CASE REPORT

Atypical evolution of collapsing FSGS in extreme elderly: case report

Evolução atípica de GESF Colapsante na velhice extrema: relato de caso

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Abstract

Introduction: Segmental and Focal Glomerulosclerosis (FSGS) is an entity characterized by glomerular damage involving the podocyte as the main target. A variant with a worse prognosis, poor response to corticosteroid therapy, and rapid progression to end-stage renal disease is recognized as collapsing FSGS. **Case Report**: A 102-year-old man with nephrotic syndrome and acute kidney injury underwent renal biopsy, revealing collapsing FSGS. He achieved an excellent response to immunosuppressive treatment, presenting renal recovery, and was discharged from dialysis treatment. **Discussion**: Diagnosis and definition of treatment in the elderly are challenging, and each case must be individualized and have functionality and risk assessed in a naturally immunosuppressed population.

Keywords: segmental and focal glomerulosclerosis; nephrotic syndrome; elderly.

Resumo

Introdução: Glomeruloesclerose Segmentar e Focal (GESF) é uma entidade caracterizada por lesão glomerular que envolve o podócito como principal alvo. Uma variante de pior prognóstico, baixa resposta à corticoterapia, e rápida evolução para doença renal terminal é reconhecida como GESF colapsante. **Relato de Caso**: Um homem de 102 anos com síndrome nefrótica e lesão renal aguda foi submetido a biópsia renal, revelando GESF colapsante. Ele obteve excelente resposta ao tratamento imunossupressor, apresentando recuperação renal e recebendo alta de terapia renal substitutiva. **Discussão:** Diagnóstico e definição de tratamento nos idosos são desafiadores, devendo-se individualizar cada caso, avaliar funcionalidade e risco em uma população naturalmente imunossupressa.

Palavras-Chave: glomeruloesclerose segmentar e focal; síndrome nefrótica; idoso.

INTRODUCTION

Segmental and Focal Glomerulosclerosis (FSGS) is a heterogeneous entity characterized by a pattern of glomerular injury involving the podocyte as the main target, causing effacement of podocyte processes and, subsequently, detachment and apoptosis. Initially, this process is focal, usually in the juxtaglomerular region. Due to the small capacity for regeneration, the remaining podocytes are overloaded, causing the injury to spread, developing a more diffuse and global pattern[1].

It is clinically characterized by proteinuria, typically in the nephrotic range (> 3.5 g/day), hypoalbuminemia (< 3.5 g/dL), hypercholesterolemia and peripheral edema, characterizing a nephrotic syndrome as presentation in approximately 50-60% of adults affected[2].

The prevalence of FSGS has been increasing worldwide. Although epidemiological studies are regionally influenced by local factors, such as access to renal biopsy, the annual incidence varies from 0.2 to 1.8/100,000 inhabitants/year[3]. A variant with a worse prognosis, presenting with frank nephrotic syndrome, poor response to corticosteroid therapy, and rapid progression to end-stage renal disease, is recognized as collapsing FSGS, characterized by segmental or global collapse of the glomerular tuft with hyperplasia and hypertrophy of overlying visceral epithelium, intense effacement of podocyte processes, without immune deposits[4].

Although initially related predominantly to HIV infection, posing as the main type of nephropathy in these patients, other secondary causes must be investigated, e.g. parvovirus B19, EBV, CMV, Covid; pamidronate, alpha-interferon, anabolic steroids, heroin; autoimmune diseases (e.g. SLE, Still's disease); neoplasms (e.g. multiple myeloma, leukemia), among others[5].

In general, patients present with intense proteinuria within a pure nephrotic syndrome have a higher rate of progression to end-stage chronic kidney disease and need for dialysis, with a predilection for young and black adults[6]. Treatment with immunosuppression in the elderly is subject to questioning, given that this group is naturally immunosuppressed and predisposed to infections[7].

The present work aims to report the case of a centenarian

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elderly man who was diagnosed with nephrotic syndrome and acute kidney injury. The diagnostic and therapeutic difficulties in this age are discussed, in addition to showing the clinical evolution over six months.

CASE REPORT

A 102-year-old patient, previously independent, reported one month before admission the onset of progressive edema in lower limbs, dyspnea at medium exertion, foamy urine, and nocturia. Two weeks later, the edema progressed to anasarca, seeking medical attention and being prescribed furosemide. He initially improved slightly but developed oliguria and worsening anasarca and was taken to a tertiary hospital.

He was a former alcoholic and current smoker, consuming approximately four (4) artisanal cigarettes per day since he was 12. He had no relevant comorbidities or family history of glomerulopathies or neoplastic diseases.

Upon admission in July 2023, he was normocardial, hypertensive (BP 159 x 81 mmHg), eupneic, and in good general condition. He had a 3+/6+ pansystolic heart murmur, normal lung auscultation, abdominal wall, and extremity edema with 3+/4+ in lower limbs. Initial examinations demonstrated urinary dipstick with proteinuria (4+), serum albumin of 2.2 mg/dL and serum creatinine of 2.66 mg/dL with urea of 72 mg/dL, hemoglobin 15.7 mg/dL, leukocytes 8,200 and platelets 242,000.

