*Arch Clin Med Case Rep 2021; 5 (3): 448-454* *DOI: 10.26502/acmcr.96550378*

## Case Report

# Focal Segmental Glomerulosclerosis Presenting as Acute Systolic Heart Failure

**Maurice Mosseri, Asseel AlBayati, Ndausung Udongwo*, Ennis Alsaadi, Swapnil Patel, Shuvendu Sen, Arif Asif**

Jersey Shore University Medical Center, Internal Medicine department, Neptune City, USA

***Corresponding Author:** Ndausung Udongwo MD, Jersey Shore University Medical Center 1945 New Jersey 33, Neptune City, USA

**Received:** 16 April 2020; **Accepted:** 07 May 2020; **Published:** 21 May 2021

## Abstract

Cardiomyopathies are present in many forms and are the result of numerous etiologies with one well-established etiology being chronic kidney disease (CKD). With recent discoveries linking early stages of CKD to profound cardiovascular disease (ischemic or non-ischemic cardiomyopathy), our focus has shifted to a seemingly inexplicable link between focal segmental glomerulosclerosis (FSGS) and non-ischemic cardiomyopathy. The cardiovascular and renal organ systems possess a unique relationship which we presume to be a bi-directional association of cause-and-effect. We present two cases in which our patients, with underlying FSGS, present with signs and symptoms of systolic heart failure.

**Keywords:** Acute systolic cardiomyopathy; Focal-segmental glomerulosclerosis; Cardiorenal syndrome; Renocardiac syndrome

## 1. Introduction

There is often a clinical overlap between the kidney and heart dysfunctions, and the term “cardiorenal syndrome” (CRS) is used to define this interaction [1]. There are 5 classifications of this syndrome according to the Consensus Conference by the Acute Dialysis Quality Group in 2008 [2] which divides the cardiorenal axis into two main groups, the cardiorenal CRS (type 1 and 2) and the renocardiac CRS (type 3 and 4). Type 3 CRS defines the acute

kidney injury (AKI) that causes acute heart failure [3]. Type 4 CRS is the chronic kidney disease (CKD) that leads to heart dysfunction [3]. Many mechanisms are proposed to explain this association, including fluid overload, metabolic acidosis, electrolyte imbalance, among others [4]. Despite the known high incidences of AKI, as of now the data is limited to characterize the details of the renocardiac (type 3 and 4) CRS [4]. To this day there is no definitive understanding of the pathophysiology and etiology of cardiomyopathies. Despite extensive research and advances in this field through the decades, from the molecular, genetic, up to clinical and radiological assessment, many classifications for myocardial diseases remain controversial. Phenotypically, cardiomyopathies can be classified into hypertrophic, dilated, and restrictive patterns. Hypertrophic cardiomyopathy is the most reported primary cardiomyopathy [5]. However, dilated cardiomyopathy (DCM) is typically genetic or acquired secondary to environmental, infectious, or systemic factors [6-8]. Although DCM predominantly affects patients at the age of 40 to 59 years of age, it can happen at any age [6, 9].

We are reporting two unique cases of two young adults (<40 years old) who both have a biopsy-confirmed focal segmental glomerulosclerosis in its early and advanced stages that presented with non-ischemic cardiomyopathies. To our knowledge, not many reports have been published to reveal the association between FSGS and cardiomyopathies.

