Contents lists available at ScienceDirect

Acta Haematologica Polonica

journal homepage: www.elsevier.com/locate/achaem

Case report/Kazuistyka

Delayed recovery of kidney function in a multiple myeloma patient treated with high cut-off hemodialysis: A case report

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ARTICLE INFO

Article history:
Received: 30.07.2014
Accepted: 29.12.2014
Available online: 07.01.2015

Keywords:
- Cast nephropathy
- Multiple myeloma
- High cut-off hemodialysis
- Kidney injury

ABSTRACT

We present a case of a 68-year-old woman with dialysis dependent acute kidney injury secondary to multiple myeloma. The treatment consisted of plasma exchange, 10 sessions of high-cut-off hemodialysis and induction chemotherapy. Free light chain concentration (FLC) was reduced from 1900 mg/l to 584 mg/l (a 70% reduction). Recovery of kidney function was observed 3 months after hospital admission and discontinuation of dialysis was possible. The case is quite unusual because of the delay in renal recovery.

Introduction

Cast nephropathy is the most common cause of renal injury in patients with multiple myeloma (MM) – it accounts for 41% of cases [1] and is responsible for up to 70% of dialysis dependent acute kidney injury in MM [2]. Previously only about 20% of patients became independent of dialysis [3]. Novel therapeutic agents – bortezomib and high cut-off hemodialysis (HCO) greatly improved renal outcome. Recovery of renal function is crucial for patients' survival. Cast nephropathy is a result of excessive production of free light chains (FLC) by plasma cells. There is a proved relationship between serum FLC reduction and kidney function recovery in patients diagnosed with cast nephropathy [4]. Removal of serum FLC can be done by plasma exchange or hemodialysis using high cut-off dialyzer. While effectiveness of plasmapheresis is disputable, results from studies with HCO are very encouraging and suggest that HCO improves clinical outcome. We would like to present a case of a patient who had delayed renal recovery – 3 months after treatment with HCO.

Case report

A 68-year-old female was admitted to the I Department of Nephrology and Transplantation with Dialysis Unit due to

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http://dx.doi.org/10.1016/j.achaem.2014.12.003

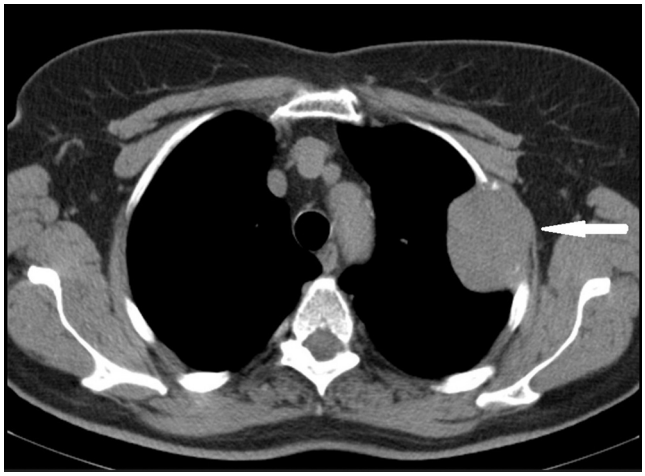

Fig. 1 – Computed tomography of the chest. Soft tissue masses: 45 × 51 mm located at the left second rib (arrow)

oliguria and acute kidney injury (AKI). Medical history revealed bone pain lasting for about 6 months (mostly in the back) and a computed tomography performed 2 weeks previously showed soft tissue masses: 45 mm × 51 mm located at the left second rib (Fig. 1), 17 mm × 36 mm at the left seventh rib, 20 mm × 31 mm at the right seventh rib and costal lesions in the thoracic vertebras – Th2, Th5, Th6, Th8-12. Two days before hospital admission a fine needle aspiration biopsy of the tumor located in the second rib was performed.

On admission laboratory tests revealed: serum creatinine 6.17 mg/dl, urea 115 mg/dl, white blood cells $7.95 \times 10^9\,l^{-1}$, platelets $157 \times 10^9\,l^{-1}$, hemoglobin 9.6 g/dl, calcium 10.92 mg/dl and serum total protein 63.8 g/l. Renal ultrasonography showed kidneys of normal size and echogenicity with no evidence of obstruction. Serum protein electrophoresis was remarkable for a paraprotein in the gamma region. Lambda light chains were detected by immunofixation in both serum and urine. The results from tumor biopsy identified MM cells. During hospitalization a bone marrow biopsy was performed and confirmed a diagnosis of multiple myeloma (40% plasma cell infiltration). Serum lambda FLC concentration was 1900 mg/l. Patient received 5 plasma exchanges within the first week. During each session one plasma volume was replaced. Consulting hematologist prescribed dexamethasone and cyclophosphamide as initial chemotherapy. After plasma exchanges serum lambda FLC concentration was even higher compared to the baseline value (3370 mg/l), serum creatinine rose (10.03 mg/dl) and daily urine output decreased (to 300 ml per day). Initially, standard hemodialysis was started (4 sessions), and afterwards patient received 10 session of HCO (Theralite™, Gambro HCO 2100 dialyzer, Lund, Sweden), each of 8 h duration. Serum lambda FLC decreased to 584 mg/l but neither urine output nor renal function improved. Patient was dialysis dependent, 4-h sessions with standard high flux membranes trice a week were performed. She was transferred to Hematology Department for further treatment. There she was started on bortezomib, melphalan and predisone (VMP). After 3 months an increase in urine output was observed and dialysis was discontinued. Creatinine level stabilized at 1.34 mg/dl (estimated glomerular filtration rate was 41 ml/min/1.73 m^2) and she stays independent of dialysis to date.

