A Case Report on Primary Collapsing Glomerulopathy in a Filipino Post-partum Female and An Updated Review of Literature

Kristine May F. Valmoria, MD and Raymond S. Alonso, MD

Division of Nephrology, Department of Medicine, Philippine General Hospital, University of the Philippines Manila

ABSTRACT

Collapsing Glomerulopathy (CG) is a rare entity presenting as nephrotic syndrome and rapidly progressive renal deterioration. It has been first identified among African-American patients and subsequently dubbed HIV-associated nephropathy after a number of patients with HIV were found to have CG. It has re-emerged recently among patients with COVID-19. To our knowledge, this is the first case of primary collapsing glomerulopathy in the country to be published.

The case is a 36-year-old Filipino female admitted due to bipedal edema which started 2 weeks post-partum. She has no comorbidities and social history was negative for illicit drug use. Initial work up showed hypoalbuminemia and diffuse hepatic disease on ultrasound. She was referred to a gastroenterologist where albumin infusion and paracentesis was done but with no improvement. She developed anasarca and was admitted. Paracentesis obtained minimal ascitic fluid. Serum ascites albumin gradient was low and baseline laboratories showed high creatinine, hypoalbuminemia, and albuminuria. 24-hour urine protein was 11 grams, ANA and anti-DsDNA were negative and c3 and c4 levels were normal. Hepatitis profile was negative for infection. Abdominal CT scan revealed multiple hypoenhancing lesions. Tumor markers CA-125, CA 19-9 and CA 15-3 were high. Breast ultrasound showed simple breast cyst. Gynecology consult was called where pap smear was negative for atypical cells. Surgery service recommended monitoring for the pancreatic and breast lesions. Kidney biopsy was delayed due to new onset bacterial pneumonia. COVID-19 RT-PCR test was negative. Patient was discharged improved with no edema. On follow up, the kidney biopsy result came out to be collapsing glomerulopathy. HIV test was then done and was negative. Bipedal edema and albuminuria recurred. She was started on tacrolimus. She has been on regular follow up and currently has no edema, no proteinuria and normal creatinine level.

This is an interesting case as the primary glomerular disease has been masked by the earlier laboratory findings which led us to think of liver disease then a paraneoplastic nephrotic syndrome. Ultimately, the renal biopsy revealed the diagnosis. This serves as an index case for primary collapsing glomerulopathy in a Filipino patient on remission after being treated with tacrolimus.

Keywords: nephrotic syndrome, glomerulosclerosis, immunosuppression therapy

Paper was presented virtually at the World Congress of Nephrology 2022, February 24-27, 2022, Kuala Lumpur, Malaysia.

eISSN 2094-9278 (Online)
Published: February 15, 2024
https://doi.org/10.47895/amp.vi0.6457

Corresponding author: Kristine May F. Valmoria, MD
Division of Nephrology
Department of Medicine
Philippine General Hospital
University of the Philippines Manila
Taft Avenue, Ermita, Manila 1000, Philippines
Email: kmf.valmoria@gmail.com
ORCiD: https://orcid.org/0000-0002-0857-168X

INTRODUCTION

Collapsing Glomerulopathy (CG) variant of Focal Segmental Glomerulosclerosis (FSGS) is designated when at least 1 glomerulus shows segmental or global obliteration of the glomerular capillary lumina by wrinkling and collapse of glomerular basement membranes in association with hypertrophy and hyperplasia of the overlying podocytes.[1] CG is a rare entity representing ~4.7% of biopsies with

focal segmental glomerulosclerosis.[2] While in a more recent single-center study in the United States, 1.4% of all kidney biopsies performed showed CG.[3]

In the Philippines, among all patients who underwent kidney biopsy showing GN, FSGS is the second most common GN at 16%, but there is no data on the subtypes.[4] To our knowledge, this is the first case of primary collapsing glomerulopathy to be published in the Philippines. It presents with nephrotic syndrome and a more rapidly progressive renal deterioration form of FSGS compared to other variants, responding poorly to treatment. Historically, CG has first been identified among African-American patients with aggressive glomerulonephritis. Subsequently, it has been called HIV-associated nephropathy (HIVAN) after nine patients with HIV infection were found to have CG. The pathogenesis of CG is related to podocyte dedifferentiation, deregulation of the cell cycle and transformation towards a proliferative phenotype that leads to the disappearance of mature podocyte markers.[5] Recently, it has re-emerged among patient with COVID-19 dubbing it as the new HIVAN.[6]

This paper discusses a case of Primary Collapsing Glomerulopathy seen in our institution. An updated review of primary CG is performed with a focus on cases diagnosed after the publication of Columbia Classification.

CASE PRESENTATION

The case is a 36-year-old Filipino female admitted due to anasarca. She had no known comorbidities. Her present illness started 3 months prior to admission when she noted bipedal edema 2 weeks post-partum of her third pregnancy. She initially sought outpatient consult with her obstetrician where work up showed hypoalbuminemia and diffuse hepatic disease on ultrasound. Liver enzymes and creatinine levels were normal at the time. She was given low dose loop diuretic and referred to a gastroenterologist where albumin infusion and paracentesis was done. Diuresis was increased but still with progression of edema. She also developed exertional dyspnea and 2-pillow orthopnea and was subsequently admitted at the Philippine General Hospital. Her family history was pertinent for diabetes mellitus, hypertension, ovarian cancer, myoma, and heart disease. She is gravida 3 para 3 (1203), with no complications in all the pregnancies. Social history was negative for intravenous or illicit drug use.

