Full House Nephropathy Without Serologic Markers: A Case Report

Nefropatia "Full-House" Sem Marcadores Serológicos: Caso Clínico

André Garrido [1], Andreia Martins[1], Rita Manso[2], Marta Cabral[1], Helena Loureiro[1]*

***Corresponding Author**/Autor Correspondente
André Garrido [ajagarrido@gmail.com]
Hospital prof. Doutor Fernando Fonseca, IC19, 2720-276 Amadora, Portugal
ORCID iD: André Garrido https://orcid.org/0000-0002-7577-978X

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Abstract

A full-house immunofluorescence pattern in a kidney biopsy is most commonly a presentation of lupus nephritis. In the absence of characteristic serologic markers of systemic lupus erythematosus, it determines a rare diagnostic and therapeutic challenge.

A fourteen-year-old female adolescent with sickle cell anemia presented with nephrotic syndrome, pneumonia, empyema and arterial hypertension. The histopathology of the kidney biopsy revealed a proliferative glomerulonephritis with a full-house pattern. Autoantibodies and the direct antiglobulin test were negative and no complement consumption was detected. Other possible etiologies were ruled out. Remission was achieved with high dose corticosteroids and mycophenolate mofetil. All other systemic lupus erythematosus clinical and laboratory criteria remained negative during the follow-up of three years.

This case report aims to contribute to the awareness of a rare clinical entity, emphasizing the necessity of a correct treatment and a regular long-term follow-up.

Resumo

A constatação de um padrão *full-house* na imunofluorescência renal é frequentemente associada a nefrite lúpica. Na ausência de marcadores serológicos de lúpus eritematoso sistémico, este padrão constitui um raro desafio diagnóstico e terapêutico.

Expõe-se o caso de uma adolescente de catorze anos de idade, drepanocítica, que se apresentou com síndrome nefrótico, pneumonia, empiema e hipertensão arterial. O exame antomo-patológico renal revelou uma glomerulonefrite proliferativa com padrão *full-house*. A pesquisa de autoanticorpos foi negativa, não foi detetado consumo de complemento e o teste de Coombs direto foi normal. As outras etiologias possíveis foram descartadas. A remissão foi conseguida com corticoides em alta dose associados a micofenolato de mofetil. Não foram identificados outros critérios clínicos ou laboratoriais de lúpus eritematoso sistémico no seu seguimento posterior.

Este caso procura alertar para a existência desta entidade rara, relevando a importância do seu correto tratamento e de um seguimento a longo prazo.

Keywords: Adolescent, Antibodies, Antinuclear; Fluorescent Antibody Technique; Lupus Lupus Nephritis

1. Departamento da Criança e do Jovem, Hospital Prof. Doutor Fernando Fonseca, E.P.E., Amadora, Portugal. **2.** Serviço de Anatomia Patológica, Hospital Prof. Doutor Fernando Fonseca, E.P.E., Amadora, Portugal.

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Introduction

A full-house immunofluorescence pattern is characterized by an intense deposition of a wide range of immune complexes and complement components in glomerulus histologic examination. It is most commonly a presentation of lupus nephritis (LN)[1] and, in absence of characteristic serologic markers, it determines a rare diagnostic and therapeutic challenge.[2,3] Other described etiologies are infection by hepatotropic virus or human immunodeficiency virus, and other nephropathies such as membranoproliferative glomerulonephritis, Henoch-Schönlein purpura and IgA nephropathy.[4,5] Treatment should be directed to the underlying disease or similarly to LN when no etiology is found. However, compared to LN, it can present a faster progression to end-stage renal disease.[6] The subsequent progression to systemic lupus erythematosus (SLE) has also been described and long-term follow-up is recommended.[4,5]

Case Report

A fourteen-year-old female adolescent with sickle cell anemia (SCA), born and resident in Angola, presented to our hospital after three months of hospitalization in her country of birth. At admission she had a nephrotic syndrome (22 g of urine protein/24 hours) with arterial hypertension and pneumonia complicated with empyema, for which she had already received treatment with prednisolone (0.75 mg/kg/day), nifedipine and antibiotics. Prednisolone was increased to 2 mg/kg/day and nifedipine was changed to enalapril, due to its renal protective effect. Respiratory stabilization was achieved in the first days with thoracocentesis and adjustment of antibiotics. A few hours after red blood cell transfusion, she developed altered mental status and seizures. The brain magnetic resonance imaging revealed a posterior reversible encephalopathy syndrome (PRES) pattern and the neurological symptoms were controlled with levetiracetam.

A kidney biopsy was performed and the histopathological examination with optical, immunofluorescence and electron microscopy revealed a proliferative glomerulonephritis with mesangial and capillary immune complexes deposits: IgA (+++/++++), IgM (++/++++; focal), IgG (+++/++++), C1 (++++/++++), C3 (++; focal) and C4 (+++/++++; focal), also known as "full-house" pattern, suggestive of LN (Fig. 1). According to the International Society of Nephrology/Renal Pathology Society (ISN/RPS) 2003 classification[7] these aspects were consistent with a class IIIA LN. Some microscopic abnormalities (partial collapse of glomerular tuft and thickness of basal membrane of the Bowman capsule) were indicative of chronic ischemia compatible with the underlying disease.