Discussion

Renal insufficiency is common in MM. Acute kidney injury complicating MM should be quickly reversed because survival of patients depends on renal function recovery. The main aim of treatment is a quick reduction of the amount of monoclonal light chains. It can be achieved by a simultaneous decrease in the production of FLC using chemotherapy and lowering levels of circulating serum FLC using extracorporeal methods like plasma exchange or hemodialysis with HCO dialyzer.

Our patient did not have any dialysis indications at admission to the hospital. That is why we decided to start plasma exchanges even though their utility in MM is questionable. The usual regimen of plasmapheresis is 5–7 exchanges within 7–10 days. A decrease of minimum 50% of serum FLC is probably required for recovery of kidney function [4]. In our case we did not observe a positive effect – FLC levels even increased after procedure. A randomized trial with 97 patients did not show any benefit of plasma exchange in acute renal failure associated with MM. Plasmapheresis with chemotherapy was compared to conventional chemotherapy alone. The authors found no differences in probability of death, dialysis dependence or glomerular filtration rate lower than 30 ml/min per 1.73 m^2 at 6 months [5]. However the main limitation of this study – the lack of renal pathology confirmation – is probably the reason why the results are in contrary to a more recent trial, which showed effectiveness of plasmapheresis when plasma exchange was used in combination with bortezomib [6].

Currently, high cut-off dialysis is the most efficient method of removing FLC [7]. High cut-off dialyzer has a membrane with large pores, with a permeability for substances with molecular weights up to 45 kD. It is therefore very effective at removing kappa and lambda light chains which have molecular weights of 22.5 kD and 45 kD respectively. HCO dialysis schedule should be extended to 8 h daily to maximize FLC removal during one session. This enables the removal of not only intravascular FLC but also FLC distributed in extravascular compartments [8, 9].

The high cut-off dialyzer was not available at our Dialysis Unit as we started dialysis in our patient, therefore we conducted her first sessions with a standard dialyzer. However, some reports even suggest using standard dialyzers for induction dialysis therapy, considering the high cost of HCO dialyzers and the necessity to shorten first dialysis sessions due to the risk of disequilibrium syndrome [10].

At the end of 10 sessions with HCO dialyzer the reduction in serum lambda FLCs was 70% which is in agreement with previous reports [2]. Despite the significant reduction in serum FLC levels we did not observe an improvement in renal function and standard dialysis sessions were started. In previous studies median time in which dialysis was

discontinued was 15–27 days and maximum time to dialysis independence was 64–120 days [2, 11]. During this time patients were still treated with HCO dialyzers. Our patient recovered renal function after over 90 days, 2 months after discontinuation of HCO dialysis sessions. Even though according to definition 3 months are needed to distinguish acute kidney injury from chronic kidney disease, our case shows that even after that time a chance remains for renal function improvement. Basnayake et al. documented 4 cases of dialysis dependent AKI due to myeloma kidney, where biopsy was performed before and after 6 weeks of treatment with chemotherapy and HCO dialysis [12]. Despite early significant reduction in FLC levels all 4 patient remained dialysis dependent at 6 weeks, although 3 of them recovered renal function at 51, 67 and 105 days. Their 6-week biopsy showed a reduction in the number of tubules with casts but an increase in index of chronic damage. In one patient there was a reduction in the degree of interstitial infiltrate. In this study even patients with significant chronic damage still achieved late renal recovery [12].

Bortezomib with high dose dexamethasone is considered the treatment of choice for patients with renal impairment due to MM [13]. In our patient initial chemotherapy with high dose dexamethasone and cyclophosphamide was started at the beginning of the dialysis. Bortezomib based chemotherapy regimen has been postponed due to infectious complications. Reported median time to response in patients treated with bortezomib is 38 days [14]. During that time serum FLC levels can be controlled by HCO dialysis to prevent irreversible damage to the kidneys. The findings from previous studies recommend initiation of HCO dialysis combined with chemotherapy as early as possible [15].

The first limitation in management of our case is lack of renal biopsy to confirm cast nephropathy diagnosis. Patient had acute kidney injury, serum FLC levels above 1500 mg/l, with low urinary albumin excretion (30 mg/dl in urine dipstick). Although only kidney biopsy confirms a definitive diagnosis the aforementioned clinical symptoms give us the right to diagnose cast nephropathy with high probability. Second limitation is a postponement in chemotherapy (due infectious complications and lack of availability of bortezomib in the nephrology department).

We therefore report a case of patient successfully treated with HCO dialysis. Effect of treatment was observed 3 months after hospital admission. In our opinion this delayed effect is worth mentioning considering a very good renal response. After 3 months of continuous dialysis therapy and 2 months after the discontinuation of HCO dialysis such a result was unexpected but fortunately for the patient not impossible.

Authors' contributions/Wkład autorów

According to order.

Conflict of interest/Konflikt interesu

None declared.

Financial support/Finansowanie

None declared.

Ethics/Etyka

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform Requirements for manuscripts submitted to Biomedical journals.

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