Upon admission to the emergency room, an indwelling bladder catheterization and a non-contrast abdominal tomography were performed, ruling out an obstructive component. Intravenous diureticotherapy (furosemide 80 mg/day) and hydrosaline restriction (intake of up to one liter of fluids and up to two grams of sodium chloride) was instituted, and he was transferred to the nephrology ward.

Despite adjusting the furosemide dose, the patient did not achieve weight loss within the target (0.5 to 1 kg/day) and had a urine output of around 900 ml/24h. On the eighth day of hospitalization, it was initially associated with hydrochlorothiazide and later spironolactone; however, even with doses of furosemide 2.5 mg/kg, spironolactone 50 mg/day, and hydrochlorothiazide 50 mg/day, he still had weight gain, and it was decided to prescribe on the twelfth-day albumin 20% 10 g/day before each furosemide.

During hospitalization, 24-hour proteinuria was collected, which showed a result of 7.7 grams. An investigation of secondary causes of nephrotic syndrome was carried out. Screening for the main sites of neoplasia, autoimmunity tests, and serology tests were negative. Electrophoresis of serum proteins demonstrated an isolated monoclonal peak in alpha fraction, but immunofixation of serum and urinary proteins showed the absence of monoclonal components.

The patient's renal function worsened (initial creatinine 2.66 mg/dL and urea 72 mg/dL increased to creatinine 3.11 and urea 133) throughout the hospitalization. Ultrasonography of the kidneys and urinary tract and Doppler of the renal arteries were performed, which demonstrated normal-looking kidneys, no signs of chronicity, and ruled out renal vein thrombosis.

As this was a nephrotic syndrome in a previously healthy extremely elderly patient associated with worsening renal function, without a secondary etiological factor, a kidney biopsy was performed, which demonstrated glomeruli with hyperplastic and proliferated podocytes, reactive nuclear changes, forming pseudocrescents compressing capillary loops (Figure 1); mild interstitial fibrosis without increased inflammatory cellularity (Figure 2), and mild tubular atrophy with acute tubular injury (Figure 3). Immunofluorescence demonstrated deposits of IgM and Kappa chains (2+ in 4+) in loops, global and diffuse, and Lambda chains (2+ in 4+) in loops, segmental and diffuse. Result compatible with a diagnosis of collapsing FSGS.

Figure 1. glomeruli with hyperplastic and proliferated podocytes, with reactive nuclear changes, forming pseudocrescents compressing capillary loops.

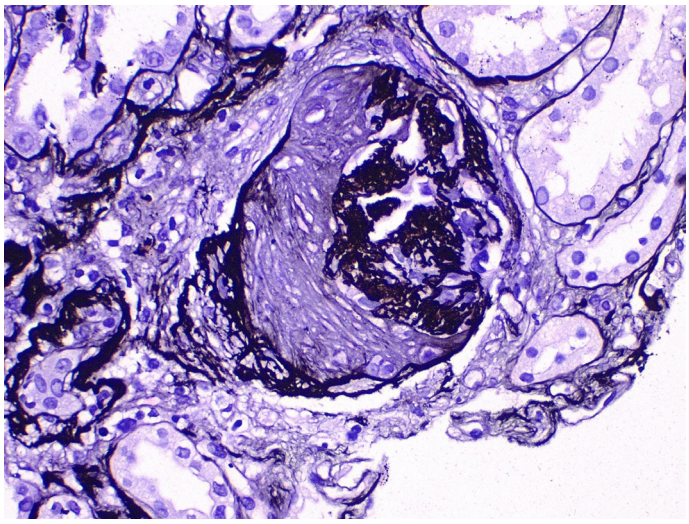


Figure 2. mild interstitial fibrosis without increased inflammatory cellularity

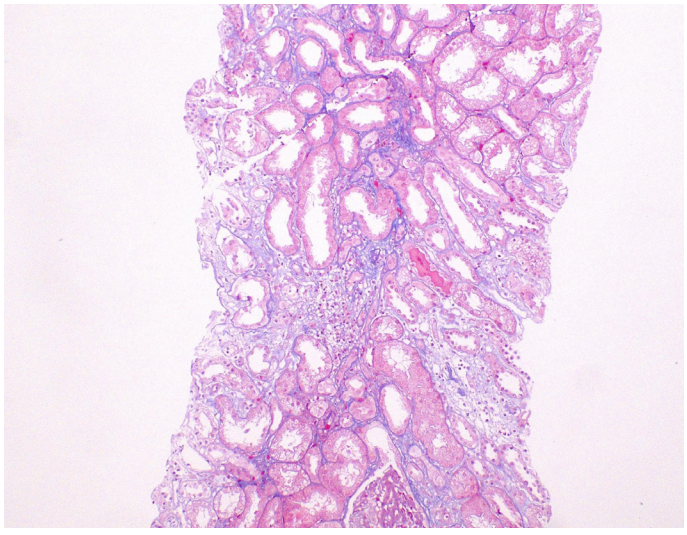
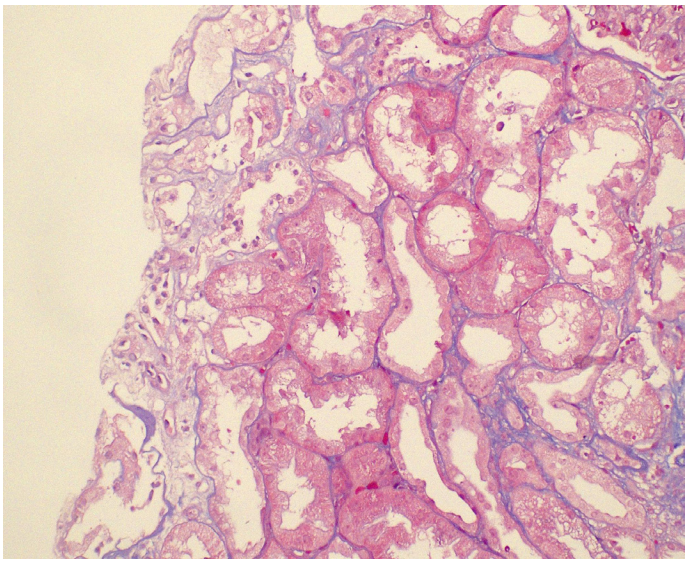


