

## IgD MULTIPLE MYELOMA COMPLICATED OF ACQUIRED FACTOR XI DEFICIENCY: A CASE REPORT

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### ABSTRACT

IgD multiple myeloma (MM) is a rare isotype of multiple myeloma, comprising less than 2% of all cases. IgD myeloma characterized by aggressive presentation and shorter overall survival than other subtypes of MM. Acquired deficiency of coagulation factor can complicate hematological malignancies; bleeding depends on level and on the factor deficiency. Factor XI deficiency is relatively low risk spontaneous bleeding. There are few cases of IgD MM described in the literature especially complicated with factor deficiency. We report a rare case of IgD lambda multiple myeloma with acquired factor XI deficiency.

**Keywords:** Case report, IgD myeloma, Factor XI deficiency, Multiple myeloma.

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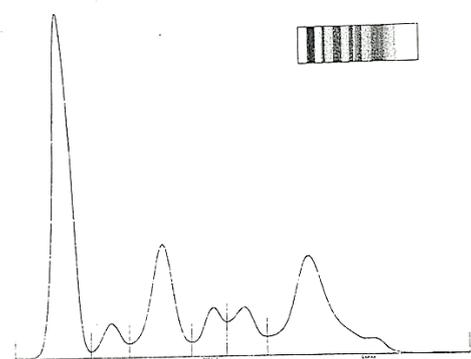
### INTRODUCTION

Multiple myeloma (MM) accounts for 1% of all cancers and approximately 10% of all hematologic malignancies [1]. Immunoglobulin D (IgD) myeloma is a rare isotype that comprises 1–2% of MM patients [2] , IgD MM is characterized by an aggressive clinical course with worse overall survival (OS) and a high frequency of complications [3]. We report a case of IgD lambda MM with acquired factor XI (f XI) deficiency.

### CASE PRESENTATION

A 47-year-old male patient, with no particular medical history, was referred to our unit for intense bone pain. Bilateral lower leg pain impeded walking and was described as 3 out of 10. The symptoms evolved in the context of alteration of the general condition without sphincter disorders.

The clinical examination found a performance status at 1, anemic syndrome, no osteoarticular abnormalities, and decreased segmental muscle strength to 4/5 in lower limbs on neurological examination. Otherwise, the rest of the somatic examination was normal. The hemogram showed non regenerative normocytic normochromic anemia at 6 g/dl. Neutrophil and platelet counts were normal. Bone marrow aspiration showed 12% invasion by plasma cells. A serum protein electrophoresis demonstrated hypoalbuminemia at 30 g/l, and hypergammaglobulinemia with a monoclonal peak at 4.9 g/l (**Figure 1**). Serum immunofixation objectified monoclonal IgD Lambda protein. Bence-Jones proteinuria was positive. The 24-hour proteinuria was 0.77 g/l. Renal function was impaired (urea=0.79 g/L, creatinine=23 mg/L with creatinine clearance at 33 ml/min.



**Figure 1:** Serum protein electrophoresis showing hypergammaglobulinemia with a monoclonal peak

Corrected calcemia was normal at 98 mg/l. Skull and long bones X-Ray showed diffuse lytic lesions (**Figure 2**) and a chest CT scan showed diffuse lesions involving the axial and peripheral skeleton. Beta2-microglobulin was increased to 5.32 mg/L.



**Figure 2:** X ray of skull showed diffuse lytic lesions (Red arrows)

Homeostasis assessment found prolonged partial thromboplastin time (PTT) to 166.6 seconds (control: 30 seconds) and a normal prothrombin time test (PT) at 88% (normal between 70 and 100%). The Rosner index to 3.4% and an assessment of coagulation factors objectified a factor XI deficiency returning to 03%.

