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CARDIOPATHY AND CHRONIC RENAL FAILURE IN A DIABETIC PATIENT

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ABSTRACT

Chronic kidney disease (CKD), is a worldwide public health issue, and it is under diagnosed and under-treated, which limits the implementation of early interventions that may prevent or delay its clinical course. The present study, aimed to illustrate the association between diabetes and arterial hypertension, contributing to the genesis of renal dysfunction, the therapeutic strategies for this nephropathy and its limitations. The patient had a 29-year history of type 2 diabetes, hypertension and left ventricular hypertrophy, diabetic retinopathy 4 years previously, chronic kidney disease, due to diabetic nephropathy and right diabetic foot with double-digit amputation. For the past 9 months, she had been undergoing hemodialysis 3 times weekly for 4 hours, each time via a left arm arteriovenous fistula. The patient's medications included oral hypoglycemic and antihypertensive. She was admitted to hospital emergency, presenting the following complaints: hypotension, hypervolemia, dyspnoea, dizziness and asthenia. Ten days after admission, the patient died, due to hydroelectrolytic disturbance, systemic arterial hypertension, chronic renal failure and *Diabetes mellitus*. In this study, the patient had diabetes for a long time and did not adequately control blood glucose, which contributed to the development of hypertension and late detection of heart disease and chronic renal failure, due to diabetes.

KEYWORDS: Hypertension, Diabetes, Chronic Kidney Disease, Hemodialysis & Cardiovascular Disease

INTRODUCTION

Diabetes mellitus (DM) is a disease of worldwide importance that has become a public health problem. Accounting for 90% of cases of diabetes, type 2 diabetes mellitus is a chronic metabolic disorder that is characterized by insulin resistance and high blood glucose levels (hyperglycemia). The number of cases of type 2 DM has almost quadrupled, since 1980 (WHO, 2014).

The chronic hyperglycemia of type 2 DM, is associated with long-term complications, including the damage, dysfunction, and failure of the heart, kidneys, blood vessels, and other organs (Bravo *et al*., 2015; Yu *et al*., 2017). The cardiovascular diseases, due to diabetes are the leading cause of death in patients, with chronic kidney disease (CKD) in renal replacement therapy, by hemodialysis (London, 2003). Cardiovascular mortality in these individuals is 10 to 20 times more frequent, than in the general population (Foley *et al*., 1998).

The spectrum of the cardiovascular diseases, due to diabetes can be described as the combination of changes in myocardial perfusion (ischemic process), altered myocardial function (metabolic processes), structural changes (hypertrophy or ventricular dilatation), and atherosclerosis affecting the peripheral and central vascular system. In chronic kidney disease, there is evidence that, all these processes can occur simultaneously and in the end, contribute to a higher occurrence of cardiovascular diseases, in this population (Sarnak and Levey, 2000).

Diabetic nephropathy affects 30% to 40% of individuals, with type 1 diabetes mellitus and 10% to 40% of those with type 2 DM, representing the main micro vascular complication of diabetes and the major cause of end-stage renal failure, in all the world (Reddi and Camerini-Davalos, 1990). It is a clinical syndrome, comprising the following features: albuminuria, progressive reduction, in glomerular filtration rate (GFR) and hypertension (Uwaezuoke, 2017).

OBJECTIVES OF THE STUDY

The present case aims to illustrate the association between diabetes and arterial hypertension, contributing to the genesis of renal dysfunction, the therapeutic strategies for this nephropathy and its limitations.

METHODS

Clinical Case

M. H, 59 years old, female, married and a housewife. Patient was admitted to a hospital emergency room, in the state of Mato Grosso do Sul, Brazil, presenting the following complaints: hypotension, hypervolemia, dyspnoea, dizziness and asthenia. At the time she had a blood pressure of 90 x 60 mmHg, despite the use of antihypertensive medication, for twenty four months. There were 60 days, she had lower limb edema, progressive and ascending, and decreased urinary volume. A patient with chronic renal failure and underwent a hemodialysis session nine months ago, three times a week, with fistula in the left upper limb for hemodialysis. On the fifth day of admission, she presented periods of agitation and blood pressure 100x80 mmHg. The sixth day of hospitalization presented difficulty swallowing and pressure 100x60 mm Hg. On the seventh day, she underwent hemodialysis, alternating periods of prostate and agitation, with blood pressure equal to that of the previous day. After nine days of hospitalization, with the use of oral hypoglycemic, antihypertensive drug and hemodialysis treatment, the patient was referred to the Intensive Care Unit (ICU), due to hypotension during a hemodialysis session. After eleven hours in the ICU, she died due to hydro electrolyte disturbance, systemic arterial hypertension, chronic renal failure and *Diabetes mellitus*.

