Crossing the Line Between Monoclonal Gammopathy of Undetermined Significance (MGUS) and Monoclonal Gammopathy of Renal Significance (MGRS)

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Introduction

MGRS:
Entity Defined in 2012 and refined in 2017.
Any B cell or plasma cell clonal lympho-proliferation with:

- One or more kidney lesions related to the produced monoclonal immunoglobulin
- No tumor complications, end-organ damage or current hematological criteria for specific therapy

Aim

Highlight the importance of MGRS diagnosis

Objectives

- Underline Subtlety of MGRS diagnosis.
- Reveal Importance of timely diagnosis due to the hasty and insidious onset.
- Highlight the importance of clone-directed therapy use even with the absence of Myeloma Defining criteria.
- Show importance of combining renal and hematologic evaluations in patients with unexplained kidney injury and the presence of monoclonal immunoglobulins.

Case Presentation

- Woman aged 68.
- Seropositive for Rheumatoid arthritis treated with methotrexate.

Timeline

02/2025

- IgM Lambda spike: 2.3 g/L – Free Light Chain Ratio (FLCR) and Labs normal
- Pet CT negative - Bone Marrow Studies deferred

03/2025

- Faint IgM Lambda spike; FLCR normal (0.47)
- Grade II anemia, Acute Kidney Injury (Creatinine = 6mg/dL) - elevated LDH=407 - Nephrotic-range proteinuria (5g)
- Bone Marrow studies negative for plasma-cells presence - IgM Lambda deposits and cryo-plugs on pathology of kidney biopsy
- Started on VCD (Bortezomib, Cyclophosphamide, Dexamethasone) protocol

04/2025

- Normalization of creatinine and resolution of anemia

Results

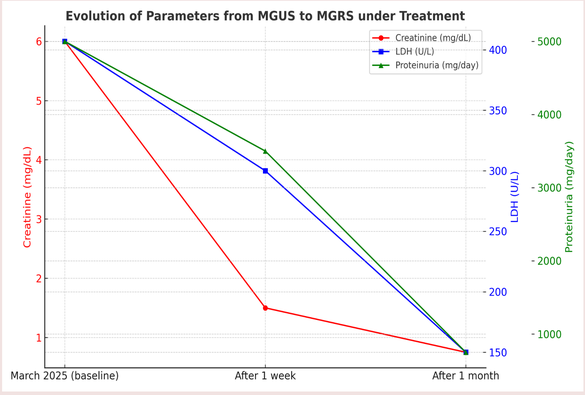


Table 1: Parameters evolution one week and one month after diagnosis

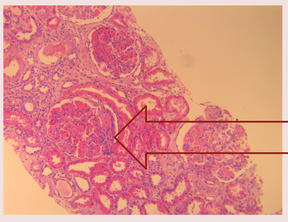
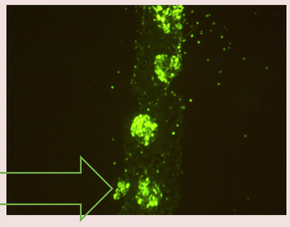


Image 1: Hematoxylin and Eosin staining of cryo-plugs

Image 2: Immunofluorescence of lambda chains deposition



Treatment Plan

Cycle (28 Days) 4 cycles	Day 1	Day 8	Day 15
Bortezomib 1.3 mg/m² SC/IV weekly	✓	✓	✓
Cyclophosphamide Cyclophosphamide: 300 mg/m² PO/IV weekly	✓	✓	✓
Dexamethasone 40 mg PO/IV weekly	✓	✓	✓

Take Home Messages

- MGRS can rapidly evolve from an MGUS-like presentation.
- Kidney injury may be the only sign of progression.
- Early, clone-directed therapy is crucial to preserve renal function which damage is rapidly reversible.
- Multidisciplinary approach improves outcomes.

References

1. *The evaluation of monoclonal gammopathy of renal significance: a consensus report of the International Kidney and Monoclonal Gammopathy Research Group*

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