CASE REPORT

Cast nephropathy with acute renal failure treated with high cut-off haemodialysis in a patient with multiple myeloma

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We report a case of a Chinese woman who presented with multiple myeloma and acute renal failure due to cast nephropathy, with an extremely high serum lambda free light chain concentration. She was successfully treated with chemotherapy and high cut-off extended haemodialysis. High cut-off haemodialysis is a new treatment modality which can achieve rapid free light chain clearance. This may contribute to a better renal outcome and overall prognosis for patients with multiple myeloma.

Introduction

Multiple myeloma (MM) is a haematopoietic malignancy of terminally differentiated plasma cells in the bone marrow. It occurs more often in the elderly. Renal failure in MM is associated with very high mortality and morbidity. The serum creatinine level increases in about 50% of patients at the time of diagnosis and 20% have a serum creatinine level of greater than 176 μmol/L.[1] About 10% of patients become dialysis dependent, which is associated with greatly increased morbidity and mortality.[2,3]

Renal pathology associated with MM includes cast nephropathy in 41%, AL amyloidosis in 30%, light chain deposit disease in 19%, and chronic tubulointerstitial nephritis in 10%.[4] The major cause of renal failure is cast nephropathy. Normally, free light chains (FLC) are filtered across the glomerulus and completely reabsorbed and metabolised by the proximal tubules. Excessive production of monoclonal FLC in MM, however, results in the burden of filtered FLC exceeding the resorption capacity of the proximal tubules. The excess FLC then co-precipitates with Tamm-Horsfall protein in the distal tubules, resulting in cast formation, tubular obstruction, and finally, acute renal failure.[5]

Renal recovery is strongly associated with an early reduction in serum FLC level.[6] Plasma exchange has been used for FLC removal but has yielded conflicting results.[6-8] Haemodialysis (HD) using a Gambro High Cut-Off (HCO) 1100 dialyser (Gambro Dialysatoren GmbH, Hechingen, Germany) has been shown to achieve efficient FLC removal, which may lead to better renal outcomes.[9-11] This report describes the case of a Chinese woman with MM and acute renal failure due to cast nephropathy, who responded well to the HCO-extended HD treatment.

Case report

A 74-year-old Chinese woman with a history of De Quervain's thyroiditis, taking thyroxine replacement therapy, presented in September 2009 with bone pain first noted 6 months previously. Initial blood tests showed a normocytic, normochromic anaemia, with a haemoglobin level of 90 g/L (reference range, 125-175 g/L) and a normal white cell count. The erythrocyte sedimentation rate was 73 mm/h (reference range, <20 mm/h). Serum albumin (42 g/L), globulin (24 g/L) and calcium (2.5 mmol/L) levels were all normal. She had normal renal function when tested 2 years previously but her creatinine level measured 180 μmol/L (reference range, 62-115 μmol/L) on presentation. Urine culture and urinalysis were normal. A bone scan showed no evidence of bone metastasis. Skeletal survey for myeloma features was negative. Urine for Bence Jones protein was positive, with lambda light chains detected by immunofixation. The serum paraprotein concentration of lambda light chains was 2.2 g/L. She was referred to a haematologist for further assessment. Bone marrow aspiration showed 64% plasma cell infiltration which confirmed the diagnosis of MM (stage 3b). Serum beta-2-microglobulin level was raised (18.5 μg/mL; reference range, level 1.1-2.4 μg/mL). Serum lambda FLC level was 10 500 mg/L (Freelite; The Binding Site, Birmingham, UK; reference range, 5.7-26.3 mg/L). She started treatment on a CTD regimen (oral cyclophosphamide 300 mg weekly, thalidomide 100 mg daily, and dexamethasone 20

