Hydrochlorothiazide/ibuprofen/olmesartan medoxomil

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Drug misuse and acute tubular injury: case report

An 81-year-old man developed acute tubular injury during treatment with hydrochlorothiazide, olmesartan medoxomil and ibuprofen misuse [*routes not stated; not all indications stated*].

The man presented with complaints of progressive fatigue and shortness of breath six days after being diagnosed with COVID-19. He reported sore throat, myalgia, intermittent dry cough, poor appetite, and loss of smell, taste and nausea. Moreover, he had diarrhoea and an episode of urinary incontinence. He was admitted for hypoxic respiratory failure, required high-flow oxygen. At the admission, he had been receiving treatment with unspecified chemotherapy and androgen deprivation therapy for prostate cancer. His medical history was significant for hyperlipidaemia, hypertension, prediabetes, chronic kidney disease stage 3 and hypertension. He was a former smoker. His home medications included olmesartan medoxomil [olmesartan] 20mg twice daily and hydrochlorothiazide 12.5mg daily. Additionally, he had a history of ibuprofen use 400-800mg per day for years for chronic neck pain (drug misuse). On the admission, a repeat SARS-CoV-2 PCR via nasopharyngeal swab tested positive. Additionally, his serum creatinine level was found to be elevated, which was suggestive of acute kidney injury (AKI) associated with COVID-19. Meanwhile, urinalysis revealed 3-10 RBCs per high power field, nephrotic range proteinuria of 4.6g per 24 hours, glycosuria and tubular epithelial cells. He had anaemia and hypoalbuminaemia. Kidney ultrasound showed bilaterally increased parenchymal echogenicity consistent with chronic kidney disease. Concurrently, based on chest radiograph, he was diagnosed with COVID-19 pneumonia. Hence, he was enrolled in a randomised placebo-controlled clinical trial of lenzilumab, where he was administered with an off-label lenzilumab 600mg for 3 doses for COVID-19 pneumonia along with unspecified antibiotics. He also received treatment with an off-label IV methylprednisolone for 5 days due to COVID-19 pneumonia. In addition, due to increasing D-dimer, heparin was started. Over the first few days of the admission, his creatinine remained elevated. However, he did not require dialysis as he maintained excellent urine output. On day 4 of the hospital admission, his kidney biopsy revealed acute tubular injury (ATI) and early membranous nephropathy. Subsequently on hospital day 7, his respiratory status worsened requiring intubation, mechanical ventilation and initiation of unspecified vasopressors. Despite the measures, his AKI was slowly recovering but creatinine remained elevated. Later, he experienced shock, which subsequently worsened. He was given continuous dialysis. However, he died of shock on hospital day 16.

The man's kidney pathological examinations were subsequently performed. The glomeruli revealed segmental mild mesangial hypercellularity and mesangial expansion, with thickening of their basement membranes. The tubulointerstitial compartment exhibited diffuse ATI, tubular protein reabsorption granules, mild tubular atrophy and interstitial fibrosis, and very mild mononuclear cell infiltrate without tubulitis. There was moderate arteriosclerosis and arteriolar hyalinosis. In situ hybridisation staining for the presence of SARS-CoV-2 RNA was performed, which failed to reveal evidence of viral RNA in the kidney. Electron microscopy showed abundant small granular sub-epithelial electron-dense deposits without or associated with early basement membrane spike formation. The glomerular basement membrane lamina densa was thickened. There was mild mesangial sclerosis with segmental mesangial electron-dense deposits, without sub-endothelial deposits. Abundant tubuloreticula inclusion bodies were seen in the endothelial cell cytoplasm. Podocytes exhibited severe foot process effacement. Pathologically, a diagnosis of membranous nephropathy (stage I to early stage II) was made. Later investigations showed COVID-19-related immune response and the high-grade proteinuria had unmasked his underlying membranous nephropathy. Additionally, it was concluded that the hydrochlorothiazide, olmesartan medoxomil, and ibuprofen misuse had contributed to the development of ATI.

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