Upon assessment on admission, she had a BMI of 23, had pale conjunctivae, and the skin did not show any signs of embolic or vascular phenomenon. Pulmonary exam was significant for bibasal decreased breath sounds. The abdomen was distended and was positive on fluid wave test. There was grade 3, pitting, bilateral edema of all extremities.

She was initially admitted under gastroenterology service where paracentesis was attempted on the 2nd hospital day but with minimal turbid ascitic fluid obtained. Serum ascites albumin gradient was low and baseline laboratory results showed elevated creatinine at 1.65 mg/dl, hypoalbuminemia at 1.6 g/dl, cholesterol at 831.54 mg/dl, mild hypokalemia, and urine microscopy of +3 albumin. She was then referred to renal service and further testing showed a 24-hour urine protein of 11 grams. Hepatitis profile was negative for infection. Patient was started on losartan and statin alternating with fenofibrates. Whole abdominal CT scan results came out which revealed massive ascites, bilateral pleural effusion, a hypoenhancing pancreatic tail lesion, hepatic foci, multiple lymphadenopathies, and right breast cyst and left breast nodule. Hence, the primary consideration has been revised to nephrotic syndrome secondary to malignancy probably pancreatic or ovarian. Serum tumor markers showed high CA-125, CA 19-9 and CA 15-3. Breast ultrasound showed simple breast cyst, right and intramammary duct ectasia, bilateral. Table 1 shows the summary of laboratory results during admission. Diuresis was started for symptomatic relief of edema. She was referred to gynecology service where pap smear was negative for intraepithelial lesion or malignancy. Surgery consult was also called and an assessment of pancreatic tail focus – Intraductal Papillary Mucinous Neoplasm was made and they recommended observation and serial monitoring of the said lesion. As co-managing services considered malignancy less likely, a kidney biopsy was scheduled but temporarily delayed due to a new onset bacterial pneumonia. SARS-CoV-2 was ruled out via RT-PCR testing. Infectious disease was called who gave clearance for kidney biopsy after lysis of fever, due antibiotics, and a negative blood culture. There was resolution of edema, patient had no complaints and creatinine upon discharge was 139 mmol/L. Pending pathologic diagnosis, patient was discharged on the 12th hospital day and added high dose prednisone at 1 mg/kg in her medications.

On follow up at the outpatient clinic, other laboratory findings came out which showed: negative ANA and anti-DsDNA, and normal c3 and c4 at 0.889 g/L and 360 mg/l, respectively. Repeat albumin/creatinine ratio from a spot urine test was 731 mg/g. The kidney biopsy findings came out to be collapsing glomerulopathy variant of focal segmental glomerulosclerosis, acute tubular injury, and mild interstitial fibrosis and atrophy as seen in Figure 1. Immunofluorescence microscopy as seen in Figure 2 shows negative staining for Anti-IgA, C3, C1q; trace mesangial staining for anti-IgG, fibrinogen and IgM; 1+ focal granular vascular staining for IgM. HIV test was done and came out negative. She was then started on tacrolimus at 2 mg/day.

DISCUSSION

Literature review and methods

A search in PUBMED was performed using the search terms “collapsing glomerulopathy” and “collapsing FSGS.” Case reports, case series, and retrospective studies on primary collapsing glomerulopathy reported after the institution of Columbia classification in adults were reviewed for patient

characteristics, treatment, and outcome. CG secondary to or associated to infection, autoimmune disease, malignancy and medications, studies involving solely children, and papers without full text were excluded. Figure 3 shows the flow diagram of the study selection process done in this literature review.

The literature is limited regarding *collapsing glomerulopathy*, most of which have been associated to infection, malignancy, and autoimmune disease. To date, the exact incidence of primary CG among adults is unknown. No clinical trials have been done on the treatment for primary CG. The first report on CG was among six African-Americans

Table 1. Summary of Laboratory Tests Done on Admission

Laboratory Test	Result
Hemoglobin	129
Hematocrit	38
White blood cell	72
Platelet count	553
Total cholesterol	831.54 mg/dl
HDL	55.21 mg/dl
LDL	693.39 mg/dl
Triglycerides	424.78 mg/dl
BUN	14.61 mg/dl
Creatinine	1.65 mg/dl
AST	18 U/L
ALT	5 IU/L
Albumin	1.6 g/dl
Sodium	134 mmol/L
Potassium	3.2 mmol/L
Chloride	111 mmol/L
Calcium	7.24 mg/dl corrected
Magnesium	2.19 mg/dl

Laboratory Test	Result
Urinalysis	
Color	Light yellow
Transparency	Hazy
Glucose	+1
Albumin	+3
Blood	+2
PH	7
Nitrite	(-)
Leucocytes	(-)
Specific gravity	1.015
RBC	8/hpf
WBC	5/hpf
Bacteria	102/hpf
Mucus thread	10/hpf
24-hour urine protein	11 g/d
Abdominal CT scan	Massive ascites, bilateral pleural effusion, a hypoenhancing pancreatic tail lesion, hepatic foci, multiple lymphadenopathies, and right breast cyst and left breast nodule
Spot urine albumin / creatinine ratio	731 mg/g