The diagnosis of IgD multiple myeloma, with International Staging System (ISS) at 1, associated with acquired factor XI deficiency was made. The patient was treated with VDT regimen (bortezomib, dexamethasone, thalidomide) with bisphosphonates. The Patient achieved complete remission after 6 VDT cycles: Absence of monoclonal in serum electrophoresis and immunofixation, and only 2% plasmacytes invasion in bone marrow aspiration.

Hemostasis assessment (PTT at 36 seconds). Renal function, serum calcium, and complete blood count were normal.

During the follow-up, the patient had a fall resulting in a femoral neck fracture, requiring a total hip replacement, the patient refused autologous stem cell transplantation, and was kept on thalidomide maintenance therapy. The evolution was favorable with the maintenance of complete remission for two years and a normalization of the PTT.

## DISCUSSION

Multiple myeloma (MM) is a clonal plasma cell neoplasm, The diagnosis requires  $\geq 10\%$  clonal bone marrow plasma cells or a biopsy proven plasmacytoma plus evidence of one or more multiple myeloma defining events (MDE): CRAB (hypercalcemia, renal failure, anemia, or lytic bone lesions) attributable to the plasma cell disorder bone marrow clonal plasmacytosis  $\geq 60\%$ , serum involved/uninvolved free light chain (FLC) ratio  $\geq 100$  (provided involved FLC is  $\geq 100$  mg/L), or  $>1$  focal lesion on magnetic resonance imaging [1] Survival in multiple myeloma has improved significantly in the last 15 years [4].

IgD MM is characterized by a more aggressive clinical course with a high frequency of renal failure, hypercalcemia, amyloidosis, extra-medullary plasmacytomas (EMP), extra-osseous lesions, hepatosplenomegaly, generalized lymphadenopathy and a poor prognosis [3]

FXI deficiency can be acquired or congenital, acquired factor inhibitors are rare events [5]. The risk of bleeding in conditions of fXI deficiency is relatively low and correlation between factor levels and symptoms is very poor; in these persons hemorrhage is usually provoked, exacerbated by trauma or surgical procedures [6]. There was no hemorrhagic syndrome in this case, the thromboprophylaxis is also mandatory in myeloma in particular treated with immunomodulatory agent, therefore it is necessary to evaluate hemorrhagic risk and thrombosis.

Few cases of inhibitors against FXI in association with malignancies were reported in the literature. Acquired factor XI inhibitor in chronic lymphocytic leukemia was described in a 71 year old man in 1992 [7]; another case of FXI deficiency was reported in gastrointestinal adenocarcinoma series of 71 patients within 10 years [8] and another in association with thymoma in A 45-year-old man[9].

The approach to treatment of symptomatic newly diagnosed multiple myeloma is dictated by eligibility for autologous stem cell transplantation ASCT and risk-stratification. Generally, patients are

treated with approximately 3-4 cycles of induction therapy prior to stem cell harvest. After harvest, patients can either undergo frontline ASCT or resume induction therapy delaying ASCT until first relapse [10]. The maintenance therapy is indicated following treatments: lenalidomide is the standard of care for maintenance therapy for most patients. [10]. A study comprising 365 patients with IgD myeloma by the Asian Myeloma Network (AMN) showed that patients who received immunomodulators (thalidomide) had relatively longer OS. Patients who received ASCT had a median OS of 45.7 months, slightly longer than 35 months for non-ASCT patients [11]. A study comprising 365 patients with IgD myeloma by the Asian Myeloma Network (AMN) showed that patients who received immunomodulators (thalidomide) had relatively longer OS. Patients who received ASCT had a median OS of 45.7 months, slightly longer than 35 months for non-ASCT patients [11].

## CONCLUSIONS

IgD Multiple myeloma is an unusual isotype of MM characterized by aggressive clinical presentation and shorter overall survival. Acquired FXI deficiency is also uncommon. The new treatment strategies, autologous stem cell transplantation, promise to improve outcomes.

## CONFLICT OF INTEREST

There are no competing interest to declare.

## FUNDING

Not applicable.

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