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Truly Aggressive IgD Myeloma? Excellent Responses from Case Series

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INTRODUCTION

Immunoglobulin D (IgD) multiple myeloma is an uncommon and particularly aggressive variant, accounting for only 1–2% of all multiple myeloma cases [1]. It is characterized by severe clinical manifestations, primarily affecting younger patients, and is associated with a poor prognosis, with overall survival rates lower than those observed in other multiple myeloma subtypes [1].

Due to its rarity, the available literature on IgD myeloma is limited, with most reports dating back to the 1960s and 1980s. Despite advancements in therapeutic approaches, limited studies focus on the clinical follow-up and treatment response of patients with IgD myeloma. This study seeks to provide a detailed description of IgD multiple myeloma, highlighting its clinical, biological, and therapeutic characteristics. The goal is to contribute to the existing body of knowledge and improve the clinical management of this rare entity.

METHODS:

We conducted a retrospective study at the Hematology Department of the University Hospital Center of Tangier (Morocco). Patient data were collected from archived medical records and the hospital's internal database.

Inclusion criteria were as follows:

- Diagnosis of multiple myeloma based on the 2014 International Myeloma Working Group (IMWG) criteria: bone marrow plasmocytosis >10% or histologically confirmed plasmacytoma, along with at least one CRAB-SLIM criterion.
- Detection of IgD immunoglobulin on serum protein immunofixation.

Treatment response was assessed according to the 2016 IMWG response criteria.

RESULTS:

Five patients were identified who met the inclusion criteria, diagnosed between December 2022 and August 2025, with a median follow-up period of 37 months until March 2026. The median age of the cohort was 55 years, and all patients resided in rural areas, working as farmers. All presenting with bone pain and PET bone lesions. Bone marrow plasmocytosis ranged from 2% to 39%, and serum protein electrophoresis revealed a monoclonal peak in the gamma region, with an average concentration of 12.3 g/l. immunofixation confirmed IgD kappa multiple myeloma (Figure 1). Renal insufficiency was noted in two patients, without the need for dialysis. No patient exhibited organ involvement or histological evidence suggestive of secondary AL amyloidosis. FISH revealed high-risk features in 2/5 patients (del17p n=1, gain1q21 n=1); non-contributory in 3/5 due to low plasma cell yield.

Treatment regimens were based on the triplet combination of VTD (n=4) and VRD (n=1), achieving complete response (CR) (n=2), very good partial response (VGPR) (n=2), and progression (n=1). The four responders subsequently received high-dose Melphalan (Mel200) followed by autologous stem cell transplantation, resulting in CR. The median time to relapse was 13.5 months; these patients were subsequently initiated on second-line therapy comprising DRd [CR (n=1), ongoing (n=3)]. The fifth patient (progression on VRD) is on ongoing D-Kd.

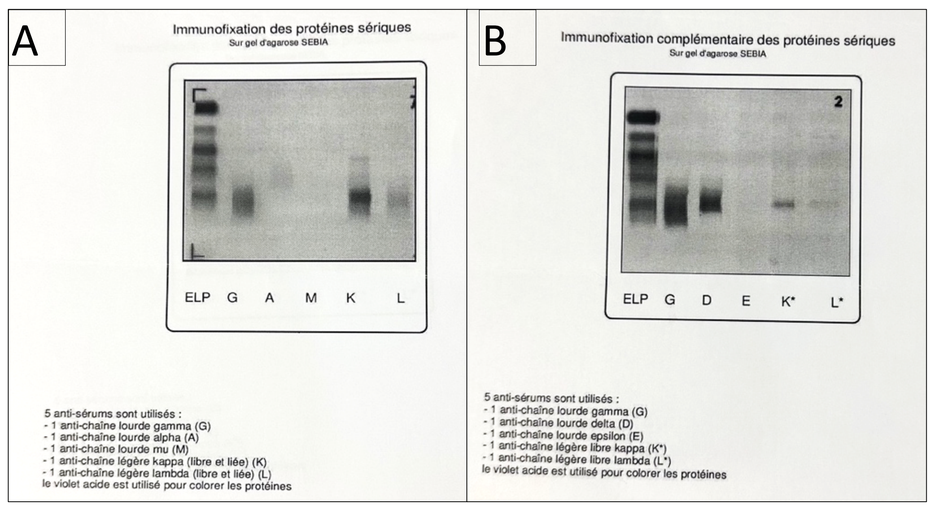

Figure 1: Serum protein immunofixation (A) and its complement (B) confirming IgD Kappa multiple myeloma diagnosis

DISCUSSION

Our cases join established IgD multiple myeloma literature regarding young age at diagnosis, lambda light chain predominance, and small gamma-region monoclonal peaks that may mimic light-chain myeloma [2,3]. However, they contradict reported frequencies of AL amyloidosis (~19%) [4] and exceed historical overall survival of 13-21 months in IgD myeloma [1,2].

High-risk cytogenetics occurred in 40% (2/5 patients), consistent with 33-53% literature rates [1]. Contemporary triplet induction followed by autologous stem cell transplantation yielded excellent responses even in high-risk cases, challenging IgD multiple myeloma's traditionally poor prognosis.

These findings underscore modern triplet therapy's impact and advocate for larger, multicenter series to optimize management strategies.

CONCLUSION

Although rare, this IgD multiple myeloma series of young patients (median 55 years) demonstrates bone pain as a principal initial presentation, high-risk cytogenetics in 2/5 patients, but excellent initial responses to standard therapy including high-risk cases. The median relapse time of 13.5 months challenges the traditionally poor prognosis. Larger series needed to refine treatment strategies.

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