

## TENOFOVIR INDUCED ACUTE KIDNEY INJURY IN A PATIENT WITH UNILATERAL RENAL AGENESIS DESPITE INITIALLY NON-IMPAIRED RENAL FUNCTION

B. T. Schleenvoigt, A. Stallmach, M. W. Pletz

Division of Gastroenterology, Hepatology and Infectious Diseases, Jena University Hospital, Jena, Germany

### Abstract

Nephrotoxicity is observed in 1.6 % of patients treated with tenofovir disoproxil fumarate (Fux 2007).

### CASE REPORT

We report a 37 year old late presenting HIV positive male patient. He was admitted with wasting, chronic diarrhoea and oesophageal candidiasis. Serology confirmed HIV-1 infection, viral load was 55.000 copies/mL (Abbott Realtime HIV-1, RT-PCR). CD4 + cells were 77 / $\mu$ L, and the CD4/CD8 ratio was 0.11. An agenesis of the right kidney with a contra-lateral hypertrophy was detected by abdominal ultrasound. However, normal values for creatinine (75  $\mu$ mol/L) and urea (5.6 mmol/L) did not suggest an impaired renal function (GFR-MDRD 108 mL/min). In addition, history revealed no risk factors for renal insufficiency (no diabetes mellitus, non-smoker, no hypertension). Concomitant medication did not contain drugs in appropriate doses with known high potential for nephrotoxicity (trimethoprim 160mg three times per week, sulfamethoxazol 800mg three times per week, folic acid 5 mg twice daily, diflucan 100mg daily, ceftriaxon 2g daily, pantoprazol 40 mg twice daily, enoxaparin 40 mg s.c. daily, mirtazapin 15 mg daily). Because of the high viral load and the deteriorated clinical condition we decided to start an antiretroviral regimen as soon as possible. Since HLA-B5701 test result was pending, Abacavir was not an option and we started with tenofovir, emtricitabin plus raltegravir to achieve fast reduction of viral load (Lennox 2009). An extensive literature research did not reveal any data on tenofovir in patients with renal agenesis.

Two days after initiation of ART laboratory monitoring of the renal function showed steadily increasing values for urea and creatinine reaching maximal levels of 14.2 mmol/L and 172  $\mu$ mol/l, respectively on day 6 despite intravenous volume substitution (GFR-MDRD 41.5mL/min). The patient developed acute kidney injury according to the RIFLE criteria (Bellomo 2004) When HLA-B5701 was tested to be negative; the NRTI backbone was switched from tenofovir plus emtricitabin to abacavir plus lamivudin. After discontinuation of tenofovir renal parameters restored within 36 hours to baseline values (GFR-MDRD 104.5 mL/min) and remained at normal values during the further course.

The most frequent mechanism of tenofovir induced kidney failure is supposed to be tubular necrosis due to mitochondrial toxicity. Tubular necrosis can result in hypophosphataemia, glucosuria, and in a decrease of

GFR due to intrarenal feed back mechanisms (e.g. by vasoconstriction of the Vas afferens). A recent renal biopsy study in 13 cases of tenofovir nephrotoxicity revealed toxic acute tubular necrosis, with distinctive proximal tubular eosinophilic inclusions representing giant mitochondria visible by light microscopy (Herlitz 2010). Electron microscopy showed mitochondrial enlargement, depletion, and dysmorphic changes. As in our case significant recovery of renal function occurred in all these patients after discontinuation of tenofovir, including in four patients who required transient hemodialysis.

Since its introduction in 2001 the nucleotide analogue tenofovir is one of the most frequently used substances in HIV treatment. Our case showed that tenofovir can induce a renal damage in patients with renal agenesis despite initially non-impaired renal function. Due to our experience we suggest that tenofovir should not be used in these patients regardless of a normal renal function.

### REFERENCES

- Bellomo R, Ronco C, Kellum JA, et al. Acute renal failure - definition, outcome measures, animal models, fluid therapy and information technology needs: the Second International Consensus Conference of the Acute Dialysis Quality Initiative (ADQI) Group. *Crit Care*. 2004 Aug;8(4):R204-12. Epub 2004 May 24.
- Fux CA, Simcock M, Wolbers M, et al. Tenofovir use is associated with a reduction in calculated glomerular filtration rates in the Swiss HIV Cohort Study. *Antivir Ther*. 2007;12(8):1165-73.
- Lennox JL, DeJesus E, Lazzarin A, et al. Safety and efficacy of raltegravir-based versus efavirenz-based combination therapy in treatment-naïve patients with HIV-1 infection: a multicentre, double-blind randomised controlled trial. *Lancet*. 2009 Sep 5;374(9692):796-806. Epub 2009 Aug 3.
- Herlitz LC, Mohan S, Stokes MB, Radhakrishnan J, D'Agati VD, Markowitz GS. Tenofovir nephrotoxicity: acute tubular necrosis with distinctive clinical, pathological, and mitochondrial abnormalities. *Kidney Int*. 2010 Dec;78(11):1171-7. Epub 2010 Sep 1.

Received: March 29, 2011 / Accepted: May 17, 2011

### Address for correspondence:

Prof. Dr. Mathias W. Pletz  
Abt. für Gastroenterologie, Hepatologie und Infektiologie  
Universitätsklinikum Jena  
Erlanger Allee 101  
07740 Jena  
Germany  
E-mail: mathias.pletz@med.uni-jena.de