Biclonal Evolution or Class Switch?
A Rare Journey from IF-Negative IgM Renal Amyloidosis to IgA Multiple Myeloma

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Introduction

AL amyloidosis and Multiple Myeloma (MM) are part of the plasma cell dyscrasia spectrum, yet their coexistence with immunoglobulin class discordance challenges the conventional model of linear clonal progression.

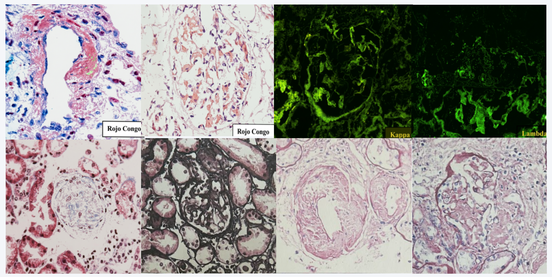
We report an exceptional case where IF-negative renal amyloidosis with IgM positivity preceded high-burden IgA MM, raising the question of whether this represents clonal class switching or a biclonal process.

Case Description

September 2023

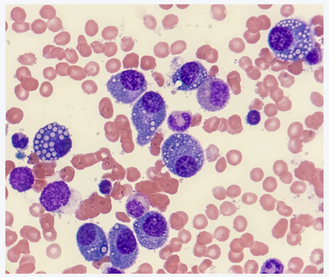
A 63-year-old female presented with nephrotic syndrome (proteinuria 3.98 g/24h, eGFR 54 ml/min).

Renal biopsy confirmed AL amyloidosis with Congo Red-positive glomerular and vascular deposits and subepithelial "spicules." Immunofluorescence was negative for Kappa and Lambda light chains, with isolated IgM positivity.



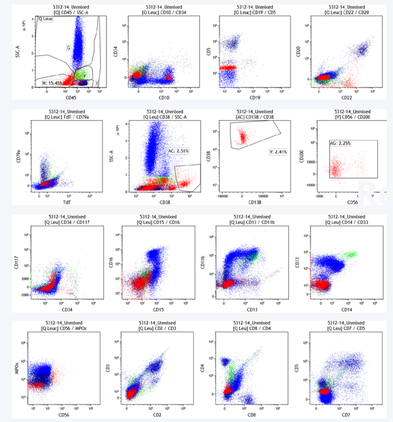
September 2024

A rising IgA paraprotein signaled clonal evolution.



December 2025

Bone marrow aspirate revealed 60% pathological plasma cells (CD45+, CD56+, CD200+, CD38+, CD138+, HLA-DR+), confirming IgA MM ISS II.



Discussion

This case presents two biologically compelling dilemmas.

First, IF-negative amyloid deposits in the setting of an ultimately IgA-secreting clone suggest the amyloidogenic clone may have operated below light chain detection thresholds at onset, consistent with low-secretory clonal behavior.

Second, the IgM-to-IgA discordance raises the possibility of heavy chain class switch recombination within a single evolving clone, or parallel expansion of a distinct IgA clone that eventually dominated the marrow.

Both phenomena are described in the literature but remain exceedingly rare.

The finding of 60% marrow infiltration alongside established renal fibrosis (20–25%) illustrates how biologically aggressive a seemingly indolent clonal origin can become, reinforcing that amyloidosis should never be considered a static endpoint.

Conclusion

This case challenges the assumption that AL amyloidosis and subsequent MM share a simple, unidimensional clonal relationship.

Immunoglobulin class discordance may signal biclonal disease or clonal evolution with class switching distinctions with meaningful biological and therapeutic implications.

This case underscores that understanding clonal identity from the outset is essential to anticipate disease trajectory in plasma cell dyscrasias.

References

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