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Case Report

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Case report: Cardio-renal syndrome with concomitant cardio-hepatic syndrome in a severe aortic stenosis patient

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Abstract

Cardio-renal syndrome and cardio-hepatic syndrome are recently described as complicated pathophysiology and therapy. We report the case of a 58-year-old man who was brought into the emergency service with acute dyspnea. On arrival, the patient status presented with congestion and oliguria. Furthermore, both renal and liver injuries were found in this severe aortic stenosis patient. The patient was treated with ventilation support, percutaneous aortic balloon valvuloplasty, intravenous loop diuretic, and vasopressor and inotrope infusion. After aortic valve angioplasty on day 2, the patient's state including acute heart failure signs and symptoms improved. Moreover, renal and liver functions gradually recovered without consequences.

Background

Unstable systemic hemodynamics in acute heart failure causes various detrimental effects on organs. In recent years, the heart-kidney and heart-liver interactions have been investigated under the terms "cardio-renal syndrome (CRS)" and "cardio-hepatic syndrome (CHS)", respectively [1,2]. Each syndrome is divided into five subtypes based on the combined dysfunction of the heart and the kidney or the heart and the liver. While type 1 CRS is characterized by acute and rapid worsening of the heart leading to acute kidney injury, type 1 CHS describes the relationship between abnormal liver function tests and the the severity of acute heart failure. The main pathophysiological mechanisms of type 1 CRS and CHS are congestion and abnormal reperfusion in the heart, the kidney and the liver. Other compounding effects of type 1 CRS include neurohormonal activation, hypothalamic-pituitary stress reaction, inflammation and immune cell signaling, oxidative stress and failure of counter-regulatory mechanisms [3]. Some important mechanisms of CHS have been previously described such as venous congestion, backward failure, decreased hepatic blood flow, decreased arterial saturation and sinusoidal thrombosis [4].

The mortality rate for aortic stenosis remains high and is commonly caused by rheumatic disease in Vietnam. Severe symptomatic aortic stenosis is a fatal condition that requires immediate treatment. We report a case of severe aortic stenosis with cardio-renal syndrome and cardio-hepatic syndrome.

Case presentation

A 58-year-old man was admitted to the emergency department for acute dyspnea. After taking a too much salt meal, the patient reported dyspnea and fatigue three days prior. His past medical history included severe aortic stenosis three years prior, but he refused any intervention or surgical treatment. He had no history of kidney and liver diseases. He also had no history of drug abuse and did not take any medications or alcohol. On admission, the patient's state was critical with a blood pressure of 95/60 mmHg, a heart rate of 110 beat per minute, jugular venous distention, crepitant rales at the bases of the lungs, hepatomegaly, and oliguria. Electrocardiogram on admission showed sinus rhythm, left axis and left ventricular hypertrophy. Bedside echocardiography showed tricuspid severe aortic stenosis with an area of 0.5 cm^2 and mean gradient of 22 mmHg. Other significant abnormal findings were left ventricular dilation (Dd 78 mm, Ds 70 mm), ejection fraction of 24%, systolic pulmonary artery pressure of 50 mmHg, moderate mitral valve regurgitation and mild pericardial effusion. Initial serum laboratory results included white blood cells of 12 G/L (75% neutrophils), red blood cells of 5.1 T/L, urea of 6 mmol/L, creatinine of 70 µmol/L, aspartate aminotransferase (AST) of 182 UI/L, alanine aminotransferase (ALT) of 683 UI/L, troponin T of 181.7 ng/L and N-terminal pro B-type natriuretic peptide of 4138 pmol/L. His electrolytes levels for postassium and sodium were 5.1 mmol/L and 140 mmol/L, respectively.

The patient was transported to the intensive care unit. Non-invasive positive pressure ventilation and intravenous loop diuretic were immediately applied. Tracheal intubation and mechanical ventilation were performed three hours after admission because of respiratory failure. Aortic valve replacement or transcatheter aortic valve implantation was considered, but his family refused.

On day two, his clinical condition worsened with unstable hemodynamics. His blood pressure was 80/50 mmHg, heart rate 120 bpm and urine output 0.4 ml/kg/hour. On the other hand, his serum laboratory results also showed worsening renal and liver function. His urea, creatinine, and AST and ALT sharply increased to urea of 17 mmol/L, creatinine of 130 µmol/L, AST of 2016 UI/L, and ALT of 2305 UI/L. The patient agreed to emergency percutaneous aortic

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balloon valvuloplasty and noradrenalin and dobutamine infusion. After balloon inflation, aortic valve gradients were measured and showed a significantly reduction, from 30 mmHg to 3 mmHg. Bedside echocardiography showed an aorta valve area improvement (AVA of 1.0 cm^2) and aortic valve gradient of 5 mmHg. Patient was controlled by continuous furosemide infusion and ventilation support.

