider giving the same dose as an infusion over one hour or longer[3] to prevent a sudden buildup of crystals in renal tubules.
- Oral therapy can significantly reduce this risk [4].
- Rarely chronic renal impairment can result from aciclovir nephropathy[6].

Clinical History: 53 year old male with headache and seizures. Normal lymphocytic meningitis on microscopy, mild afebrile. Technique: Routine pre and post contrast sequences including diffusion weighting performed. Imaging findings:
- Hypertensivity of the right medial temporal lobe concerning predominantly to the amygdala. The diffusion sequence reveal stenosis area of obstruction in the temporal side, cortical and the lacuna in no rights side. Due to the area of involvement no encephalitis is of prime consideration but others infective disorders could also involve these areas (less common).
- Blood lesion response does not reveal haemorrhage or infarction. Enlargement and subtle shift to high amphotamin.
- Contrast study does not reveal any significant enhancement in the right temporal lobe or leptomeninges.
- No hydrocephalus. Apparent space lesision due to an remote acute hyperintensity of the right medial temporal lobe.
- An additional review in clinical blood by imaging performed. Providing opinion may be obtained ASAP. Clinical team alerted.

References