

Cardiorenal syndrome: Resistant to diuretics, sensitive to ultrafiltration

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ABSTRACT

Cardiac and renal diseases are becoming increasingly common today, and are seen to frequently coexist, thus causing a significant increase in the mortality rate, morbidity, complexity of treatment and cost of care. Syndromes describing the interaction between heart and kidney have been defined and classified; however, never as a result of a consensus process. Though the incidence of cardiorenal syndrome is increasing, the associated pathophysiology and effective management are still not well understood. For many years, diuretics and ultrafiltration, have been the mainstay of treatment for cardiorenal syndrome, although a significant proportion of patients develop resistance to diuretics, and even deteriorate while on diuretics. Here, we will discuss one such patient who failed to respond to the optimum doses of diuretics; however, his blood urea and serum creatinine touched the baseline levels post-ultrafiltration.

Key words: Cardiorenal syndrome, ischemic heart disease, ultrafiltration

INTRODUCTION

Cardiorenal syndrome is a term connoting the intersection between cardiac and renal dysfunctions, most frequently in patients with heart failure. Although the underlying mechanisms have not been fully characterized, this presentation in the setting of acute decompensated heart failure and in chronic heart failure is associated with poor short- and long-term outcomes. Cardio-renal syndrome can be diagnosed in the following conditions: Hypervolaemia in advanced renal failure, co-occurrence of heart and kidney failure (eg, ischemic heart disease and obstructive arterial disease), malignant hypertension leading to the development of simultaneous heart and kidney failure,

and bilateral renal artery stenosis, or unilateral renal artery stenosis of the only kidney. Clinical and laboratory symptoms of cardio-renal syndrome include progressive heart and kidney failure with refractory hypertension and vascular disease, difference in size of the kidneys by more than 1.5 cm, and reversible creatinine level increase caused by angiotensin convertase inhibitors.

CASE REPORT

A 58 year old male, a known case of ischaemic heart disease with Type 2 Diabetes mellitus and hypertension, who had been admitted for cerebellar stroke 2 months back, came with complaints of dry cough- (more at night), gradually increasing breathlessness (New York Heart Association, NYHA Grade-I to start with and displaying gradual progression to NYHA Grade IV in a period of 3 days), and swelling all over the body with minimal abdominal distension. Patient was admitted in Intensive Cardiac-Care Unit (ICCU). On admission, his blood pressure (BP) was 170/100 mmHg; pallor and icterus were present, and

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jugular veins showed distension. Also, facial puffiness was present along with bipedal pitting oedema. Per abdominal examination was suggestive of moderate ascites with no organomegaly. Respiratory system examination revealed bilaterally reduced breath sounds at lung bases, with a stony dull note and extensive scattered coarse crepitations.

On investigation, his total leukocyte count was 18900/cmm, and blood sugar levels were constantly on higher side. His liver function test report was as follows: Total bilirubin-2.8 mg/dl; direct bilirubin-1.2 mg/dl; indirect bilirubin-1.6 mg/dl; serum glutamic pyruvic transaminase (SGPT)-23 IU; serum glutamic oxaloacetic transaminase (SGOT) -61 IU; alkaline phosphatase-175; blood urea-90 mg/dl and serum creatinine-3 mg/dl. Electrocardiography (ECG) was showing sinus bradycardia with ST segment depression in inferior, anterior, lateral leads with left ventricular hypertrophy (LVH) and multiform ventricular premature beats. 2-D Echocardiography revealed all four heart chambers to be dilated with concentric left ventricular (LV) hypertrophy, global hypokinesia, LV ejection fraction of 37%, moderate LV systolic dysfunction, grade III diastolic dysfunction, mild mitral regurgitation, moderate tricuspid regurgitation and moderate pulmonary artery hypertension. Urine output was less than 30ml/hr. Chest radiograph was suggestive of bilateral hydrothorax. Ultrasonography of the abdomen and pelvis showed bilateral pleural effusion with moderate ascites with dilated inferior vena cava (IVC) and portal vein while the kidneys appeared smaller in size. The provisional diagnosis turned out to be Cardiorenal Syndrome (CRS) Type II which was finally confirmed by a cardiologist's expert opinion.

During his stay in ICCU, he was treated with immediate haemodialysis (mainly ultrafiltration), medical intervention with nitrates, antiplatelets and furosemide, along with other supportive care. After one session of haemodialysis, his general condition improved and his serum creatinine level came down to 1.8 mg/dl [normal range → 0.8-1.6 mg/dl]. After being stable for one day, his urine output reduced, for which he was started on intravenous furosemide (60-mg bolus followed by continuous infusion of 5 mg/hour), which showed only a moderate diuretic response (1800 to 2000 mL/day). This was continued for 2 days. However, he continued to be oliguric and gained 2 kg of body weight on the third day of intravenous (IV) furosemide, and serum creatinine and blood urea nitrogen concentrations rose from 1.8 to 2.7 mg/dL and from 53 to 125 mg/dL, respectively. Thus, suspecting the diuretic resistance in CRS, he was dialysed immediately on the 4th day which led to dramatic improvement and drop in blood urea level to- 33 mg/dl and serum creatinine level to 1.4 mg/dl. Antibiotic cover was given with Moxifloxacin 400 mg IV per day. He was also put on low salt and a strict diabetic

diet along with subcutaneous regular human insulin daily as per his body-requirement. He was monitored for cardio-pulmonary status and input-output records round the clock. Further management with oral furosemide showed gradual improvement in his cardiorenal status by lowering renal markers and improved urine output to around 2000 ml per day, thus making him totally symptom-free. Patient was later on discharged in a haemodynamically stable condition, and was advised regular once a week haemodialysis (ultrafiltration) along with other supportive care.