Background

Diabetic patient for twenty-nine years, always in irregular treatment, using oral hypoglycemic agents (sitagliptin, 100 mg) and always with inadequate glycemic control; right diabetic foot with double-digit amputation, difficulty with ambulation, diabetic retinopathy four years ago. Two years ago, she developed hypertension, which was treated with hydrochlorthiazide, 25 mg. The patient also presented with left ventricular hypertrophy, depression and anxiety disorder. The last two diseases were not treated.

Laboratory and Medical Examinations

Glycemia: 269 mg/dl; erythrocytes 2.95 million/mm^3; hemoglobin 7.9 g/dl; leukocytes 3,300/mm^3; platelets 216,000/mm^3; potassium: 6.4 mmol/l; sodium: 140 mEq/l; calcium: 9.1 mg/dl; magnesium: 2.3 mg/dl; chlorine: 103 mEq/l; creatinine: 5.3 mg/dl; albumin: 2.7 g/dl; urea: 171 mg/dl; pyruvic transaminase: 48 U/l. Urine examination revealed the presence of glucose and proteins.

Ultrasonography of the abdomen: liver with normal volume and absence of vascular and ductal alterations; cholecystectomy, biliary and extrahepatic bile ducts, without abnormalities, pancreas with normal volume and normal textural echogenicity, spleen with normal volume and texture, abdominal aorta with normal path, right and left kidney with cortical-medullary thickness of 1.8 cm and 1.9 cm, measuring 104.8 mm and 102.7 mm, respectively. Both kidneys had a

smooth surface, a normal form, preserved cortico-medullary echogenicity, with good visualization of the pyramids, hyperechogenic renal sinus and absence of calyx and urinary bladder dilatation, smooth and thin wall with anechoic content.

Chest x-ray showed an increased cardiac area and thickened bronchial weave in both lungs. Electrocardiogram: sinus rhythm and left ventricular overload. Echocardiogram: 26 mm aorta, right ventricle measuring 22 mm, left ventricle measuring 68 mm in diastole and 56 mm in systolic, ventricular function with ejection fraction of 0.37 and a systolic fraction of 0.18, inter ventricular septum with 10 mm of thickness and decreased movement, tricuspid valve with discrete insufficiency, mitral valve with moderate insufficiency; normal pulmonary and aortic valves and pericardium with discrete effusion.

DISCUSSIONS

The number of patients with chronic kidney disease is increasing worldwide, on an alarming scale. The magnitude of the problem is so great that, it has led the medical authorities to consider it as a public health problem. The number of deaths from CKD has risen by 82.3%, in the last two decades, despite increased availability and advances in the field of renal replacement therapy (Lozano *et al*., 2012).

US Renal Data System Annual Data Report (2016), indicate mortality rates in end-stage renal disease patients undergoing standard hemodialysis, to be 16.9%. The number of end-stage renal disease patients receiving renal replacement therapy is estimated at > 1.4 million, with an annual growth rate of 8% (White *et al*., 2008).

CKD is one of the widely recognized and notorious indicators for hospitalization, cardiovascular events, cardiovascular and non-cardiac mortality, and all-cause of mortality CKD also affects cognitive impairment and quality of life (Park, 2014).

The unfavorable evolution of CKD is mainly, due to the frequent association of cardiovascular co morbidities and the relatively early occurrence of complications, typical of renal disease. Thus, treatment of arterial hypertension, preferably with angiotensin converting enzyme inhibitors (ACEI) and/or angiotensin 1 receptor blockers, glycemic control in diabetics, maintenance of proteinuria <1.0 g/day, and the correction of anemia, changes in calcium and phosphorus, correction of metabolic acidosis and prevention of malnutrition are fundamental interventions, to provide optimal clinical control of CKD (Parmar, 2002).

Antihypertensive therapy aims at both renal and cardiovascular protection, since chronic renal insufficiency and DM are independently associated, with a significant increase in mortality from cardiovascular causes. The pressure target in this population should be 130x80 mm Hg, according to the guidelines of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC 7), on the management of hypertension in the presence of chronic kidney disease, however, even lower values (< 125x75 mm Hg) are warranted in nephropathies with proteinuria greater than 1000 mg/day (K/DOQI, 2004).

The pharmacologic armamentarium for the treatment of hypertension notably includes β-blockers, (dihydropyridine) calcium channel blockers, and renin-angiotensin system (RAS) inhibitors. Less commonly used classes in dialysis patients comprises central α agonists, peripheral α antagonists, and direct vasodilators. Diuretics constitute another antihypertensive modality in patients with normal urine output or mild oliguria, but their utility is limited in end-

stage renal disease; aside from loop diuretics (in patients with residual kidney function), class members are infrequently prescribed. In dialysis patients, hypertension can be managed by agents in one or more classes; for patients who have also been diagnosed with heart failure, β-blockers and RAS inhibitors may be efficacious through mechanisms, other than blood pressure reduction (Bakris *et al*., 2016).