## 2. Case Presentation

### 2.1. Case 1

A 32-year-old African-American male with a history of hypertension and undetermined stage 3 chronic kidney disease, presented to the emergency department with complaints of progressive substernal chest pain that started one month ago. He described the pain as dull in quality with a severity of five on a ten-point scale. He described the chest pain as being intermittent, lasting two to four minutes aggravated by physical activity and sexual intercourse. It was associated with exertional shortness of breath and a non-productive cough. However, he denied pain radiation, leg swelling, fever, chills, recent illness, or travel history. He also denied any previous episodes in the past. His symptom was associated with a non-productive cough. No travel history or sick contacts were elicited. Patient was found to be in no acute distress, with no remarkable findings on physical examination. Vital signs on presentation included blood pressure of 247/166 on mmHg on the left arm and 245/160 on right arm, heart rate of 82 beats per minute, respiratory rate of 18 breaths per minute and oxygen saturation of 97% on room air. Laboratory testing revealed potassium of 3.6 mmol/L [3.5-5.2 mmol/L], blood urea nitrogen of 17 mg/dl [3.5-5.2 mmol/L], creatinine of 1.98 mg/dl [0.61-1.24 mg/dL] with proteinuria of 100 mg/dL on urinalysis [normal range is negative], random urine protein 137 mg/dL, protein-creatinine ratio 975.8 mg/dL [0-200 mg/dL], glomerular filtration rate of 39 mL/min [>60 mL/min/1.73m*2], troponin of 0.04 ng/mL [<0.08 ng/mL], and brain natriuretic peptide of 558 pg/mL [0-100 pg/mL]. His Electrocardiogram showed normal sinus rhythm with left ventricular hypertrophy, left atrial

enlargement, ST-segment depression in inferior leads (I, II), lateral leads (I, aVL, V5 and V6) with T wave inversions in all leads, except V1-V3. Chest x-ray showed a mildly enlarged cardiac silhouette. CT- angiogram of the chest, abdomen and pelvis confirmed left ventricular hypertrophy, with no aortic dissection, pulmonary embolism, and no nodules or masses were noted on adrenal glands or kidneys. The patient's condition was stabilized with nitroglycerin infusion at a rate of 5 mcq/min that was uptitrated to achieve a goal of blood pressure 190/80 mmHg within the first hour. He also received intravenous pushes of labetalol 20 mg, intravenous pushes of metoprolol 5 mg, two doses of intravenous hydralazine 10 mg 4 hours apart, and a dose of 325 mg of aspirin tablet orally (chewable). Within 6 hours of his presentation, the blood pressure was stabilized to 162/95 mmHg and he was free of chest pain. The patient was admitted to the hospital for the management of hypertensive emergency with end-organ damage to the heart and kidneys. Cardiology service was consulted for further recommendations in the management. Type II Non-ST-segment elevation myocardial infarction, secondary to hypertensive emergency was diagnosed, after cardiac catheterization. Echocardiogram showed heart failure with reduced ejection fraction of 41%-45%, with moderate global hypokinesis, mild mitral regurgitation and severely increased left ventricular wall thickness. Cardiac magnetic resonance imaging showed findings consistent with a biventricular non ischemic cardiomyopathy with an ejection fraction of 36%, and severe concentric left ventricular hypertrophy.

Patient's hospital course was uncomplicated and a workup for secondary causes of hypertension was implemented. Results for aldosterone, aldosterone to renin ratio, plasma and 24-hour urine metanephrines, thyroid stimulating hormone and renal artery doppler ultrasound were unremarkable. With increased renal echogenicity noted on renal ultrasound and worsening kidney function, Nephrologist recommended renal biopsy. Oral anti-hypertensive medications were started incrementally. Blood pressure was stabilized. He was discharged on the following medications: Amlodipine 10 mg daily, isosorbide mononitrate 120 mg daily, losartan hydrochlorothiazide 100-25 mg daily, metoprolol succinate 100 mg daily and hydralazine 25 mg three times a day. Renal biopsy showed focal segmental glomerulosclerosis. Patient was scheduled for outpatient follow up with cardiology and nephrology.