DISCUSSION

The term “Cardiorenal Syndrome” is generally used to describe the presence or development of renal dysfunction in patients with cardiac dysfunction. Although most patients with this presentation are volume overloaded, some patients may not be in congestive cardiac failure (CCF) and may suffer from low cardiac output. Renal dysfunction is one of the most powerful independent adverse prognostic predictors in heart failure patients. Cardiac dysfunction and renal dysfunction often occur concomitantly as they share common causes and pathogenic mechanisms. Diabetes and hypertension are among the most important causes of both heart failure and chronic kidney disease, and thus they are frequently associated with the cardiorenal syndrome and worsening renal function in patients hospitalized for heart failure,^[1,2] just as in our case. Renovascular disease has also been implicated, especially in some case series, but there is inadequate data to determine its prevalence or mechanistic role in cardiorenal syndrome.^[3]

Cardiorenal syndrome is common, with an estimated glomerular filtration rate (GFR) of less than 60 mL/min/1.73 m² is present in 33% of the patients with a recent myocardial infarction and left ventricular dysfunction or heart failure, and in up to 64% of the patients admitted for acute decompensated heart failure.^[4]

Five subtypes of the syndromes have been identified and defined, as follows:

- Acute Cardio-Renal Syndrome (Type 1): An acute worsening of cardiac function leading to renal dysfunction;
- Chronic Cardio-Renal Syndrome (Type 2): Chronic abnormalities in cardiac function leading to renal dysfunction;
- Acute Reno-Cardiac Syndrome (Type 3): An acute worsening of renal function causing cardiac dysfunction;
- Chronic Reno-Cardiac Syndrome (Type 4): Chronic abnormalities in renal function leading to cardiac disease;

- Secondary Cardio-Renal Syndromes (Type 5): Systemic conditions causing simultaneous dysfunction of the heart and kidney.

In CRS Type II, the background pathophysiology is thought to be poor cardiac output that leads to activation of renin-angiotensin-aldosterone system (RAAS) and negative myocardial remodelling. Although this concept is the prevailing one, it may not be the only pathophysiologic mechanism leading to worsening renal function. The feed-forward mechanisms of Ang II and increased inflammatory markers and reactive oxygen species further exacerbate these abnormalities.^[5] At present, there is no therapeutic intervention with proven benefit in outcomes in this setting, but reasonable treatment objectives include maintaining renal perfusion by maintaining arterial pressure, decongesting the patient to lessen central venous pressure, avoiding excessive diuresis, and maintaining as much as possible treatment with neurohormonal antagonists that are known to prolong survival and to prevent readmissions. Novel approaches in the form of the uses of nesiritide and adenosine antagonist (BG9719), vasopressin V₂ receptor antagonist (tolyaptan) are undergoing investigation. Role of diuretic agents are as follows:

Diuretics

Diuretics are a mainstay of treatment of patients with acute decompensated heart failure as they relieve fluid retention and congestion. However, high doses or excessive use of diuretics is associated with worsening renal function, at least in part by activating tubuloglomerular feedback and neurohormonal activation. Diuretic resistance is a hallmark of advanced heart failure and cardiorenal syndrome. It also increases renal dysfunction as measured by an increase in serum creatinine and declining GFR.^[6,7]

Ultrafiltration

New devices using venovenous ultrafiltration provide a relatively simple approach to mechanical fluid removal, making this approach available in a variety of clinical settings. Compared with diuretic treatment, ultrafiltration is not associated with as much neurohormonal activation. It also facilitates greater and more rapid removal of fluid and, especially, of salt than does aggressive diuresis. One study suggested that although ultrafiltration was not associated

with either greater symptom improvement or better renal function in a prospective randomized trial compared with furosemide, there was an apparent reduction in readmissions for heart failure between 30 and 90 days after discharge — a potentially important finding but one that requires replication.^[8] Therefore, we want to conclude that most of the current therapies in use may not have the desired outcome on renal function; hence, good clinical judgement is essential for proper patient management. Diuretics act only as supportive care, and the mainstay of treatment is ultrafiltration. Patients diagnosed to be having CRS should be immediately treated with ultrafiltration along with diuretics as an add-on therapy, as, if not treated with ultrafiltration, these patients may require re-admission to the hospital in their near future, with the only treatment option as ultrafiltration. Further, —in depth studies are still necessary to understand the exact pathophysiology of cardiorenal syndrome and to determine an effective means of therapy in order to improve the patient outcome.

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