Laboratory Test	Result
Tumor Markers	
AFP	1.25
CEA	2.6
CA125	2901 (H)
CA 19-9	89.91 (H)
CA 15-3	91.2 (H)
ANA	negative
Anti-DsDNA	negative
c3	0.889 g/L
c4	360 mg/l
Trans-vaginal ultrasound	Normal uterus with thin endometrium, normal ovaries, moderate ascites
PAP smear	Negative for intraepithelial lesion or malignancy
Breast ultrasound	Simple breast cyst, right and intramammary duct ectasia, bilateral
COVID-19 RT-PCR	negative
ALP	105 IU/L
PT %	94 %
PT-INR	1.05
HBsAg	Non-reactive

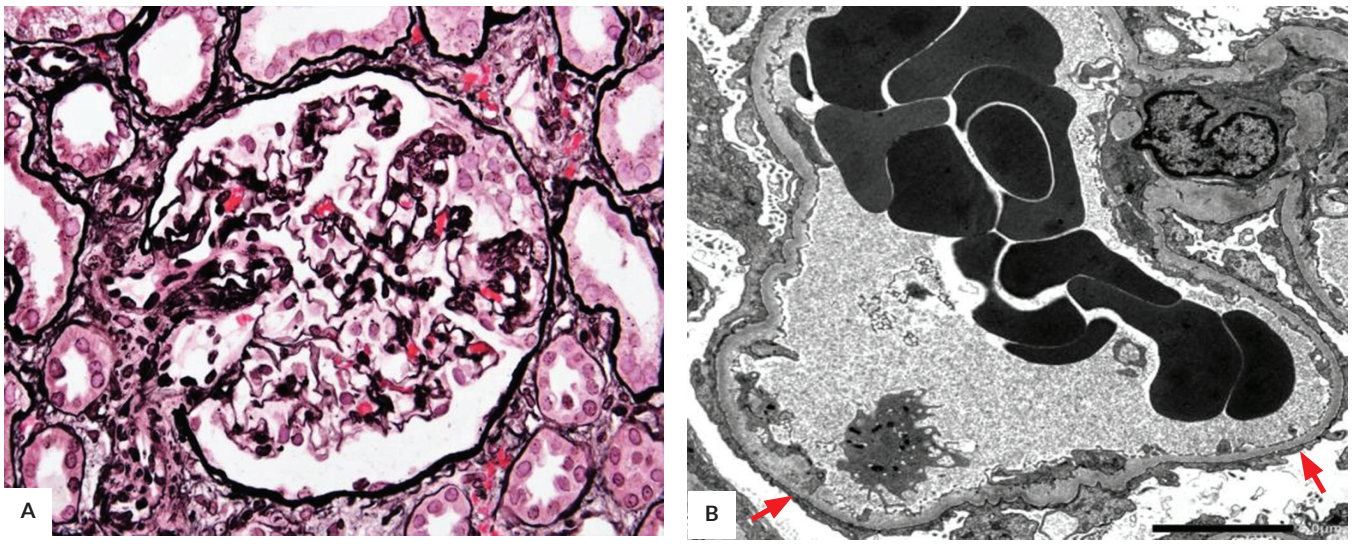

Figure 1. **(A)** Light microscopy with Periodic Acid Silver Stain (PAAg) showing glomerular collapse or wrinkling of capillary loops surrounded by hypertrophic visceral epithelial cells *(asterisk)*. **(B)** Electron microscopy showing widespread podocyte foot process effacement *(arrows)*. No tubuloreticular inclusions are identified.

