Case Report

Crit Care & Shock (2011) 14:19-23

Continuous venovenous hemodiafiltration, impedance cardiography and critical care nephrology: a case study of chronic myeloid leukemia-associated acute renal failure

Tao Wang, Huici Ma, Yaling Bai, Junxia Zhang, Jinsheng Xu

Abstract

Chronic myeloid leukemia (CML) is a hematologic malignancy characterized by clonal myeloproliferation of cells in the myeloid line, expressing the BCR-ABL fusion gene responsible for the oncogenic effect of the CML. Although the leukemic cells are minimally invasive, renal dysfunction is a known complication of the disease. Acute renal failure (ARF) caused by leukemic infiltration is relatively rare and often responds well to chemotherapy. We described an 80-year old CML patient who developed anuric ARF and was treated in our critical care nephrology (CCN) with hydrocarbamide in combination with impedance cardiography (ICG)-guided continuous venovenous hemodiafiltration (CVVHDF). Urine output was resumed and renal function improved within 1 day and 1 week, respectively. The chemotherapy and CVVHDF appeared to be effective therapeutic paradigm, whereas the use of ICG may offer extra guarantee especially in hemodynamically unstable patients. CCN could play a leading role in managing a broader spectrum of diseases rather than the adjunctive one of renal replacement therapy.

Key words: Acute renal failure, chronic myeloid leukemia, CVVHDF, hemodynamic monitoring, critical care nephrology.

Introduction

Chronic myeloid leukemia (CML) is a myeloproliferative disease characterized by clonal expansion of myeloid cells, with the aberrant BCR-ABL fusion gene as the pathognomonic cytogenetic anomaly. (1) Leukemic cells are minimally invasive and their proliferation is largely confined to hematopoietic tissues: primarily to the blood, bone marrow, spleen and liver. (2) Although rare, renal involvement in CML has also been reported. (3-5)

In addition to parenchymal infiltration of leukemia cells, CML can adversely impact on the kidneys in several ways. (4) Acute renal failure (ARF) of the renal origin, in turn, is associated with increased hospital mortality of CML patients. (6) The treatment usually includes hydroxycarbamide-induced cytoreduction, prednisolone, and continuous renal replacement therapy. (4,5) In the latter context, continuous venovenous hemodiafiltration (CVVHDF) is believed to be the best option to treat ARF in the CML. (4) It is of particular importance that assessment of volume status be performed during CVVHDF, especially in patients with unstable hemodynamic situations. (7) A flawed fluid management, if left unattended, may further compromise tissue perfusion, exacerbate renal dysfunction and cripple hemodynamic stability. (7) As such, impedance cardiography (ICG) is a valuable method of evaluating

From The 4th Hospital, Hebei Medical University, Shijiazhuang 050011, China (Tao Wang, Huici Ma, Yaling Bai, Junxia Zhang, and Jinsheng Xu)

Address for correspondence:
Jinsheng Xu
Department of Nephrology
The 4th Hospital, Hebei Medical University, Shijiazhuang 050011, China
Tel: +86-311-86095668
Fax: +86-311-86086919
E-mail: nephrology2009@hotmail.com

hemodynamic parameters. (8)

We reported here a case of ARF in CML that was successfully treated with chemotherapy, and CVVHDF under concomitant ICG monitoring.

Case report

An 80-year-old man presented with progressive elevation of serum creatinine (Scr) for 1 month and acute anuria for 1 day was admitted. A diagnosis of CML with gene rearrangement of the BCR-ABL had been made 1 year prior to admittance. The patient had a history of hypertension and coronary heart disease for 30 and 20 years, respectively. Current medications included amlodipine, metoprolol, losartan and sustained-release nitrate glycerin. He had lost 10 kg in weight over the preceding 4 weeks. On examination, blood pressure was 159/72 mmHg. The patient was not anemic and there was patchy ecchymosis on the flexor aspect of the lower left extremity. Pulmonary auscultation was clear and heart rate was 75 beats/minute with regular rhythm and 2/6 grade systolic murmur. Moderate splenomegaly was found without concurrent lymphadenopathy and hepatomegaly. Both lower extremities had slight pitting edema.