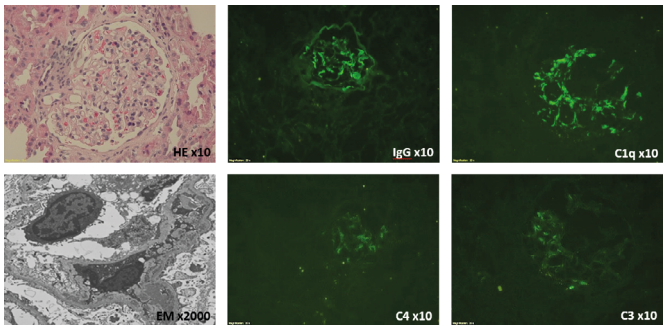

Figure 1. Histopathology examination of kidney biopsy: optical microscopy (hematoxylin eosin [HE], 10x) with mesangial proliferation; immunofluorescence (10x) with a "full-house" pattern; electron microscopy (EM, 2000x) with electrodense mesangial deposits.

At this point all other SLE clinical and laboratory criteria were reviewed but they were absent except for possible neuropsychiatric lupus, hemolytic anemia and lymphopenia (800 cells/µL). Complement levels were high (C3 184 mg/dL and C4 68.2 mg/dL [RV C3 90-180 mg/dL, C4 10-40 mg/dL]) and antinuclear antibodies (ANA) were negative at admission while receiving prednisolone 0.75 mg/kg/day and more than two months from the last blood transfusion. Other autoantibodies (anti-dsDNA, anti-Sm, anti-phospholipid, anti-SSA/Ro, anti-SSB/La, anti-RNP and antiribosomal P protein antibodies) at the time of histologic diagnosis (with three weeks on high dose corticosteroids) were negative, as direct antiglobulin test. C3 and CH50 were normal (C3 158 mg/dL, CH50 85.7 U/mL [RV 41.7-95.1 U/mL]), C4 remained high (48.8 mg/dL) and reevaluation of ANA negative. Serum immunoglobulins were in the normal range. The erythrocyte sedimentation rate (ESR) was high at presentation (140 mm/h) and decreased later. No kidney failure occurred. No stored serum from Angola was available.

Pseudomonas aeruginosa was isolated from the pleural empyema and the blood cultures were negative. Other infectious causes were ruled out (herpesvirus, parvovirus B19, hepatovirus, human immunodeficiency virus, *Treponema pallidum*, *Mycobacterium tuberculosis*, *Mycoplasma pneumoniae, Streptococcus pyogenes* and *pneumoniae*). Ophthalmologic evaluation was normal. Left ventricular hypertrophy with mild mitral valve regurgitation were documented by echocardiography. Abdominal and kidney ultrasounds with Doppler revealed a spleen scarring and enlarged kidneys with increased parenchymal echogenicity with poor corticomedullary differentiation.

Complete clinical and laboratory remission was achieved in two weeks of receiving high dose prednisolone. However, after

definite diagnosis at the end of the third week, induction LN treatment with mycophenolate mofetil (MMP) was started (600 mg/m2 every 12 hours), in addition with prednisolone, hydroxychloroquine and enalapril. The disease remained controlled with this treatment except for a transient episode of noninfectious bilateral gonarthritis with ESR elevation (60 mm/h) and spontaneous resolution. MMP and enalapril were discontinued two years after considering nonadherence and evidence of long-term absence of proteinuria. Prednisolone was restarted (5 mg/day), in association with hydroxychloroquine.

Three years after the diagnosis all laboratory criteria remained negative/normal range, no renal flares occurred and no other clinical pattern suggestive of common specific organ involvement of SLE was observed.

Discussion

A full-house nephropathy is commonly seen in SLE patients. When present, it determines the extensive search for other Systemic Lupus International Collaborating Clinics (SLICC) criteria for LES, as has been done in our patient. We should emphasize that the patient was under corticosteroids and after several blood cell transfusions every time that serologic markers were performed. Such events may mislead in the interpretation of negative markers, as they can be false negative at the beginning of MMP and remain negative thereafter. High complement levels instead of the expected consumption by SLE could be justified by the concomitant infectious process; however, they remained normal after its resolution.

Concerning the possible clinical SLE criteria present in our patient, the authors consider that all of them could be explained by other etiologies, questioning the definitive diagnosis of SLE. PRES can be triggered by corticosteroids, arterial hypertension and red blood cell transfusion. Hemolytic anemia is also present in SCA. Transitory lymphopenia (800 cells/µL) is found in acute infectious states such as the respiratory infection by *P. aeruginosa* and with high dose prednisolone. However, less frequent etiologies of the full-house pattern glomerulonephritis were excluded by clinical, laboratory and histologic investigation.

It seems also unlikely that SCA could justify those histological changes. The sickle cell kidney disease patterns described in literature are commonly focal segmental glomerulosclerosis, membranoproliferative glomerulonephritis and/or thrombotic-like microangiopathy or associated with immune-complexes but the deposits are usually of C3, IgG and IgM and fine (+/++++ or ++/++++).[8–10] Also, rare cases of focal proliferative glomerulonephritis with immune-complex deposits and pauci-immune glomerulonephritis have been described in patients with SCA but in these cases an infectious relation was frequently established, mainly caused by Parvovirus.[11,12] In accordance with literature,[2,4,5] this patient was treated similarly to proliferative lupus glomerulonephritis. MMP was chosen instead of cyclophosphamide due to its similar efficacy and better safety profile.[13–15] An immediate and steady favorable clinical and laboratory response was achieved, which is uncommon with LN. However, the possibility of a progression to overt SLE cannot be excluded and a regular long-term follow-up is being carried out.

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AG, AM, RM, MC e HL: Conceção, recolha de dados, investigação e escrita do artigo

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AG, AM, RM, MC and HL: Conception, data collection, research and article writing.

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