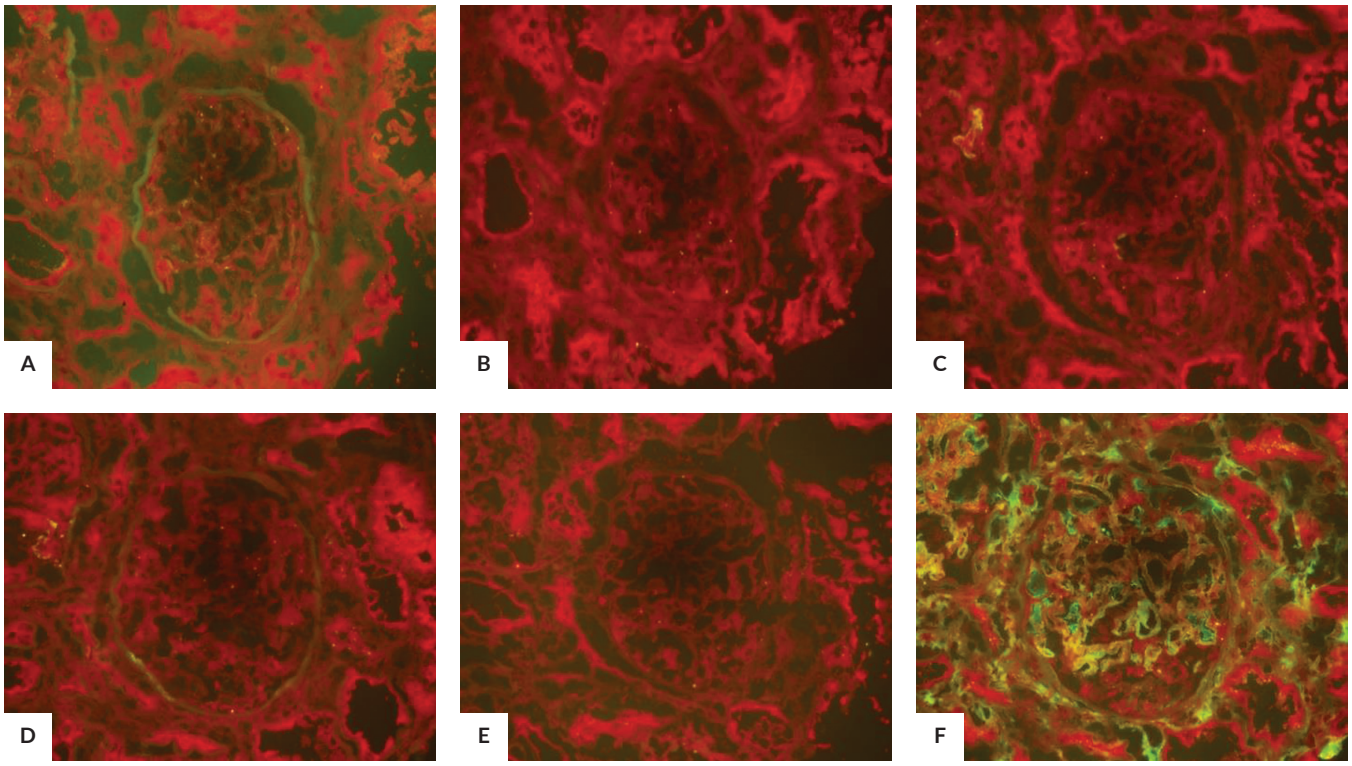

Figure 2. Immunofluorescence slides. **(A)** anti-human IgG, **(B)** antihuman IgA, **(C)** antihuman IgM, **(D)** antihuman C3, **(E)** antihuman C1q, **(F)** antihuman fibrinogen.

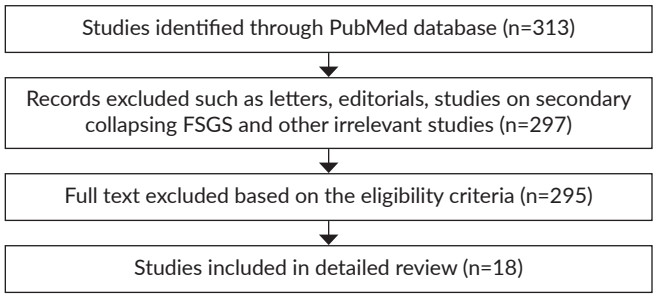

Figure 3. Selection process of studies included in the literature review.

and presented with rapidly progressive renal failure, nephrotic syndrome negative for HIV as reported by Weiss and colleagues in 1986.[7] In 1994, Detwiler et al. reported 16 predominantly African-American patients, with rapidly progressive renal failure, proteinuria, and segmental to global glomerular tuft collapse.[8] Shimamura in 1995 reported a case of a 30-year-old black female with CG but had the following unusual features: the glomeruli had bright fluorescence to IgG and C3, electron dense epimembranous deposits, little evidence of interstitial fibrosis, and tubuloreticular structures.[9] Haas et al. from the University of Chicago reviewed kidney biopsies done from 1974-1993 and revealed 21 cases with features of primary CG.[2] In 1996, another review of kidney biopsies done from 1974-1993 in the Renal Pathology Laboratory at Columbia-Presbyterian Medical Center was done by Valeri and coworkers and were able to identify 43 cases to manifest collapsing features. Twenty-six patients first had a trial of prednisone but none went into remission. Overall, the remission rate in this study was 14%.[10] In Macedonia, another review of kidney biopsies was done by Grcevska et al. in 1999 showing 16 specimens with idiopathic CG. Seven patients were treated with steroids and eight patients with a combination of cyclophosphamide and steroids. They experienced no reduction in proteinuria or progression of renal failure.[11] Another paper published in 1999 by Laurinavicious and coworkers identified patients who underwent kidney biopsy in their institution from 1979 to 1997. There were 18 HIV CG patient and 42 non-HIV CG patients. They saw that predominance of CG among African-American patients were only noted among those with HIV, but not for those without. In the non-HIV group, 23 patients received steroids and had good response while seven revealed partial remission and 14 were steroid resistant. Six patients received cytostatic therapy yielding two patients with normal creatinine at the end of follow up but with no relief in nephrotic syndrome. Three patients were treated with cyclosporine with one patient becoming cyclosporine dependent while the other two did not respond.[12] In 2002, a 35-year-old black male presented with flu-like symptoms, nephrotic syndromes, and progressive renal failure. Pulse therapy was done and patient was on hemodialysis where