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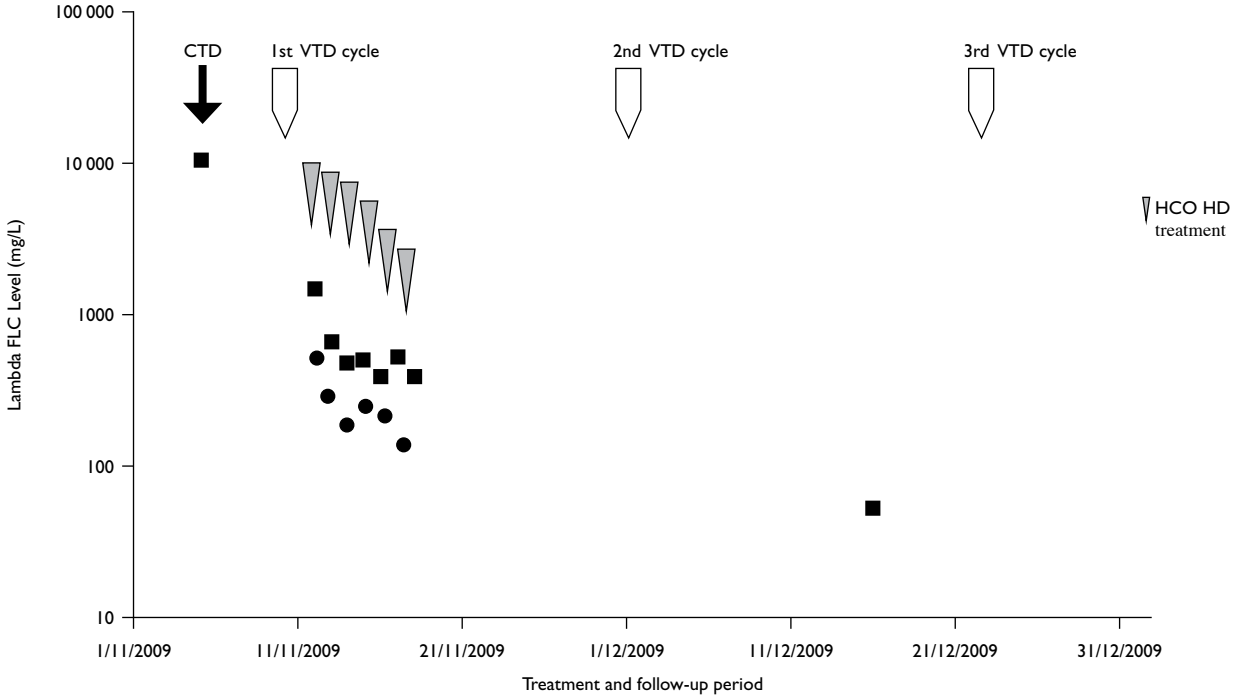
以高滲透血液透析治療因管型腎病引致的急性腎衰竭和多發性骨髓瘤

本文報告一名華籍多發性骨髓瘤女病人因管型腎病引致急性腎衰竭，其血清遊離輕鏈濃度相當高，後用化療及高滲透血液透析成功控制病情。高滲透血液透析是一種新的治療方法，能有效清除血清中遊離輕鏈。此療法可能有助改善腎功能及控制多發性骨髓瘤的病情。

mg weekly) on 6 November 2009 and subsequently changed to a VTD regimen (bortezomib [Velcade; Janssen, Auckland, New Zealand] 1.3 mg/m^2 twice weekly for 2 weeks, followed by a resting period of 10 days; thalidomide 100 mg daily; and dexamethasone 20 mg weekly) 4 days later. However, her creatinine level increased to 547 μmol/L, with decreasing urine output. Renal ultrasound was normal and 24-hour urine for protein was 1.6 g per day (reference level, <0.15 g/day).

In view of her deteriorating kidney function, HCO HD treatment was offered. A double-lumen catheter was inserted over the right internal jugular vein for access. The HCO HD was undertaken for 8 hours with a Gambro HCO 1100 dialyser, and the Gambro AK 200 Ultra S machine (Gambro, Stockholm, Sweden). Blood flow was 180 to 200 mL/min and dialysate and flow was 300 to 400 mL/min. Two U8000S ultrafilters (surface area 2.1 m^2; polyamide S membrane) were installed to the Gambro AK 200 Ultra S machine to safeguard water quality during the treatment course. Tinzaparin at a dose of 2000 units, 1000 units, and 1000 units was given at commencement, the third hour, and sixth hour of treatment, respectively. The pre-dialysis serum lambda FLC level was 1490 mg/L. Six daily sessions (from 12 to 17 November 2009) of HCO HD were given. The change in lambda FLC levels during treatment is shown in the Figure. In view of the potential for significant albumin loss during treatment, 100 mL 20% albumin was given immediately after each session of HCO HD. Her initial serum albumin level was 32 g/L which remained static (31-33 g/L) during the entire treatment period. The woman's urine output, renal function, and FLC level improved gradually during treatment (Fig). Therefore, further HCO HD was not performed. No significant haemodynamic instability or metabolic disturbance was observed during the treatment period. Renal biopsy was performed after



		Lambda FLC level (mg/L) during HCO HD on different days in November 2009					
		1st (12th)	2nd (13th)	3rd (14th)	4th (15th)	5th (16th)	6th (17th)
Pre-HCO HD	■	1490	673	479	505	393	516
Post-HCO HD	●	626	314	235	282	251	112

FIG. Lambda free light chain (FLC) level during the treatment period

HCO HD denotes high cut-off haemodialysis, CTD cyclophosphamide/thalidomide/dexamethasone, and VTD Velcade/thalidomide/dexamethasone

a course of HCO HD which confirmed the diagnosis of cast nephropathy. One month after HCO HD, her lambda FLC level was 52 mg/L. She was on her fourth cycle of VTD treatment at the time of submission of this case report. The woman remained dialysis free 3.5 months after the onset of the disease, with her creatinine level stabilised at 150 μmol/L.

