CASE REPORT

Early use of PEPA dialyzer for light chains removal and for the recovery from myeloma cast nephropathy: A case report

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Abstract

Chemotherapy and extracorporeal treatment reduce serum free light chains (FLCs) allowing the recovery of acute kidney injury (AKI) caused by myeloma cast nephropathy (MCN). We report the first case of recovery from AKI in a patient with MCN who underwent the removal of FLCs using the PEPA filter, with an undisclosed cut-off, combined with chemotherapy for multiple myeloma (MM).

Keywords: Multiple myeloma, cast nephropathy, free light chains, dialysis, Bortezomib, PEPA (Poly Ester Polymer Alloy)

INTRODUCTION

Acute kidney injury (AKI) is found in 40% to 60% of patients presenting with multiple myeloma (MM). At diagnosis, 15% to 20% of these patients have severe renal injury requiring renal replacement therapy.[1,2] Myeloma cast nephropathy (MCN) is the most common renal manifestation (90%) in MM.[2] Reduction of serum free light chains (FLCs) is the primary aim to restore renal function during MCN.[3] Renal failure is one of the most common causes of death, second only to infection.

CASE REPORT

A 52-year-old man with MCN underwent chemotherapy for MM combined with the extracorporeal removal of FLC using the PEPA hemodialysis filter. The patient was admitted to the orthopedic clinic for acute low back pain with loss of lower limb function. Spine MRI showed a plasmacytoma with lambda FLC monotypic restriction. He promptly underwent surgery for intralesional excision of the T4-T5 lesion with ample decompressive laminectomy. Blood tests and urinalysis showed AKI: plasma creatinine was increased to 2.1 mg/dL (RIFLE class = Injury) and dipstick urinalysis revealed a proteinuria of 30 mg/dL; urinary output was regular (almost 2000 ml/day). Subsequently he was admitted to the Nephrology, Dialysis and Renal Transplantation Unit at S.Orsola Hospital for a diagnostic workup and treatment planning.

On admission his blood pressure was 135/70 mmHg controlled with a combination of angiotensin receptor blockers and Ca-antagonists, his pulse was regular 83 bpm. Nephrotic proteinuria (17 g/day) and a reduced glomerular filtration rate 33.5 ml/min (CKD-EPI) were observed. Lambda FLCs were 11,940 mg/L, whereas total serum protein and albumin were 7.6 and 2.55 g/dL, respectively. No alteration of serum and urinary electrolytes was noted. Serum IgA concentration was abnormal (3032 ng/mL). Positive serum and urinary immunofixation for IgA lambda and free lambda FLCs were found. Renal ultrasound demonstrated regular size (bipolar diameter 12 cm) and effective cortical perfusion (RI: 0.6). Cardiac examination showed a normal biventricular function with a 61% ejection fraction of the left ventricle. Renal biopsy was obtained at the left lower pole. Histological examination disclosed evidence of

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MCN (Figure 1). The patient was treated with Bortezomib (Velcade 1.3 mg/m^2, Janssen Cilag Spa, Beerse, Belgium) twice a week for four times (days 1, 5, 8, and 11) then once a week, and Dexamethasone (Soldesam 80 mg/week, Laboratorio Farmacologico Milanese S.r.l, Varese, Italy). Extracorporeal treatment for the removal of FLCs was prescribed regardless of renal function. Vascular access was a temporary central jugular venous catheter (19.5 cm long, diameter 11.5 French, Mahurkar, Medtronic, MN, USA). Extracorporeal treatment was obtained by means of on-line hemodiafiltration (HDF) using the Poly Ester Polymer Alloy dialyzer (Nikkiso FDY 210 GW, 2.1 m^2 membrane surface area, Kuf 73 ml/h/mmHg, membrane cut-off undisclosed by the manufacturer). To achieve optimal FLCs removal during each 4-hour dialysis session, the FDY dialyzer was replaced with a new one at the second hour. No anticoagulation was required. Each treatment was carried out without dehydration because the patient had an effective urinary output. The patient underwent seven extracorporeal treatments: before and after each of these FLCs, albumin, parathyroid hormone and β2-microglobulin were measured. The reduction rate per session (RRs) was calculated as follows:

$$RRs = \left(C_{pre} - C_{post}\right)/C_{pre} x\, 100$$

where C_{pre} is the predialysis solute level, and C_{post} is the postdialysis solute concentration. The measured values during dialysis have not been corrected for the hemoconcentration due to weight loss because no weight loss was prescribed.