Primary Collapsing Glomerulopathy in a Filipino Female

Table 2. Published Cases of Collapsing Glomerulopathy

Author	Year Published	Country	Patient Race	Type of Study	Comorbidities	Indication for biopsy	Number of CG cases	Mean age	Male %	Treatment	Remission rate	Progressed to ESRD
Yamakazi et. al.[15]	2016	Japan	Japanese	Case report	Hypertension, hyperlipidemia, mental disorder	Acute nephritic-nephrotic syndrome	1/1	81	0	Oral prednisolone, Oral cyclosporine Hemodialysis LDL apheresis	0	100%
Stokes et. al.[16]	2006	USA	Black (53.6%)	Cross-sectional	-	-	56/225	31.2 ± 2.3	46.4%	Steroid ACE/ARB CNI Cytotoxic	13.2%	65.3%
Thomas DB et. al.[17]	2006	USA	-	Cross-sectional	-	-	22/197	38 ± 12	45%	-	18%	67%
Deegens et. al.[18]	2008	The Netherlands	Dutch (96%)	Cross-sectional	-	-	5/93	63 ± 18	60%	ACEi/ARB Steroid Cytotoxic	40%	70%
Nada et. al.[19]	2009	India	-	Cross-sectional	-	-	4/210	46 ± 10	75%	-	-	-
Taneda et. al.[20]	2012	Japan	-	Cross-sectional	-	-	13/80	39.9 ± 4.1	69.2%	Steroid Immunosuppressant ACEi/ARB LDL apheresis Hemodialysis	44.4 %	30%
Testagrossa et. al.[21]	2012	Brazil	-	Cross-sectional	-	-	48/131	-	-	-	-	-
Das et. al.[22]	2012	India	Indian	Cross-sectional	-	-	9/65	-	-	-	-	-
D'Agati et. Al.[23]	2013	USA	Black (63%)	Clinical trial	-	-	16/138	16.5 (2-38)	50%	-	13%	47%
Arias et. Al.[24]	2013	Colombia	Hispanic	Cross-sectional	-	-	10/129	11.9 (3-66)	60%	-	22.2%	33.3%
Shakeel et.al.[25]	2013	Pakistan	Pakistani	Cross-sectional		Idiopathic nephrotic syndrome	22/184	32.3 ± 13.8	59.1%	-	-	-
Kwon et. al.[26]	2014	Korea	Korean	Cross-sectional	-	-	1/111	84	0	RAAS blockade Steroid	100%	0
Swarnalatha et. al.[27]	2015	India	-	Cross-sectional	-	-	5/116	33.5 ± 23	-	Steroid Cyclophosphamide Cyclosporine	-	60%
Ramachandran et. al.[28]	2013	India	-	Case report	none	Steroid-resistant nephrotic syndrome	1/1	19	100	Oral corticosteroid Cyclophosphamide Cyclosporine Tacrolimus Mycophenolate mofetil Rituximab	100%	0
Dieng et. al.[29]	2020	Senegal	-	Cross-sectional	-	-	1/58	-	-	RAAS Corticosteroid	-	-
Padala et. al.[30]	2020	Georgia, USA	African-American	Case report	Pseudotumor cerebri	-	1/1	25	100	Oral corticosteroid	100%	0
Ahuja et. al.[31]	2014	India	Indian	Cross-sectional	-	-	30/3314	27.35	83%	Oral corticosteroid Calcineurin inhibitors Hemodialysis	-	30%
Husain et. al.[32]	2017	Saudi Arabia	Arab	Cross-sectional	-	-	31/31	28	65%	Steroids IV Cyclophosphamide Mycophenolate mofetil ACEi IV pulse therapy	45%	26%

patient was transiently weaned from but ultimately became hemodialysis dependent. In 2003, Shamari et al. from the University of British Columbia reported three cases of CG co-existing with membranous nephropathy. All three specimens showed CG and numerous epimembranous electron-dense deposits along the GBM, which shows some spiking between deposits. One patient was Chinese who was given prednisone but fell into ESRD. He underwent peritoneal dialysis but died a few years later from refractory congestive heart failure. The second case was a Filipino female treated with prednisone then intravenous (IV) cyclophosphamide. There was improvement and cyclophosphamide was later switched to MMF. However, patient developed progressive and persistent increase in creatinine. The last case was a North American male who was given prednisone and azathioprine which were both stopped as patient improved.

He relapsed and was given MMF but later on switched to cyclophosphamide IV but still ended up on hemodialysis.[13]

Since the report of Weiss et al. of CG as a new etiology in 1986, several other cases of CG either primary or idiopathic, as well as secondary and genetic forms have emerged. In 2004, a group of renal pathologists convened at Columbia University to reach a consensus of terms and their usage, as well as to establish a uniform approach to the different morphological subtypes of FSGS for future clinicopathologic studies. Since then, CG has been classified as one of the five morphologic subtypes of FSGS namely: Perihilar variant defined as at least one glomerulus with perihilar hyalinosis, with or without sclerosis, >50% of glomeruli with segmental lesions must have perihilar sclerosis and/or hyalinosis; Cellular variant defined as at least one glomerulus with segmental endocapillary hypercellularity occluding lumina, with or

without foam cells and karyorrhexis; Tip variant defined as at least one segmental lesion involving the tip domain (outer 25% of tuft next to origin of proximal tubule); Collapsing variant defined as at least one glomerulus with segmental or global collapse and overlying podocyte hypertrophy and hyperplasia; and lastly, Not Otherwise Specified (NOS) variant defined as at least one glomerulus with segmental increase in matrix obliterating the capillary lumina. There may be segmental glomerular capillary wall collapse without overlying podocyte hyperplasia.[14]

Table 2 shows the updated list of papers on primary/idiopathic CG as defined by the Columbia Classification, including those listed in previously published case reports and reviews. Our own literature review in this paper revealed five more published case reports and cross-sectional studies.

