Focal segmental glomerulosclerosis – Corticotherapy response: A case raport

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ABSTRACT

Focal segmental glomerulonephrosis (FSGS) is a renal disorder with significant presence of proteinuria (usually in the nephrotic range) and glomerular damage, which affects children and adults. The diagnostic finding is made by means of renal biopsy, where podocyte alterations will be observed. The objective of this study is to report the case of a patient diagnosed with focal segmental glomerulonephrosis. The case report is of a 27-year-old Caucasian female patient who presented with edema of the extremities of the lower limbs and foamy urine. The findings described by light microscopy and immunofluorescence characterize a case of FSGS. After the tests, the patient started using 40 mg/day of furosemide and 20 mg/day of prednisone, in addition to pulse therapy with methylprednisolone, with a new increase in 24-hour proteinuria, recurrent hospitalizations and clinical decompensation in anasarca. Treatment with cyclophosphamide alternated with methylprednisolone was initiated, with improvement in proteinuria since then. Corticosteroids are the choice for the treatment of FSGS, although there is uncertainty about the risks and benefits. In cases of non-remission with corticosteroid therapy, cyclosporine associated with prednisone is chosen, which can cause total remission in many patients. Mycofelonate mofetil may be used as an alternative in non-responders. If resistance persists and with frequent protein increases, a regimen with cyclophosphamide in association with prednisone and with constant follow-up is indicated. The use of calcineurin inhibitors has shown positive effects in the treatment of FSGS. To date, the mechanisms involved in FSGS have not been accurately described, a fact that hinders the treatment of this pathology, and it is crucial that current and future studies comprehensively examine individuals to identify the characteristics of those who respond and those who do not respond to the treatment of the disease.

Keywords: Therapy, Focal segmental glomerulonephrosis, Prednisolone.

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INTRODUCTION

Focal segmental glomerulonephrosis (FSGS) is a renal disorder with significant presence of proteinuria - usually in the nephrotic range and glomerular damage, which affects children and adults. It is believed that primary FSGS is of autoimmune origin and secondary FSGS is that with histological characteristics of podocytary damage caused by various mechanisms such as viruses, drugs, and adaptive, the former being the most common, caused by a chronic overload of the nephrons (GAUCKLER, 2023).

The degree of proteinuria at the onset of the pathology presupposes the level of FSGS, which is an indicator of renal glomeruli damage. However, the diagnostic finding is made through renal biopsy, where podocyte alterations will be observed (GARCIA, 2020).

There are still few evidence-based studies for the treatment of FSGS in adults, however, intervention with immunosuppressants is still recommended, specifically in primary FSGS with nephrotic syndrome, the initial recommendation is to use glucocorticoids, the most common being methylprednisolone and prednisolone, and for patients with contraindication to GC, the use of calcineurin inhibitors can be used. such as tacrolimus and cyclosporine. The choice of therapeutic method should be based on the patients' experience, comorbidities, and goals (GAUCKLER, 2023).

From this perspective, knowledge about FSGS is necessary, considering that this is a progressive kidney disease with a significant number of patients who progress to loss of renal function. The objective of this study is to report the case of a patient diagnosed with focal segmental glomerulonephrosis.

CASE REPORT

A 27-year-old Caucasian female patient developed edema of the extremities of the lower limbs. After two months, he also observed the presence of foamy urine. She denies smoking and alcoholism, denies the use of medications, and has a negative family history of hypertension, diabetes or nephropathies. The patient started follow-up in nephrology, with the following test results: serum creatinine 0.9 mg/dL; urea 32 mg/dL; triglycerides 253mg/dL; serum albumin 2.86g/dL; proteinuria of 9,497mg/24h. The levels of RF, ANA, anti-DNA and serology for HIV, HCV and HBV were negative. Components C3 and C4 were normal. Ultrasonography of the urinary tract showed no abnormalities.

