

## Clinical Report

# Successful delivery of chemotherapy to treat small-cell prostate cancer in a patient undergoing haemodialysis

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### Abstract

We report on the successful treatment of small-cell prostate cancer in a patient undergoing haemodialysis. The therapeutic regimen included 300 mg/m<sup>2</sup> of carboplatin and 50 mg/m<sup>2</sup> of etoposide coupled with radical radiotherapy. Adjustments to the patient's haemodialysis prescription included the use of high flux, a larger dialyser surface area and an increased dialysis time. The parameters used aided tolerance to the drug, allowing the delivery of safe, effective treatment. At an interval of over 12 months post-treatment the patient shows no clinical evidence of recurrent disease. This case provides evidence to encourage the use of chemotherapy in otherwise potentially undertreated haemodialysed patients.

**Keywords:** chemotherapy; ESKD; haemodialysis; prostate; small-cell

## Background

Accounting for <2% of all prostatic primary tumours [1], small-cell carcinoma of the prostate is a rare, yet highly aggressive variant form of prostate cancer for which optimal treatment strategies have not been established. Prognosis is very poor, with median survival times from diagnosis ranging from 5 to 17.5 months [2]. The most adopted treatment for small-cell of the prostate is cisplatin-based chemotherapy coupled with radiotherapy. However, delivery of chemotherapy in patients with concurrent end-stage renal disease (ESRD) can be hindered as drugs like cisplatin are primarily removed by haemofiltration.

## Case report

A 51-year-old man was referred with a 4-month history of dysuria, haematuria and increasing pelvic pain. He had a background history of ESRD secondary to polycystic kidney disease requiring dialysis. At the time of initial review he had performance status 2 due to pain but had previously been fit and well.

Rectal examination revealed a nodular prostate but nothing else of note. Blood results were within normal range, including a PSA at 1.2 µg/mL, and a cystoscopy was unremarkable. Transrectal ultrasound-guided biopsies however identified small-cell carcinoma. A pelvic MRI scan showed disease extending outside of the prostate into the right seminal vesicle, but without evidence of nodal

disease. Further CT imaging showed no evidence of metastasis. The case, reviewed at a multi-disciplinary consultation with urology, medical oncology, radiation oncology and pathology, was felt to represent limited stage small-cell carcinoma of the prostate.

To maximize the patient's chance of cure, it was intended to treat his disease with sequential chemoradiotherapy to the prostate. In our centre, this would usually involve a regime including cisplatin chemotherapy. This however has significant nephrotoxic potential. Carboplatin, an alternative platinum-based chemotherapy agent which is less nephrotoxic and reported (albeit in series of no more than three patients) to be well tolerated by haemodialysis patients [3–5], was considered. Nephrology advice was sought early to adjust the haemodialysis prescription to the kinetics of carboplatin in ESRD.

Carboplatin 300 mg/m<sup>2</sup> on Day 1 and etoposide 50 mg/m<sup>2</sup> on Day 1 and Day 3 of a 21-day cycle were administered. Dialysis was carried out on Day 1 and Day 3, 2 h after chemotherapy (early in the drug elimination phase, when protein binding is low). Sequential radical radiotherapy to the prostate and seminal vesicles was given using standard hypo-fractionated intensity modulated radiotherapy of 57 Gray in 19 fractions over 4 weeks.

The patient, who was on extended haemodialysis schedules, had a body weight of 124 kg with significant residual renal function (RRF 1 L/day) with minimal interdialytic weight gains, the volume management complicated by steroid therapy. He would perform six 3-h sessions per week independently using constant site cannulation, high-flux FX100 polysulphone dialysers (Fresenius™), Tinzaparin

anticoagulation and A232 dialysis fluid. Post-chemotherapy he underwent high-flux haemodialysis using an identical prescription but for over 4 h, using blood flow of 320 mL/min and dialysate flow of 800 mL/min. The high flux, larger dialyser surface area and increased time were adjustments made given the higher total body water to maximize diffusive clearance of the drug.

After the first of four intended cycles of chemotherapy, the patient enjoyed a complete resolution of his severe pelvic pain. He developed Grade 3 thrombocytopenia (carboplatin has a well-known myelosuppressive effect), and was moved to a 28-day cycle from cycle 2. Interval scans after two cycles showed a complete disease response. Treatment was stopped after three cycles due to persistent grade 2 thrombocytopenia, but he proceeded to radiotherapy to the prostate and seminal vesicles with concurrent prophylactic cranial irradiation (25 Gray in 10 fractions over 2 weeks). All radiotherapy was well tolerated without significant toxicity. At an interval of over 12 months post-treatment there is no clinical evidence of recurrent disease and the patient continues to be on frequent haemodialysis with well-maintained RRF.

## Discussion

The low incidence and aggressive nature of small-cell carcinoma of the prostate have contributed to the lack of systematic therapeutic studies from which to gather evidence-based data to guide its treatment. The literature, largely consisting of case reports and small series [6], is even scarcer for complex cases or where comorbidity is present. Treatment decisions are therefore based, as in this case, on empirical considerations and data published from a handful of patients, which highlights the need for a wider reporting of treatment strategies used that can serve as guide.

RRF contributes significantly to dialysis adequacy and overall patient outcome in terms of survival. RRF preservation is therefore vital, especially for patients unlikely to be early candidates for transplant. High dose carboplatin has recognized nephrotoxic potential and has been reported to cause interstitial nephritis and direct tubular toxicity often resulting in acute kidney injury [7]. The oxidative renal injury is both dose-dependent and time-dependent, as evidenced by renal anti-oxidant depletion, enhanced lipid peroxidation, platinum content, plasma creatinine BUN, and blood urea levels in rat models [8].

Overall, patient outcome should be considered in relation to the likely survival from both cancer and dialysis. Both carry a poor prognosis although for patients on dialysis it is often inferior to many cancer diagnoses. The dosing of platinum compounds therefore has to take into

account efficacy, patient toxicity profile and comorbidity to maximize patient outcome. The clinical circumstances in this case defined the need for combining a stable drug profile with minimal nephrotoxicity and preservation of RRF.

In the described case study, elimination of the drug through extended dialysis sessions (through adjustments to frequency and time in relation to dosing) aided tolerance and preservation of RRF. Close collaboration within the multi-disciplinary team led to safe, effective treatment of an ESRD patient with limited stage small-cell carcinoma of the prostate. A nonconventional haemodialysis regimen might be an effective strategy for higher doses of chemotherapy with nephrotoxic agents, for those afflicted by ESRD and cancer, although studies with corresponding AUCs to define drug kinetics are required to investigate the effect of HD timing and frequency in chemotherapy regimens.

*Conflict of interest statement.* The authors declare no competing interests. This article has not been published previously in whole or part elsewhere.

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