### 2.2. Case 2

A 28-year-old African American male with a history of hypertension presented to the emergency department complaining of sudden onset of lightheadedness and high blood pressure measurement at home (211/130 mmHg). He reported having "tunneled vision" that lasted for about 30 seconds. He also reported that he has been experiencing shortness of breath at night for the last 4 weeks, non-productive cough with yellowish sputum since then, and also noticed progressive bilateral lower limbs swelling. He denied any hearing loss, tinnitus, loss of consciousness, chest pain, or palpitation. Review of systems was significant for bi-temporal headache. He was noncompliant with his antihypertensive medication. He endorsed smoking two packs per day for nine years, and

drinking alcohol socially, the last drink was more than four weeks. He denied any use of recreational drugs, especially cocaine. Family history was remarkable for hypertension and coronary artery disease.

Vital signs showed blood pressure of 199/141 mmHg on left arm and 190/140 mmHg on right arm, heart rate of regular 122 beats per minute, respiratory rate of 31 breaths per minute, and pulse oximetry of 97% on room air. On physical examination, he was not in acute distress. He was alert, oriented to person, place and time. Cardiac examination revealed audible S1, loud S2 with no murmurs, rubs, and gallops. No jugular venous distension was found. Bilateral lower extremity pitting edema up to the mid-legs was noted. Laboratory tests showed potassium of 5.6 mmol/L [3.5-5.2 mmol/L], blood urea nitrogen of 10 mg/dL [3.5-5.2 mmol/L], creatinine of 1.33 mg/dL [0.61-1.24 mg/dL], troponin of 0.32 ng/dL [<0.08 ng/mL], and brain natriuretic peptide of 622 pg/mL [0-100 pg/mL],. Troponin trended down subsequently. Urinalysis revealed proteinuria. 24-hour urine protein-level was 210 mg/(24.h) (reference range; 0 to 150 mg/(24.h). Urine drug screen was negative. Electrocardiogram showed normal sinus rhythm, with signs of left atrial enlargement, left ventricular hypertrophy, and T-wave inversion on lead I, and V4-6 suspicious for left ventricular strain. Chest x-ray showed an enlarged cardiac silhouette. This was a new finding compared to the previous chest X-ray four years ago. His blood pressure improved to 162/85 mmHg, after receiving multiple doses of labetalol 20 mg intravenously. In addition to stabilizing his blood pressure, lasix 40 mg intravenously and hydrochlorothiazide PO 12.5 mg were added to manage acute decompensated heart failure symptoms. He was transferred to the telemetry floor for monitoring.

Transthoracic echocardiogram showed severely enlarged left atrium, mild mitral and aortic valve regurgitation, and severely reduced left ventricular systolic function, with an ejection fraction of 21-25%. Right and left heart catheterization showed mildly elevated filling pressures with low cardiac output, and patent non-diseased coronary arteries. Cardiac Magnetic resonance imaging showed bi-ventricular dysfunction and severe global hypokinesis, with left ventricular ejection fraction of 21%. No scar tissue, infiltrative cardiomyopathy, nor myocarditis signs were present. Other workup (e.g. Anti-nuclear antibodies, metanephrines, normetanephrines) was unremarkable. Ultrasound guided kidney biopsy showed FSGS. Blood pressure stabilized and he was discharged on the following oral medications: spironolactone 25 mg daily, sacubitril-valsartan 24-26 mg twice daily, isosorbide dinitrate 20 mg three times daily, hydralazine 25 mg three times daily, carvedilol 25 mg twice daily, and amlodipine 10 mg daily. The patient was further discharged on a wearable cardioverter-defibrillator (LifeVest). One month after discharge, his blood pressure reading on follow-up visit was 130/80 mmHg. Cardiology and nephrology follow up was advised for closer monitoring of newly diagnosed non-ischemic cardiomyopathy and FSGS, respectively.