Ideally, a little quantity of albumin is filtered in the glomerulus, and is accompanied by its near-complete re absorption in the tubules. Thus, increased urinary albumin excretion is accepted, as a well-established biomarker of glomerulopathy, as well as tubulopathy because in the latter, there is reduced re absorption of the filtered albumin (Uwaezuoke, 2017).

In this study, the authors evaluated clinical-laboratory parameters, known to be related to CKD in diabetic and hypertensive patients. When serum creatinine levels are ≥ 1.5mg/dl for women and ≥ 2.0 mg/dl for men, nephrological follow-up is recommended, as proposed by the American National Institutes of Health (NIH, 1994). The CKD staging according to the estimated glomerular filtration rate from the last serum creatinine registry showed that, the patient was in stage 5 of the disease (serum creatinine > 5 mg/dl).

Rigorous glycemic control is essential in diabetic patients, particularly those with CKD. The glycemia in the evaluated patient was 269 mg/dl and, on most days of hospitalization, the glycemia was > 110mg/dl. Although most of the evidence relates to the benefits of strict blood glucose control in relation to CKD prevention, it is clear that, maintaining a euglycemic state should be pursued to promote the prevention or decrease of macro vascular and micro vascular complications of diabetes (UK Prospective Diabetes Study, 1998).

As renal replacement therapy, renal transplantation has been consolidated as an elective therapy for patients on dialysis, independently of age, sex, diabetic and non-diabetic patients, with a significant increase in life expectancy. This increase is more relevant in young diabetic patients aged 20 to 39 years, with an increase in survival over dialysis for 17 years. Patients between 60 and 74 years of age, diabetics and non-diabetics, had an increase in survival of three and five years, respectively (Wolfe *et al*., 1999).

Adults on dialysis are at increased risk of foot ulceration, which commonly precedes more serious lower limb complications, including amputation. Dialysis patients have a high burden of lower limb complications. There are markedly higher risks of foot ulceration and/or amputation, in those with previous and/or current ulceration, previous amputation, peripheral arterial disease, lower serum albumin, and foot deformity (Kaminski *et al*., 2017). The diabetic foot ulcer is affected by several factors, including patient age, educational status of the patient, weight of patient, type of diabetes mellitus, patient habits of foot self-care practice, and the presence of complicated peripheral neuropathy (Mariam *et al*., 2017).

Patients undergoing dialysis treatment are at a higher risk of impaired physical function and mobility, which are strong predictors of disability, hospitalization, falls, and death and are often associated with poor outcomes. Complications commonly encountered in this population of patients are peripheral neuropathy, amputation and heart failure.

The patient had a diabetic foot and she performed double-digit amputations on the right foot before starting the hemodialysis treatment. Patients with type 2 diabetes are more likely, to develop lower limb injuries. The time of disease should also be considered, since studies have found that there is a greater propensity to develop lesions in patients, with

more than 10 years of disease duration, in the case in question the patient had diabetes, for 29 years (Araújo and Alencar, 2009).

Usually, diabetic nephropathy is accompanied by diabetic retinopathy. Nevertheless, the absence of diabetic retinopathy does not exclude the diagnosis of diabetic nephropathy (Martínez-Castelao *et al*., 2015). Retinal micro-aneurysms and haemorrhages are the first signs of retinopathy in people, with diabetes mellitus and its presence has a high predictive value for the worsening of retinopathy (Olafsdottir *et al.,* 2014) these authors reported that, the frequency of any diabetic retinopathy increased to 68%, when the duration of diabetes was more than 20 years. The patient presented several complications of diabetes, such as, retinopathy, due to the long time she had the disease.

Dialysis patients frequently report generalized weakness, fatigue, difficulty with ambulation and decreased range of motion. The patient reported all these symptoms, besides presenting depression and anxiety. Mental disorders, including depression and anxiety are the prevalent human diseases which are associated with several metabolic diseases. Type 2 DM, as a complicated metabolic disorder, is associated with inflammation and also mental disorders. It has been hypothesized that depression and anxiety, as mental disorders may be the inducers/stimulators of inflammation in the patients suffering from type 2 DM (Hajebrahimi *et al*., 2016).

CONCLUSIONS

The public health impact of kidney disease is larger than previously appreciated, and early detection, education, intervention, and risk-factor control need to address the heavy burden of cardiovascular disease and adverse events in this vulnerable population.

To prevent the progression of diabetic kidney disease and subsequent cardiovascular morbidity and mortality entailed in patients with diabetes, it is important to personalize treatment and to set treatment goals, for individual patients depending on age, type of diabetes, and its duration.

In this study, the patient had diabetes for almost 30 years and did not adequately control blood glucose, which contributed to the development of hypertension and late detection of heart disease and chronic renal failure, due to diabetes.

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