Figure 3. Mild tubular atrophy with acute tubular injury



After biopsy results, it was decided to start corticosteroid therapy with prednisone 1 mg/kg/day; however, four days after starting treatment, the patient developed further worsening of renal function, with a rise in creatinine levels of 3.1 mg/dL to 4.2 mg/dL and urea from 133 mg/dL to 150 mg/dL, associated with oliguria, metabolic acidosis (bicarbonate 16) and pulmonary congestion, prompting the start of hemodialysis.

After optimization of dialysis therapy, the patient remained stable, without signs of congestion, with edema in regression, remaining in lower limbs bilaterally (2+/4+). Weaning from corticosteroid therapy began 14 days after its initiation to a dose of 40mg/day of prednisone, at which time the patient was granted a place in the dialysis clinic and was de-hospitalized, returning for outpatient follow-up.

Two months after hospital discharge, the patient progressed with regression of proteinuria to subnephrotic levels of 2651 mg/24h and an increase in albumin to 3.0 mg/dL, using corticosteroids at a dose of 40 mg/day of prednisone. His kidney function recovered, and he was discharged from hemodialysis approximately eight (8) weeks after starting corticosteroids.

Four months after hospital discharge, in a new outpatient consultation, the patient presented once again with subnephrotic levels of proteinuria of 2678mg/24h (maintained in relation to the last consultation) but showed an improvement in albumin to 3.7 mg/dL. It was decided to reduce the dose of prednisone to 30 mg/day and, after fifteen days, to 20 mg/day.

Six months after hospital discharge, a new outpatient follow-up observed an improvement in proteinuria levels to 1940 mg/24h and albumin to 4.1 mg/dL, in addition to maintenance of renal function, creatinine of 0.7 mg/dL and urea of 26 mg/dL. It was decided to wean the corticosteroid to 10 mg/day, after 15 days to 5 mg/day, and subsequently discontinue it.

DISCUSSION

The elderly population has particularities regarding the presentation of glomerular diseases. It has a lower functional renal reserve: a lower capacity to increase its glomerular filtration rate after physiological or pathological stimuli. Furthermore, there is a loss of nephric mass due to the glomerulosclerosis process of senescence, aggravated by comorbidities typical of this group[8]. Renal disorders include glomerulopathies, with nephrotic syndrome being one of the main manifestations.

There are peculiarities in the investigation of the elderly population, considering the risk of invasive exams, such as renal biopsy, especially in the extreme of age and in those with already compromised renal function, as there is a risk of complications, mainly hemorrhage, which can culminate in worsening of the glomerular filtration rate, precipitating dialysis therapy[9]. In the patient in question, the procedure was chosen because he was a fully functional elderly man who was presenting frank nephrotic syndrome associated with renal dysfunction, with no evidence of chronicity in laboratory and imaging tests.

Collapsing FSGS in the elderly is uncommon, but there are no precise statistics. A survey of kidney biopsies was carried out at the Hospital das Clínicas de São Paulo between 2012 and 2019 in patients over 65 years old diagnosed with nephrotic syndrome. The sample contained 44 biopsies, revealing a prevalence of FSGS of 18.18%, 9.1% of which were collapsing. The most common glomerulopathy was membranous (29.5%)[10].

There is divergence in the literature regarding the indication of immunosuppression in this age, and its benefit in relation to remission of nephrotic syndrome and survival is questioned.

In a study in 2019, 41 elderly people were evaluated and biopsied between 2000 and 2016, among which eight received immunosuppressive treatment; however, in two cases, it was necessary to suspend the medication due to psychosis, and in the others, the treatment did not demonstrate an improvement in global or renal survival[11].

Contrary to what is reported, the patient presented an excellent response to immunosuppressive treatment, showed complete recovery of renal function, and was discharged from dialysis treatment. It shows the importance of individualizing each case, weighing the risks and benefits of immunosuppression, and the need for more studies in this population.

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