## 3. Discussion

FSGS presents more commonly in the African-American population with an incidence greater in men as compared to women (1.5-2) and a mean age range between 23 to 57 years old [10-14]. Polymorphic variants (G1 and G2) in the Apolipoprotein 1 (APOL-1) gene, have been reported to increase the risk of FSGS amongst African-Americans [15, 16]. Elevated blood pressure, elevated creatinine, proteinuria, and nephrotic syndrome (NS) are some of the hallmarks of this disease. Although our patients had pertinent clinical and laboratory findings of NS. IR guided renal biopsy was done to confirm FSGS histologically. Under microscopic examination, it shows-focal and segmental destruction of capillary tufts with an increased matrix, which ultimately was visible in both our patients. FSGS is classically treated with high-dose prednisone as well as calcineurin inhibitors in patients with resistant FSGS. The cardiovascular and renal systems work together to maintain body homeostasis. If one fails, the other is affected. Cardio-renal syndromes have been grouped into five types. An acute or chronic pathology in the heart can cause pathological changes in the renal system (type 1 and 2), and vice versa (type 3 and 4) [2, 17, 18].

In 2006, the American Heart Association (AHA) defined cardiomyopathies as “a heterogeneous group of diseases of the myocardium due to a variety of causes that frequently are genetic. Cardiomyopathies either are confined to the heart or are a part of generalized systemic disorders, often leading to cardiovascular death or progressive heart failure-related disability.” Cardiomyopathies can be primary, only involving the heart or secondary involving other organ systems [2, 17, 18] Glomerulopathy resulting in cardiomyopathy in patients with FSGS is still not clearly understood [19, 20]. Kaur et al. suggested that some inflammatory mediators like; Urokinase-type plasminogen activator receptor (UPAR), CD-40 antibodies and cardiotrophin like cytokine-1 causing FSGS could play a role in cardiomyopathy [19]. Malnutrition caused by significant protein loss, could result in compensatory breakdown of protein rich cells in the body including cardiac myocytes. Furthermore, the accumulation of urea and the activation of the renin aldosterone angiotensin system (RAAS) may also play a role leading to cardiomyopathy [2, 19]. Given our patients’ focal segmental sclerosis, histological findings point to the etiology of cardiomyopathy as a secondary cause. Especially, when both patients’ MRI results ruled out ischemic cause of cardiac disease.

Cardiomyopathies can also be classified based on morphology and physiology. Some of the classifications include hypertrophic, dilated, restrictive, and arrhythmogenic right ventricular cardiomyopathy [21]. Both of our patients' cardiac imaging was significant for non-ischemic cardiomyopathy. Chronic renal damage in patients with ESRD is well documented and can lead to cardiac disease. We may be underestimating how quickly and how direly FSGS can impact the balance of the cardiovascular-renal system, or there may be another more direct underlying connection between FSGS and acute systolic cardiomyopathy in young, otherwise healthy patients. Adedoyin et al case series reported 6 cases of children who had FSGS and presented with cardiomyopathies and CHF exacerbations

[20]. However, there has been no in-depth study found on the correlation in adults. More research is needed, but it is significant and notable that this may be a broader problem than suspected.

## 4. Conclusion

The bi-directional relationship that exists between the heart and the kidneys helps to maintain the body's homeostasis. Unilateral pathology in one, gradually leads to an acute or chronic failure in the other. We believe that the pathophysiological etiology of FSGS may contribute to non-ischemic cardiomyopathy seen in both of our patients. To get a clearer understanding of this, we recommend that more cases be reported in literature, regarding FSGS causing non-ischemic cardiomyopathy. This will help with earlier diagnosis and management and could lead to a decrease in mortality.

## Conflict of Interest

No potential conflict of interest relevant to this article was reported.

## Funding Statement

This project did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## References