Treatment

In the most recent 2021 KDIGO guidelines on Glomerular Diseases, there was no treatment stated for CG as a separate disease but as a subtype of FSGS. According to this guideline, adults with steroid-resistant primary FSGS, cyclosporine or tacrolimus is recommended to be given for >6 months rather than continuing glucocorticoid monotherapy or not treating. Starting dose for tacrolimus is 0.05-0.1 mg/kg/d in 2 divided doses with a target trough level of 5-20 ng/ml. The dose at which trough level is achieved should be maintained for at least 12 months and should be slowly tapered over a course of 6-12 months.[33]

Our patient met the Columbia Classification criteria for collapsing GN with 1 out of 20 glomeruli showing segmental collapse of capillary loops with reactive podocytes. In the paper by Yamakazi, LDL apheresis was done in their patient and they proposed that it may be worth performing as it had few side effects. Persistent hyperlipidemia for prolonged periods is nephrotoxic and leads to chronic progressive glomerular and tubulointerstitial injury. LDL apheresis has been used in drug-resistant Nephrotic Syndrome (NS) patients to prevent the progression of renal disease and, in some patients, resolution of NS symptoms. Interim results of a prospective, multicenter, post- approval study of LDL-A therapy using Liposorber LA- 15 System for the treatment of drug-resistant NS in FSGS patients show partial or complete remission in few patients during 1-, 3-, 6-, and 12-months follow-up, with the majority showing improvement in eGFR.[34]

Kidney biopsy results usually come out a few weeks after the procedure so we gave our patient oral corticosteroids at 1 mg/kg prior to discharge. The patient was also given losartan 75 mg/day, rosuvastatin 10 mg/day, fenofibrate 200 mg/day and clopidogrel 75 mg/day. Upon receiving the kidney biopsy result, despite lack of predisposition or history to HIV, it was ascertained to be negative prior to starting tacrolimus. Tacrolimus trough was 1.3 ng/ml hence the dose was increased from 2 mg/day to 4 mg/day. The patient has achieved remission with this regimen.

Prognosis

Most cases of primary collapsing FSGS have poor prognosis. Incidence of end-stage renal disease is high and renal survival of patients with CG lesions is lower than FSGS. In the present study, case reports and cross-sectional studies revealed an incidence of ESRD ranging from 26-100%. The mean time from biopsy to the development of ESRD was lower in patients with CG (13 months vs. 63 months). A higher baseline creatinine on presentation, treatment-resistant proteinuria, and marked interstitial fibrosis in the renal biopsy were the main factors for the development ESRD. There are no randomized clinical trials to determine the treatment of collapsing FSGS and recommendations were based from observational studies. Results are poor, with a complete remission rate of <10% and a partial remission of 15%.[5] KDIGO defines complete remission as reduction of proteinuria at <0.3 g/d or PCR <300 mg/g (or <30 mg/mmol), stable serum creatinine, and serum albumin >3.5 g/dl (or 35 g/L). Partial remission is defined as reduction of proteinuria to 0.3-0.5 g/d or PCR 300-3500 mg/g (or 30-350 mg/mmol) and a decrease of >50% from baseline.[33]

CONCLUSION

Our experience tells of a 36-year-old Filipino female presenting with progressing edema a few months after giving birth. Her clinical course has been riddled by interesting laboratory findings that required further investigation. The initial impression was chronic liver disease due to the ultrasound findings of diffuse hepatic disease. Edema further progressed which prompted admission for a more extensive work-up. Paracentesis obtained minimal ascitic fluid with a low serum ascites albumin gradient. Additional tests were consistent with nephrotic syndrome. Secondary causes for glomerulonephritis were ruled out through serum tests such as tests for hepatitis, lupus, and complement. Clinching the diagnosis has been confounded by abdominal CT findings of multiple hypoenhancing abdominal and breast lesions with high tumor markers. Referral to surgery and gynecology was done to make sure that the diagnosis of neoplasm was not overlooked. The diagnostic process was further protracted by nosocomial pneumonia and circumstances then required that COVID-19 was ruled out. As patient recovered from pneumonia, kidney biopsy was finally done and she was discharged improved with no edema. She was sent home with medications for the general management of nephrotic syndrome. After several weeks, edema has recurred and the biopsy result serendipitously came out which revealed collapsing FSGS. Tacrolimus was then added to her medications. Three months since being given tacrolimus, the patient had normal BP, with no edema or frothy urine. The latest urine protein-creatinine ratio was 79.9 mg/g and creatinine was 78 mmol/L. The kidney biopsy finding has inclined us to a more aggressive therapy with immunosuppressants as cases of CG had shown high rates

of ESRD and no previous cases of CG among Filipinos has been reported yet which could serve as a guide for treatment in this particular population.

There are a lot of learning points in this case. There have been crucial laboratory results in the work up of this patient which have served both as clues but also as diversions. It reminds us of the importance of thorough history-taking and to be critical of laboratory results. It highlights the importance of ordering ancillary tests in the most efficient way possible specially in a setting of limited resources such as the Philippines and the importance of determining the pathologic diagnosis as soon as possible in a patient presenting with nephrotic syndrome. The patient also has been seen previously by three other doctors before being seen by a nephrologist which may show how glomerular disease is perceived as a highly specialized condition for clinicians from other specialties. Hence, more data about it should be made available to a broader audience so that nephrologists and non-nephrologists alike will be able to approach the disease more efficiently. A condition known to have a poor prognosis may not inevitably lead to a poor outcome with prompt and aggressive management.