Initial laboratory tests showed the following values: white blood cells 76.1×10^9/L, hemoglobin 102 g/L; platelets 58.0×10^9/L, blood urea nitrogen 15.2 mmol/L; Scr 440.5 µmol/L (this was preceded by the respective values of 135.7 and 338.9 µmol/L as 4 weeks and 1 day ago), serum potassium 5.4 mmol/L, serum calcium 2.0 mmol/L. Urinalysis detected 2+ protein, white blood cells of 500/µL, rare red blood cell, and occasional white blood cell casts, protein-creatinine ratio 2.65 g/g and albumin-creatinine ratio 0.51 g/g. Coagulation screen showed slight prolongation of prothrombin time and activated partial thromboplastin time. Serological test for antineutrophil cytoplasmic antibody, anti-glomerular basement antibody, cryoglobulins were negative. Immunofixation for monoclonal gammopathy was also negative. Chest radiography and tomography respectively found a CTR of 57.0% and mediastinal lymphadenopathy. A renal ultrasound showed normal size kidneys and echo enhancement of bilateral cortex without evidence of obstructive nephropathy.

Hydroxycarbamide and the pertinent supportive measures were started, followed by the CVHHDF. A 12-hour respite was given between the medications and renal replacement therapy, during which ICG (BioZ, CardioDynamics, CA, USA) was performed at the initiation and cessation. In parallel with the reduction of white blood cells count, urine output was resumed and renal function improved, whereas key serum levels of electrolytes and uric acid were maintained (**Table 1**). Initial ICG parameters showed a marked increased in intravascular fluid volume that is consistent with the volume overload of ARF, as reflected by the thoracic fluid content (**Table 2**). An impaired cardiac function was also observed, which, along with additional ICG data, were considered in the CVVHDF prescription.

Discussion

CML could exert a detrimental influence on the kidneys under heterogeneous mechanisms and renal dysfunction *per se* may put the patients at higher risk of mortality. (6) Renal dysfunction in most cases is caused by pre-renal conditions (i.e., volume depletion, heart failure or medications affecting the renin-angiotensin-aldosterone system), intrinsic renal alterations by parenchymal infiltration of leukemia cells, tumor lysis syndrome and chemotherapy-induced vascular or tubular toxicity, or post-renal causes such as obstruction of ureters from lymphadenopathy. (4) In our present case, the sudden anuria and acute elevation of Scr made the diagnosis of ARF definite. The exact mechanism, however, could not be determined without renal biopsy, due to the thrombocytopenia. Since the ARF responded well to chemotherapy, together with the facts that there was no evidence of pre- and post-renal indications, leukemic infiltration of the kidneys under these circumstances might be considered as suggested in a recent report. (5)

In our patient initial treatment with hydroxycarbamide resulted in a complete hematological response without electrolytes disturbance. Of note, the use of this cytoreductive agent may be occasionally associated with tumor lysis syndrome, requiring prophylactic measures of alkalinizing the urine, prescribing allopurinol, instituting hydration and diuresis. (9) Conceivably, continuous renal replacement therapy is a preventive option (10) and, as in our patient manifesting ARF, *bona fide* therapeutic one. Indeed, CVVHDF is effective in the treatment of ARF in

CML patients. (6)

Despite the good hemodynamic tolerance of CVVHDF, great emphasis has been directed at the volume control in ARF from a nephrologic viewpoint. (7) Volume depletion is associated with compromised cardiovascular performance, decreased organ perfusion and renal impairment. Once ARF is established, however, volume overload becomes the main problem in the fluid management. These derangements of volume status are particularly true in the critically ill patients, especially those of advanced age with cardiac comorbidity. In this regard, our patient on admission had a tolerable yet fragile cardiac function, making him extremely susceptible. Dynamic and vigilant monitoring of blood volume by the non invasive ICG method can generate pleiotropic cardiocirculatory information, highlighting blood flow, vascular resistance, contractility and fluid status. (8) Simultaneous consideration of the variables then yielded an accurate picture of the volume status, optimized the ultra filtration prescription and prevented recurrent renal injury. (11) Accordingly, another advantage is the breakup of the vicious circle predisposing to the potentially life-threatening cardiorenal syndrome. (12)

Finally, critical care units seem to be a *conditio sine qua non* for implementing these procedures, considering the technical and empirical challenges. Bellomo et al. (13) believed that a properly trained medical and nursing staff with extensive practice and experience could easily conduct the hemodynamically-tailored ultrafiltration safely and flexibly.

Conclusion

This is a case of ARF superimposed on CML which was treated in our CCN by hydroxycarbamide and CVVHDF. The therapeutic paradigm also highlights the importance of hemodynamic monitoring as an extra guarantee during the renal replacement therapy.