1. Ronco C. The Cardiorenal Syndrome: Basis and common ground for a multidisciplinary patient-oriented therapy. CardioRenal Med 1 (2011): 3-4.
2. Ronco C, Haapio M, House AA, et al. Cardiorenal Syndrome. J. Am. Coll. Cardiol 52 (2008): 1527-1539.
3. Ronco C, Bellasi A, Di Lullo L. Cardiorenal Syndrome: An Overview. Adv. Chronic Kidney Dis 25 (2018): 382-390.
4. Di Lullo L, Reeves PB, Bellasi A, et al. Cardiorenal Syndrome in Acute Kidney Injury. Semin. Nephrol 39 (2019): 31-40.
5. Argulian E, Sherrid MV, Messerli FH. Misconceptions and Facts About Hypertrophic Cardiomyopathy. Am. J. Med 129 (2016): 148-152.
6. Maron BJ, et al. Contemporary definitions and classification of the cardiomyopathies: An American Heart Association Scientific Statement from the Council on Clinical Cardiology, Heart Failure and Transplantation Committee; Quality of Care and Outcomes Research and Functio. Circulation 113 (2006): 1807-1816.
7. Stacey RB, Caine AJ, Hundley WG. Evaluation and Management of Left Ventricular Noncompaction Cardiomyopathy. Curr. Heart Fail. Rep 12 (2015): 61-67.

8. Ikeda U, Minamisawa M, Koyama J. Isolated left ventricular non-compaction cardiomyopathy in adults. J. Cardiol 65 (2015): 91-97.
9. Luk A, Ahn E, Soor GS, et al. Dilated cardiomyopathy: A review. J. Clin. Pathol 62 (2009): 219-225.
10. Kitiyakara C, Eggers P, Kopp JB. Twenty-one-year trend in ESRD due to focal segmental glomerulosclerosis in the United States. Am. J. Kidney Dis 44 (2004): 815-825.
11. Haas M, Meehan SM, Karrison TG, et al. Changing etiologies of unexplained adult nephrotic syndrome: A comparison of renal biopsy findings from 1976-1979 and 1995-1997. Am. J. Kidney Dis 30 (1997): 621-631.
12. Ali AA, Sharif DA, Almukhtar SE, et al. Incidence of glomerulonephritis and non-diabetic end-stage renal disease in a developing middle-east region near armed conflict. BMC Nephrol 19 (2018).
13. Dragovic D, Rosenstock JL, Wahl SJ, et al. Increasing incidence of focal segmental glomerulosclerosis and an examination of demographic patterns. Clin. Nephrol 63 (2005): 1-7.
14. Braden GL, Mulhern JG, O'Shea MH, et al. Changing incidence of glomerular diseases in adults. Am. J. Kidney Dis 35 (2000): 878-883.
15. Lebrun S, Bond RM. Spontaneous coronary artery dissection (SCAD): The underdiagnosed cardiac condition that plagues women. Trends Cardiovasc. Med 28 (2018): 340-345.
16. Freedman BI, Limou S, Ma L, et al. APOL1-Associated Nephropathy: A Key Contributor to Racial Disparities in CKD. Am. J. Kidney Dis 72 (2018): S8-S16.
17. Schrier RW. Cardiorenal versus renocardiac syndrome: Is there a difference? Nat. Clin. Pract. Nephrol 3 (2007): 637.
18. Ronco C, House AA, Haapio M. Cardiorenal syndrome: Refining the definition of a complex symbiosis gone wrong. Intensive Care Med 34 (2008): 957-962.
19. Kaur P, Singh B, Patel P, et al. Non-ischemic cardiomyopathy with focal segmental glomerulosclerosis. J. Community Hosp. Intern. Med. Perspect 10 (2020): 154-157.
20. Adedoyin O, Frank R, Vento S, et al. Cardiac disease in children with primary glomerular disorders-Role of focal segmental glomerulosclerosis. Pediatr. Nephrol 19 (2004): 408-412.
21. McKenna WJ, Maron BJ, Thiene G. Classification, epidemiology, and global burden of cardiomyopathies. Circ. Res 121 (2017): 722-730.

**Citation:** Maurice Mosseri, Asseel AlBayati, Ndausung Udongwo, Ennis Alsaadi, Swapnil Patel, Shuvendu Sen, Arif Asif. Focal Segmental Glomerulosclerosis Presenting as Acute Systolic Heart Failure. Archives of Clinical and Medical Case Reports 5 (2021): 448-454.