In the following days, his clinical statement improved: his hemodynamics was gradually stabilized, endotracheal tube was removed on day three, and his urine output was 1.5 ml/kg/hour. The laboratory results showed gradual decreases in creatinine, urea, AST and ALT. Creatinine and urea lowered to normal ranges on day 7. However, AST and ALT lowered to normal ranges later on day 10. The patient recovered well and was discharged on day 11.

Discussion

Worldwide, the definition of "cardio-renal syndrome" has been recently well accepted. It describes the relationship between poor cardiac and renal function. Five subtypes were defined to better understand pathophysiological activities, epidemiology, and optimal therapies. Type 1 and type 2 CRS are characterized by acute or chronic worsening of cardiac function, leading to acute or chronic poor renal function. Type 3 and type 4 CRS are characterized by acute or chronic renal dysfunction, leading to acute or chronic cardiac dysfunction. Lastly, cases where acute or chronic systemic disorders lead to cardiac and renal dysfunction are indicated by type 5 CRS [1]. Type 1 CRS occurs not only in acute heart failure, but also in acute coronary syndrome and in patients following cardiac surgery [5].

An important characteristic of type 1 CRS in patients with acute heart failure is worsening renal function (WRF). Currently, WRF during hospitalization is defined as acute kidney injury by AKIDO, in which serum creatinine increases ≥ 1.5 times baseline within 7 days, 0.3 mg/dL (26.5 μmmol/L) within 48 hours, or urine volume < 0.5 ml/kg/hour for 6 hours [6]. In clinical practice, the incidence of WRF in patients admitted for acute heart failure ranges from 11% to 40% and is related to poor prognosis during hospitalization, including length of stay in the intensive care unit and length of stay in hospital. Furthermore, WRF is associated with cardiac outcomes, renal complications, and long-term mortality [7]. Interestingly, a significantly higher proportion of acute heart failure patients have type 1 CRS compared to acute coronary syndrome or cardiac surgery patients [5].

Abnormal liver function tests (LFTs) were found in 46% to 76% of admitted patients with acute heart failure and is associated with increased short- and long-term mortality. Nevertheless, patients with abnormal AST and/or ALT presented with more signs of hypo-perfusion. Other LFTs, including total bilirubin, gama-glutamyltransferase, alkaline phosphatase, AST, and ALT, were previously described and are closely related to acute heart failure severity [8,9]. A 12-month registry found that the prevalence of elevated ALT and AST were 28% and 24%, respectively. Elevated transaminases were reported more commonly in patients with right heart failure, cardiac shock, or an ejection fraction < 45%. ALT was strongly associated with worsening renal function, longer length of stay, and intensive care unit admission [10]. While cholestatic enzymes such as alkaline phosphatase, or gama-glutamyltransferase were reported as normal or mildly elevated, transaminases were found to be more highly elevated in acute heart failure and cardiogenic shock. Moreover, LFTs were differentially elevated in systolic or diastolic heart failure [11]. To the best of our knowledge, no specific LFTs were recommended to define the term "cardio-hepatic syndrome".

Unstable hemodynamics likely plays an important role in the pathophysiology pathway of type 1 CRS. It leads to fluid retention and abnormal reperfusion in the heart and the kidney. Some remarkable cardiac mechanisms include decreasing cardiac output, venous congestion, renin-angiotensin-aldosterone activation and systemic nervous system. Decreasing renal arterial flow leads to a reduction in glomerular filtration rate. Moreover, renal venous congestion, renal interstitial pressure elevation, peri-tubular pressure elevation, impaired auto-regulation, and renal perfusion pressure reduction contribute to a complicated mechanism for type 1 CRS. A recent review demonstrated that each category of patients, including cold-pattern patients, warm-pattern patients, and warm and wet patients, have distinct mechanisms for type 1 CRS [12].