Acknowledgments

Micrographs courtesy of Dr. Sonia Chicano, Renal Pathology and Electron Microscopy Unit, Department of Pathology and Laboratory Medicine, National Kidney and Transplant Institute, Quezon City, Philippines.

Statement of Authorship

KMFV contributed in the writing and editing of the manuscript as well as procurement of the images of the kidney biopsy slides. RSA contributed in the conceptualization of work, and proofreading and editing of the manuscript.

Author Disclosure

Both authors declared no conflicts of interest.

Funding Source

None.

REFERENCES

1. Swarnalatha G, Ram R, Ismal KM, Vali S, Sahay M, Dakshinamurty KV. Focal and segmental glomerulosclerosis: does prognosis vary with the variants? Saudi J Kidney Dis Transpl. 2015 Jan;26(1):173-81. doi: 10.4103/1319-2442.148772.
2. Haas M, Spargo BH, Coventry S. Increasing incidence of focal-segmental glomerulosclerosis among adult nephropathies: a 20-year renal biopsy study. Am J Kidney Dis. 1995 Nov;26(5):740-50. doi: 10.1016/0272-6386(95)90437-9.
3. Cossey LN, Larsen CP, Liapis H. Collapsing glomerulopathy: a 30-year perspective and single, large center experience. Clin Kidney J. 2017 Aug;10(4):443-9. doi: 10.1093/ckj/sfx029.
4. Hizon MAP, Lim RS, Tan ZK, Yeo SC, Villanueva ART, Liew A. SUN-014 Epidemiology of glomerulonephritis in Southeast Asia: The GN-Special (Glomerulonephritis–Singapore-Philippines Epidemiology Cohorts in Adults) Study. Kidney Int Rep. 2019 Jul;4(7):S158.
5. Morales E, Alonso M, Gutiérrez E. Collapsing glomerulopathy: update. Med Clin (Barc). 2019 May;152(9):361-7. doi: 10.1016/j.medcli.2018.10.021.
6. Velez JCQ, Caza T, Larsen CP. COVAN is the new HIVAN: the re-emergence of collapsing glomerulopathy with COVID-19. Nat Rev Nephrol. 2020 Oct;16(10):565-7. doi: 10.1038/s41581-020-0332-3. Erratum in: Nat Rev Nephrol. 2020 Oct;16(10):614. doi: 10.1038/s41581-020-00341-y.
7. Weiss MA, Daquioag E, Margolin EG, Pollak VE. Nephrotic syndrome, progressive irreversible renal failure, and glomerular "collapse": a new clinicopathologic entity? Am J Kidney Dis. 1986 Jan;7(1):20-8. doi: 10.1016/s0272-6386(86)80052-x.
8. Detwiler RK, Falk RJ, Hogan SL, Jennette JC. Collapsing glomerulopathy: a clinically and pathologically distinct variant of focal segmental glomerulosclerosis. Kidney Int. 1994 May;45(5):1416-24. doi: 10.1038/ki.1994.185.
9. Shimamura T, Walker J. A collapsing form of glomerulopathy. Pathol Int. 1995 Jul;45(7):520-3. doi: 10.1111/j.1440-1827.1995.tb03495.x.
10. Valeri A, Barisoni L, Appel GB, Seigle R, D'Agati V. Idiopathic collapsing focal segmental glomerulosclerosis: a clinicopathologic study. Kidney Int. 1996 Nov;50(5):1734-46. doi: 10.1038/ki.1996.493.
11. Grcevska L, Polenakovik M. Collapsing glomerulopathy: clinical characteristics and follow-up. Am J Kidney Dis. 1999 Apr;33(4):652-7. doi: 10.1016/s0272-6386(99)70215-5.
12. Laurinavicius A, Hurwitz S, Rennke HG. Collapsing glomerulopathy in HIV and non-HIV patients: a clinicopathological and follow-up study. Kidney Int. 1999 Dec;56(6):2203-13. doi: 10.1046/j.1523-1755.1999.00769.x.
13. Al-Shamari A, Yeung K, Levin A, Taylor P, Magil A. Collapsing glomerulopathy coexisting with membranous glomerulonephritis in native kidney biopsies: a report of 3 HIV-negative patients. Am J Kidney Dis. 2003 Sep;42(3):591-5. doi: 10.1016/s0272-6386(03)00793-5.
14. D'Agati VD, Fogo AB, Bruijn JA, Jennette JC. Pathologic classification of focal segmental glomerulosclerosis: a working proposal. Am J Kidney Dis. 2004 Feb;43(2):368-82. doi: 10.1053/j.ajkd.2003.10.024.
15. Yamazaki J, Kanehisa E, Yamaguchi W, Kumagai J, Nagahama K, Fujisawa H. Idiopathic collapsing focal segmental glomerulosclerosis in an 81-year-old Japanese woman: a case report and review of the literature. CEN Case Rep. 2016 Nov;5(2):197-202. doi: 10.1007/s13730-016-0224-3.
16. Stokes MB, Valeri AM, Markowitz GS, D'Agati VD. Cellular focal segmental glomerulosclerosis: clinical and pathologic features. Kidney Int. 2006 Nov;70(10):1783-92. doi: 10.1038/sj.ki.5001903.
17. Thomas DB, Franceschini N, Hogan SL, Ten Holder S, Jennette CE, Falk RJ, et al. Clinical and pathologic characteristics of focal segmental glomerulosclerosis pathologic variants. Kidney Int. 2006 Mar;69(5):920-6. doi: 10.1038/sj.ki.5000160.
18. Deegens JKJ, Steenbergen EJ, Borm GF, Wetzels JFM. Pathological variants of focal segmental glomerulosclerosis in an adult Dutch population--epidemiology and outcome. Nephrol Dial Transplant. 2008 Jan;23(1):186-92. doi: 10.1093/ndt/gfm523.
19. Nada R, Kharbanda JK, Bhatti A, Minz RW, Sakhuja V, Joshi K. Primary focal segmental glomerulosclerosis in adults: is the Indian cohort different? Nephrol Dial Transplant. 2009 Dec;24(12):3701-7. doi: 10.1093/ndt/gfp328.
20. Taneda S, Honda K, Uchida K, Nitta K, Yumura W, Oda H, et al. Histological heterogeneity of glomerular segmental lesions in focal segmental glomerulosclerosis. Int Urol Nephrol. 2012 Feb;44(1):183-96. doi: 10.1007/s11255-011-9932-y.
21. Testagrossa L, Malheiros D. Study of the morphologic variants of focal segmental glomerulosclerosis: a Brazilian report. J Bras Patol Med Lab. 2012 Jun;48(3):211–5.
22. Das P, Sharma A, Gupta R, Agarwal SK, Bagga A, Dinda AK. Histomorphological classification of focal segmental glomerulosclerosis: a critical evaluation of clinical, histologic and morphometric features. Saudi J Kidney Dis Transpl. 2012 Sep;23(5):1008-16. doi: 10.4103/1319-2442.100883.