The patient underwent uneventful renal biopsy. The findings described by light microscopy and immunofluorescence characterize a case of segmental and focal glomerulonephrosis. After the tests, the patient started using 40 mg/day of furosemide and 20 mg/day of prednisone, in addition to a pulse therapy session with methylprednisolone, with a new increase in 24-hour proteinuria, recurrent hospitalizations and clinical decompensation in anasarca, requiring intravenous furosemide for

volume control. Immunosuppression was then made with mycophenolate sodium, also without success, due to intolerance to the medication. Treatment with cyclophosphamide alternated with methylprednisolone was initiated, with improvement in proteinuria since then. The patient was weaned from corticosteroids and the patient was followed up.

DISCUSSION

FSGS is a chronic, progressive pathological process. This kidney disease can be defined by the formation of a focal scar, which affects only a few glomeruli, or segmental, which can affect the lobes of some glomeruli. Such alteration leads to characteristic sclerotic lesions and is, therefore, one of the main causes of End-stage Renal Disease (ESRD). It can be classified as primary - which usually presents as nephrotic syndrome, secondary - includes glomerular hyperfiltration, or hereditary (GARCIA, 2020).

Primary FSGS is an immunologic disease accompanied by a focal pattern characteristic of glomerulosclerosis leading to complete nephrotic syndrome. (GAUCKLER et al., 2020). It is presumably caused by an unknown circulating factor and may respond to immunosuppressive treatment (SHABAKA; RIBERA; FERNÁNDEZ-JUÁREZ, 2020).

Unlike primary FSGS, the secondary and genetic forms of the disease, which are caused by the presence of the primary FSGS, have adaptive glomerular changes that lead to excessive nephron workload and hyperfiltration, do not respond to immunosuppression, but do not recur after kidney transplantation. The secondary form includes maladaptive, virus-associated, and drug-induced FSGS (SHABAKA; RIBERA; FERNÁNDEZ-JUÁREZ, 2020).

Corticosteroids are the choice for the treatment of FSGS, although there is uncertainty about the risks and benefits. It is possible to observe the relationship between lower rates of remission and treatment time greater than five weeks, and the use of corticosteroids for six months is indicated. If there is no improvement, drug resistance is proven (GAUCKLER et al., 2020 and SHABAKA; RIBERA; FERNÁNDEZ-JUÁREZ, 2020).

In cases of complete non-remission or partial remission with corticosteroid therapy, cyclosporine associated with prednisone is chosen, which can cause total remission in many patients. Mycofelonate mofetil may be used as an alternative in non-responders. If resistance persists and with frequent protein increases, a regimen with cyclophosphamide in association with prednisone and with constant monitoring is indicated (GAUCKLER et al., 2020).

The use of calcineurin inhibitors has shown positive effects in the treatment of FSGS. It is known that calcineurin is part of the T cell signaling pathway and participates in the activation of IL-2 production, promoting an immune response in several cell types. Tacrolimus monotherapy or low-dose corticosteroid monotherapy has been recommended only as second-line agents for the treatment

of adults with segmental and focal glomerulosclerosis by blocking T-cell activation and stabilizing actin directly in podocytes. However, long-term use of calcineurin leads to nephrotoxicity and its serum levels should be closely monitored (GAUCKLER et al., 2020).

The use of cyclophosphamide, cyclosporine alone or combined with steroids has demonstrated efficacy in first-line treatment in adult patients with FSGS, but has important toxic side effects such as infertility, urotoxicity, oncogenicity in years or even decades after exposure to treatment (GAUCKLER et al., 2020).

Rituximab treatment, despite the scarcity of data on its effectiveness, has changed the therapeutic landscape in the treatment of recurrent post-transplant FSGS with 44% to 50% of treated patients achieving complete remission and 20% to 25% achieving partial remission. (HARSHMAN; BARTOSH; ENGEN, 2022).

CONCLUSION

To date, the mechanisms involved in FSGS have not been accurately described, which makes the treatment of this pathology difficult. Thus, it is necessary to develop new studies on the disease in order to know the main mechanism involved in FSGS.

With advances in immunomodulatory therapy, significant improvements have been achieved. New therapies that have the potential to improve prognosis are being evaluated. Considering the diversity of FSGS manifestations and the multiple molecular pathways involved in its pathogenesis, it is crucial that current and future work comprehensively examine individuals to identify the characteristics of those who respond and those who do not respond to treatment of the disease.

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