Acute cardio-hepatic syndrome is characterized by acute heart failure, leading to acute and rapid exacerbation of liver injury, including hypoxic hepatitis, ischemic hepatitis, or liver shock. The abnormal systemic hemodynamics cause a decrease in oxygen uptake in the liver. Low cardiac output is associated with acute impaired liver perfusion and causes hepatocellular damage and necrosis. Moreover, the elevated right-sided filling pressure can compress centrilobular liver sinusoids, and increase injury of liver cells [2]. Elevated intra-abdominal pressure in acute heart failure is a potential mechanism for liver cell injury and worsening liver function [13]. These mechanisms cause acute ischemic and/or hypoxic liver injuries that can be either asymptomatic or symptomatic [4].

Venous congestion improvement, perfusion improvement, tissue oxygenation, and euvolemic achievement are essential management of cardio-renal syndrome and cardio-hepatic syndrome [2,14]. The patient should be checked whether, where and which main potential mechanisms causes volume overload. Another important feature is the present of hypo-perfusion. Bedside physical examination is the simplest way to determine clinical signs or symptoms of congestion and peripheral hypo-perfusion. Clinical profiles of acute heart failure patients can be divided into 4 groups including warm-dry, warm-wet, cold-dry, and cold-wet based on initial examination. Clinical management decisions can be easily made from patient profiles during the early phase. Pharmacotherapy such as diuretics, vasodilators, inotropic agents, and vasopressors are recommended for the management of patients' conditions [15]. One challenge of treatment is the determination of combination of drugs and optimal time of delivery for maximal effectiveness. Normally, in type 1 CRS patients with volume overload in the absence of poor blood pressure, loop diuretics remain the cornerstone of treatment. However, the optimal dose or mode of administration is still indertermined [14]. The Diuretic Optimization Strategies Evaluation trial showed that there was no overall difference in diuretic efficacy between bolus versus continuous administration and high dose versus low dose in acute decompensated heart failure. The higher dose strategy was associated with better diuresis, dyspnea improvement, and weight loss but also with an increase in creatinine level [16]. As a result, loop diuretic strategies are performed by physicians' experience in clinical practice. Monitoring of clinical status daily, especially congestion signs and symptoms, weight, and volume diuresis are recommended to achieve the correct fluid balance, reduction in congestion, and better perfusion [15]. Diuretic resistance is a challenge of treatment in CRS, it has been proven to reduce diuretic efficacy and increase clinical outcome. The recommended approach for treating diuretic resistance includes optimal loop diuretic, adding the second class of diuretics such as thiazide, metolazone, or acetazolamide, considering alternative strategies by using the third diuretic class, dopamine, or hypertonic

saline solution, and ultrafiltration. On the other hand, medications such as nonsteroidal anti-inflammatory drugs should be avoided [17]. Inotropes, vasodilator, and angiotensin-converting-enzyme inhibitors should be considered in acute heart failure patients based on clinical presentation [18]. Monitoring for recovery of liver and renal function should be checked regularly to modify doses of medications that depend on liver and hepatic metabolism [2]. Importantly, identification and management of acute aetiology in heart failure should be urgently considered to avoid further deterioration [15].

Low flow, low gradient severe aortic stenosis is defined as an aortic valve area <1.0 cm^2, a mean transvalvular pressure < 40 mmHg and a left ventricular ejection fraction <50% [19,20]. It is the most frequent severe aortic stenosis and has worse clinical events than high gradient severe aortic stenosis. A low-dose dobutamine echocardiography should be recommended to rule out pseudo-severe aortic stenosis due to incomplete valve opening [21,22]. The optimal therapy is still up for debate, and further trials are needed to determine the ideal treatment.

We report a severe aortic stenosis patient with both liver and renal injuries. We believe that unstable systemic hemodynamic in our acute heart failure patient leads to congestion and perfusion impairment in the liver and the renal. This common pathophysiology pathway of CRS and CHS causes a syndrome that we call "cardio-renal-hepatic syndrome" – which we successfully treated with percutaneous aortic balloon valvuloplasty and acute heart failure treatment therapies.

Conclusion

Cardio-renal syndrome and cardio-hepatic syndrome are complex challenges that contribute to the mortality rate of patients with acute heart failure. Congestion status and abnormal reperfusion are mentioned as cornerstone mechanisms of these severe syndromes. Clinical monitoring requires early discovery of worsening renal and abnormal liver function status after admission, particularly the first several days. Management approaches, including diuretic strategies, inotropes, vasodilator and other drugs, depend on the clinical situation. Nevertheless, acute heart failure aetiology should be detected and managed.

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