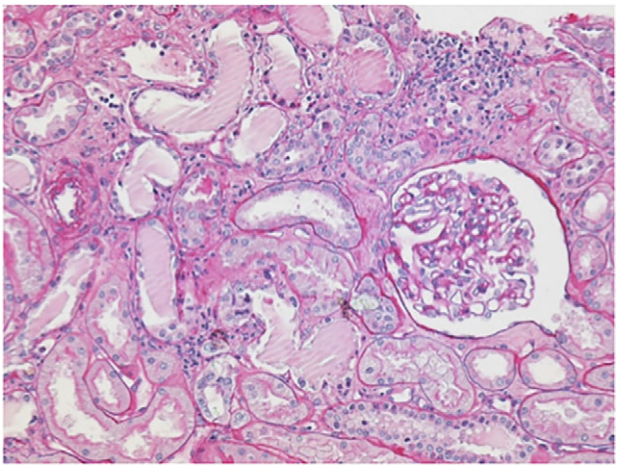

Figure 1 Periodic acid reactive Schiff Stain. Myeloma cast nephropathy. The eosinophilic casts are fractured into platelike fragments. No alteration can be seen in the glomerulus and interstitium. [Color figure can be viewed at wileyonlinelibrary.com]

Table 1 Depurative results

Sessions (n)	Lambda-FLC dialysis start (mg/L)	Lambda-FLC dialysis end (mg/L)	Lambda-FLC RRs (%)	Creatinine dialysis start (mg/dL)	Albumin dialysis start (g/L)	Albumin dialysis end (g/L)	β2-microglobulin dialysis start (mg/L)	β2-microglobulin dialysis end (mg/L)
1	9383.7	3740.6	60.1	1.79	26.5	22.3	6	2.7
2	6857.8	2014.8	70.2	1.59	25.3	21.3	5.1	2.1
3	5448.1	1593.3	70.8	1.35	25.6	21.8	5	2.3
4	697.1	368.3	49.3	1.35	25.6	23.5	3.4	1.3
5	266.7	166.9	37.4	1.2	23	22.9	1.6	1.4
6	33.5	19.4	42.1	1	27.7	25.2	2.9	1.2
7	25	12.9	48.4	1.1	27.2	25.3	2.7	1

FLC: free light chain.

Table 1 summarizes the depurative results. The extracorporeal treatment began before the chemotherapy, and the first two treatment sessions were carried out before starting Bortezomib administration. It is important to emphasize that the reduced serum concentration of lambda FLCs was obtained only by the extracorporeal treatment until the third session. Mean blood flow was 250 ± 30 ml/min, while mean convective volume was 17 ± 5 ml/min. Five drug cycles were administered, the first according to the VD (Velcade+Desamethasone) schedule then VDT (Velcade, Desamethasone and Thalidomide) in the period from September 2017 to January 2018. In March 2018, the patient underwent autologous bone marrow transplant. Our results show an effective FLCs reduction ratio (range 34%-70.8%) and after seven sessions the whole period reduction rate exceeded 99% with a complete recovery of renal function. No infectious complications were recorded.

DISCUSSION

MCN is the most frequent cause of AKI in patients with MM. The most important predictive factor for restoring renal function is the reduction of serum FLCs. This is achieved by chemotherapy drugs that kill neoplastic cells, combined with extracorporeal treatment which removes the circulating FLCs that have already been released into the bloodstream.[4] Different methods of removing monoclonal proteins have been evaluated for their ability to remove serum FLCs promptly and improve renal outcomes.[5] More recently, hemodialysis studies using a high-molecular weight cut-off (HCO) dialyzers have shown both in vitro and in vivo efficacy for FLCs removal.[6,7] A randomized controlled study, called MYRE, showed that FLCs removal with a HCO dialyzer improves patients' outcomes.[8] However, high cost, elevated protein leakage requiring albumin replacement after treatments reduce its utilization.[7] As a consequence dialyzers cheaper than HCO dialyzers, efficient in FLCs removal but without protein leakage are still wanted.

The PEPA filter is widely available and probably cheaper than dialysis with HCO filters. The PEPA filter removes kappa and lambda FLCs by both adsorption and filtration.[6,9] It was used with the HDF technique because convective techniques have proved more efficient than high flux hemodialysis in FLCs removal.[10] Nonetheless, the manufacturer does not disclose the membrane cut-off of the PEPA dialyzer. Our patient's recovery from AKI caused by myeloma cast nephropathy shows (a) HDF with PEPA dialyzer is a safe and effective technique for lambda light chains removal, which present a molecular weight of 45.000 Da; (b) the present result will be applicable to the removal of the smaller kappa light chains (m.w. 22.000 Da); (c) HDF with PEPA dialyzer can be considered as a useful "bridge" to achieve FLCs removal while awaiting chemotherapy to be commenced.

Unfortunately, we were not able to collect FLCs in the spent dialysate, so a percentage of light chains filtration or adsorption cannot be ruled out. Nonetheless, no loss of albumin was found in blood and the reduction of serum FLCs was comparable to that obtained with HCO dialyzers, which are more expensive and carry higher risks of albumin loss.

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