MEMBRANOUS NEPHROPATHY VERSUS MEMBRANOUS LUPUS NEPHRITIS – CHALLENGES IN THE DIFFERENTIAL DIAGNOSIS

Nídia Marques[1], Filipa Ferreira[1], Ana Nunes[1], Inês Ferreira[1], Roberto Pestana[2], Manuel Pestana[1]

[1]Nephrology Department, Centro Hospitalar e Universitário de São João, Faculdade de Medicina da Universidade do Porto, Oporto, Portugal

[2]Pathological Anatomy Department, Centro Hospitalar e Universitário de São João, Faculdade de Medicina da Universidade do Porto, Oporto, Portugal

Introduction

About 10-20% of patients with lupus nephritis (LN), have membranous LN (MLN), which may precede the systemic manifestations of SLE. Membranous nephropathy (MN) is the most common cause of nephrotic syndrome, classically divided into primary (80%) or secondary (20%) to systemic diseases, such as systemic lupus erythematosus (SLE), neoplasms, hepatitis B or drugs. In 2012, LN (confirmed by biopsy), without other clinical criteria for SLE, and only accompanied by ANA or positive anti-dsDNA was included in the classification criteria of the Systemic Lupus International Collaborating Clinics (SLICC).

Case Description

Identification: 48-year-old female patient, leucodermic || No relevant **past medical history** || **Family diseases:** mother - ANCA vasculitis and cousins - SLE and Rheumatoid Arthritis

2008

Subnephrotic proteinuria

Referral to the nephrology department

- Normal renal function and urinary sediment (US)
- Negative immunological study <

2010

Renal Biopsy

Diffuse thickening of the basement membrane; negative direct-immunofluorescence (IF). No results from electron microscopy (EM) were available

Suspicion of **Primary Membranous Nephropathy** (PMN))

Secondary causes excluded

2014

ANA stands out **transiently positive** (1/100)

2015

Evaluated by Rheumatology due to low back and cervical pain whose study was inconclusive

Proteinuria < 1g/24h under irbesartan

2017

Negative serum measurement of Anti-Phospholipase A2 Receptor Antibody (PLA_2R)

- US without erythrocituria
- Immunological study
  - ❖ **ANA 1/100**
  - ❖ Anti-dsDNA negative
  - ❖ Anti-nucleosome negative
- No complement consumption

September 2018

Proteinuria of 2,55g/24h

Conservative therapy optmized → **progressive worsening of proteinuria to nephrotic range**

2019

Renal Biopsy

(figure 1)

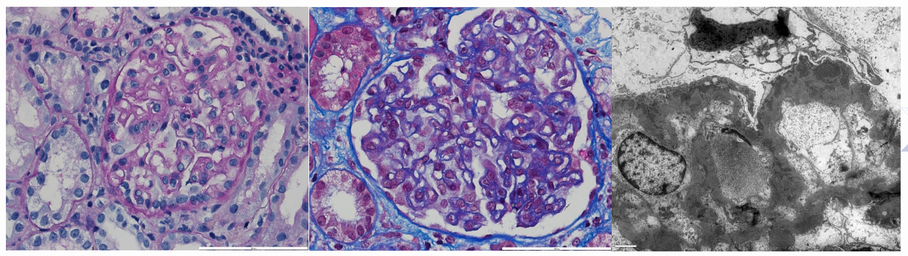

Figure 1: Renal Biopsy 2019: Thickening of the basement membrane and increased matrix, **full-house diffuse IF pattern** (image not available) and subepithelial immune deposits on **EM**

Differential Diagnosis of MLN vs. PMN

Pros MLN

- Meets the SLICC criteria
  - ❖ Positivity for ANA
  - ❖ Full-house IF

Cons MLN

- Absence of mesangial proliferation, mesangial and/or subendothelial immune deposits and tubuloreticular inclusions
- Full-house pattern is not pathognomonic for LN
- Non-specificity of ANA (detectable in 27% of population)

Positive immunohistochemistry and serum measurement of PLA_2R

→ **Primary Membranous Nephropathy**

→ **Immunossupression** with prednisolone and cyclosporine

→ **Complete remission** and **negativization of serum PLA_2R**

Conclusion

This case reinforces the **limitations of SLICC** criteria, as well as the challenge that can constitute the differential diagnosis between MLN and PMN whose course, therapy and prognosis are different. In this case, despite assuming the diagnosis of PMN, a high level of suspicion for SLE remains.

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Contact:
Nídia Marques
nidia.marques@chsj.min-saude.pt