Discussion

This is the first case of a patient with MM and cast nephropathy successfully treated with HCO HD in a public hospital in Hong Kong.

Serum FLC level depends on levels of synthesis by plasma cells and clearance by the kidney. The production of FLC in normal individuals is approximately 500 mg per day. These FLC are usually rapidly cleared and metabolised by the kidney within the proximal tubules, with a half-life of 2 to 6 hours. The kidneys can metabolise 10 to 30 g of FLC per day.[12] In MM, excessive synthesis of FLC occurs which overwhelm the absorption limit of the proximal tubules. The FLC enter the distal tubules and cause direct cellular damage and cast formation. Deterioration of renal function occurs and FLC clearance half-life is prolonged to 2 to 3 days.[13]

The molecular weight of kappa and lambda light chains are 22 kD and 45 kD, respectively. They are present in similar concentrations in serum and the extravascular compartment. The intravascular compartment contains around 20% of the total load of FLC. Exchange of one plasma volume during plasmapheresis can only remove 65% of the FLC from the intravascular compartment or 13% of the total FLC load from the body. Therefore, plasma exchange cannot achieve sustained removal of FLC.[14] Haemodialysis using conventional or high-flux dialysers is ineffective for the removal of FLC, due to their small pore size.[9] However, extended HD using a HCO dialyser, combined with chemotherapy, can provide excellent FLC clearance.[9-11] The HCO membrane is characterised by very large pores, 3 times the size of a normal high-flux filter, with a cut-off of 45 kD. These large pores can allow FLC to pass through but limit albumin loss.

The amount of FLC removed is affected by the initial serum FLC level, duration of dialysis, dialyser surface area, and dialysate flow rate. The Figure shows the change in FLC level during the treatment course. The FLC level decreased by 40 to 60% after each dialysis session, which is similar to previously published reports.[9-11] The serum FLC clearance rate was about 10 to 40 mL/min and slowed with time. Changing the dialyser during a HD session could have further increased FLC clearance.[11] The Gambro HCO 1100 dialyser has a relatively small surface area (1.1 m^2). Connection of two dialysers in a series could provide even better FLC clearance by means of increased surface area and internal filtration.[9,11] However, in view of the absence of appropriate connection tubing to use between two dialysers and the patient having a relatively small body build (approximately 50 kg), only one dialyser was used for each HCO HD session. The 8-hour extended HD was well tolerated, with no significant haemodynamic disturbance or side-effects. No bleeding or circuit clotting occurred, with low-molecular-weight heparin used during dialysis. Haemodialysis duration was similar to that used in previous studies and cases.[9-11]

Albumin loss is inevitable with the use of a HCO dialyser. Previous studies have shown that albumin loss ranges from 12 to 30 g per session of single-dialyser HD.[9,11] Albumin loss increases when two or more dialysers are used in a single session or with the addition of convective clearance (eg use of haemodiafiltration instead of HD).[11] In order to avoid significant hypoalbuminaemia, 20 g of albumin was given intravenously after each session of HCO HD treatment. We were able to maintain the patient's albumin level during the treatment period.

Back filtration is one of the potential hazards of HCO HD. As the blood compartment pressure drops along the length of the dialyser, back filtration occurs when the dialysate pressure is greater than that of the blood. Endotoxin or bacteria can be transferred from dialysate compartment to blood compartment which can lead to the development of septic shock. In order to decrease the potential risk of back filtration, the Gambro AK 200 Ultra S machine was fitted with two U8000 ultrafilters to ensure production of ultra pure dialysate throughout treatment.

The patient's FLC level decreased significantly before HCO HD treatment in response to chemotherapy. In fact, appropriate chemotherapy can suppress the FLC level to a very low level in a patient with normal renal function.[15] For those with renal impairment however, FLC clearance decreases. In these patients, the FLC level remains at a relatively high level for an extended period, even with appropriate chemotherapy. This contributes to continuous tubular destruction and possibly irreversible renal damage. With the use of HCO HD, rapid FLC clearance can be achieved which limits the damage associated with cast nephropathy.[10]

In conclusion, this case report demonstrates that extended daily HD using a Gambro HCO 1100 dialyser, in combination with appropriate chemotherapy, can suppress the FLC level in a patient with MM and cast nephropathy. This may lead to a better renal outcome and overall prognosis.

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Photo taken during an Editorial Board lunch on 19 Nov 2010, Hong Kong Academy of Medicine