Table 1. Continuous venovenous hemodiafiltration (CVVHDF) prescription and laboratory parameters

	On admission	1st session	2nd session	5th session	Unit
CVVHDF					
Ultrafiltration		5800	3000	0	mL
Net fluid removal		2000	1100	650	mL
CVP (pre- and post-CVVHDF)		16/12	12/10	10/9	cmH2O
Duration		33	20	11	h
Laboratory parameters					
Urinary output	0	680	730	2200	mL
White blood cell count	76.1	36.3	24.1	10.4	$x10^9/L$
Blood urea nitrogen	15.5	10.2	13.0	10.2	mmol/L
Serum creatinine	440.5	350.9	320.1	181.5	µmol/L
Serum potassium	5.41	4.04	4.43	4.35	mmol/L
Serum calcium	2.01	2.27	2.16	2.23	mmol/L
Uric acid	591.0	382.0	373.0	240.0	µmol/L

Table 2. Hemodynamic parameters from impedance cardiography

Hemodynamic parameters	1st session		2nd session		5th session		Normal range and unit
	Pre-CVVHDF	Post-CVVHDF	Pre-CVVHDF	Post-CVVHDF	Pre-CVVHDF	Post-CVVHDF	
Heart rate	88	77	88	76	88	76	58-86 beats/min
Systolic blood pressure	108	125	153	169	153	125	100-140 mmHg
Diastolic blood pressure	52	58	72	79	75	58	60-90 mmHg
Cardiac index	2.5	2.7	2.6	3.0	3.1	3.1	2.5-4.2 L/min/m2
Stroke index	28	35	30	39	35	41	35-65 mL/m2
Systemic vascular resistance index	1901	2025	2615	2377	2348	1841	1337-2483 dynes.s/cm5/m2
Velocity index	32	37	27	39	36	34	33-65 L/1000 s
Thoracic fluid content	64.8	59.4	62.3	55.2	50.6	41.8	30.0-50.0 L/kilo ohm
Systolic time ratio	0.51	0.48	0.49	0.48	0.43	0.41	0.30-0.50

References

1. Druker BJ, Talpaz M, Resta DJ, Peng B, Buchdunger E, Ford JM, et al. Efficacy and safety of a specific inhibitor of the BCR-ABL tyrosine kinase in chronic myeloid leukemia. N Engl J Med 2001;344:1031-7.
2. Vardiman JW, Pierre R, Thiele J, Imbert M, Brunning RD. Chronic myelogenous leukemia. In: Jaffe ES, Harris NL, Stein H, Vardiman JW, editors. Pathology and Genetics: Tumours of Haematopoietic and Lymphoid Tissues. Lyon, France: IARC Press; 2001. p. 20-6.
3. Xiao JC, Walz-Mattmüller R, Ruck P, Horny HP, Kaiserling E. Renal involvement in myeloproliferative and lymphoproliferative disorders. A study of autopsy cases. Gen Diagn Pathol 1997;142:147-53.
4. Patel TV, Rennke HG, Sloan JM, DeAngelo DJ, Charytan DM. A forgotten cause of kidney injury in chronic myelomonocytic leukemia. Am J Kidney Dis 2009;54:159-64.
5. Yuzawa Y, Sato W, Masuda T, Hamada Y, Tatematsu M, Yasuda Y, et al. Acute kidney injury presenting a feature of leukemic infiltration during therapy for chronic myelogenous leukemia. Intern Med 2010;49:1139-42.
6. Berghmans T, Meert AP, Markiewicz E, Sculier JP. Continuous venovenous haemofiltration in cancer patients with renal failure: a single-centre experience. Support Care Cancer 2004;12:306-11.
7. Bellomo R, Ronco C, Kellum JA, Mehta RL, Palevsky P, Acute Dialysis Quality Initiative workgroup. 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;8:R204-12.
8. Sodolski T, Kutarski A. Impedance cardiography: A valuable method of evaluating haemodynamic parameters. Cardiol J 2007;14:115-26.
9. Otrock ZK, Taher AT, Mahfouz RA, Makarem JA, Shamseddine AI. Acute tumor lysis syndrome secondary to hydroxycarbamide in chronic myelomonocytic leukemia. Am J Hematol 2006;81:220-1.
10. Saccente SL, Kohaut EC, Berkow RL. Prevention of tumor lysis syndrome using continuous veno-venous hemofiltration. Pediatr Nephrol 1995;9:569-73.
11. Prowle JR, Echeverri JE, Ligabo EV, Ronco C, Bellomo R. Fluid balance and acute kidney injury. Nat Rev Nephrol 2010;6:107-15.
12. Ronco C, Haapio M, House AA, Anavekar N, Bellomo R. Cardiorenal syndrome. J Am Coll Cardiol 2008;52:1527-39.
13. Bellomo R, Ronco C. Continuous haemofiltration in the intensive care unit. Crit Care 2000;4:339-45.