23. D'Agati VD, Alster JM, Jennette JC, Thomas DB, Pullman J, Savino DA, et al. Association of histologic variants in FSGS clinical trial with presenting features and outcomes. Clin J Am Soc Nephrol. 2013 Mar;8(3):399-406. doi: 10.2215/CJN.06100612.
24. Arias LF, Jiménez CA, Arroyave MJ. Histologic variants of primary focal segmental glomerulosclerosis: presentation and outcome. J Bras Nefrol. 2013 Apr-Jun;35(2):112-9. doi: 10.5935/0101-2800.20130019.
25. Shakeel S, Mubarak M, Kazi JI, Jafry N, Ahmed E. Frequency and clinicopathological characteristics of variants of primary focal segmental glomerulosclerosis in adults presenting with nephrotic syndrome. J Nephropathol. 2013 Jan;2(1):28-35. doi: 10.5812/nephropathol.8959.
26. Kwon YE, Han SH, Kie JH, An SY, Kim YL, Park KS, et al. Clinical features and outcomes of focal segmental glomerulosclerosis pathologic variants in Korean adult patients. BMC Nephrol. 2014 Mar;15:52. doi: 10.1186/1471-2369-15-52.
27. Swarnalatha G, Ram R, Ismal KM, Vali S, Sahay M, Dakshinamurty KV. Focal and segmental glomerulosclerosis: does prognosis vary with the variants? Saudi J Kidney Dis Transpl. 2015 Jan;26(1):173–81. doi: 10.4103/1319-2442.148772
28. Ramachandran R, Rajakumar V, Duseja R, Sakhuja V, Jha V. Successful treatment of adult-onset collapsing focal segmental glomerulosclerosis with rituximab. Clin Kidney J. 2013 Oct;6(5):500-2. doi: 10.1093/ckj/sft102.
29. Dieng A, Ba MA, Sy A, Ndongo M, Ndiaye B, Diawara MS, et al. Patterns of Primary Focal Segmental Glomerulosclerosis (FSGS) in adults treated in a Dakar single center: about 58 cases. Open J Nephrol. 2020 Oct 15;10(4):265-73. doi:10.4236/ojneph.2020.104026
30. Padala SA, Birkelo B, Mohammed A, Kapoor R, Mulloy L, Rawla P. Collapsing focal segmental sclerosis in an HIV-negative patient. Clin Case Rep. 2020 Jul;8(11):2166-71. doi: 10.1002/ccr3.3078.
31. Ahuja A, Gupta R, Sharma A, Bagga A, Bhowmik DM, Agarwal SK, et al. Idiopathic collapsing glomerulopathy: a clinicopathologic analysis of 30 cases. Indian J Nephrol. 2014 Jul;24(4):239-42. doi: 10.4103/0971-4065.133009.
32. Husain S. Collapsing glomerulopathy, the Saudi Arabian scenario. A study of 31 cases and a review of literature. Saudi Med J. 2017 May;38(5):509-16. doi: 10.15537/smj.2017.5.19299.
33. Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. KDIGO 2021 Clinical practice guideline for the management of glomerular diseases. Kidney Int. 2021 Oct;100(4S):S1-S276. doi: 10.1016/j.kint.2021.05.021.
34. Raina R, Krishnappa V. An update on LDL apheresis for nephrotic syndrome. Pediatr Nephrol. 2019 Oct;34(10):1655-69. doi: 10.1007/s00467-018-4061-9.