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Immunoglobulin D Multiple Myeloma, a More Aggressive Subtype

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Abstract Immunoglobulin D (IgD) multiple Myeloma (MM) is a very rare subtype of myeloma. It accounts for only 1-2% of all MM patients. It is associated with a rapidly progressive disease and poorer outcomes compared with other MM subtypes. In this case report, we present a case of a sixty-year-old man who presented to our hospital with fatigue, anemia, thrombocytopenia, and acute renal failure. His bone marrow biopsy during admission showed 75.9% of plasma cells with significant light chain burden. He was also found to have severe immunoglobulin deficiency along with a lambda to kappa ratio was <0.01. The diagnosis of IgD MM was established, and he was started on CyBorD (Bortezomib, cyclophosphamide, and dexamethasone). Our patient also required hemodialysis for his kidney failure.

Keywords: *Immunoglobulin D, multiple myeloma, renal failure, light chain nephropathy, CyBorD*

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1. Introduction

MM is a hematologic malignancy characterized by clonal proliferation of plasma B cells in the bone marrow. IgD MM is a rare subtype. It is more common in men than women, as well as patients of a younger age [1,2]. Patients usually have an aggressive disease at the time of presentation. Twenty to forty percent of those patients present with renal failure. Of those 20 to 40% of patients, 10% require renal replacement therapy at the time of presentation, while 25% require dialysis later during the disease [3,6]. The mechanism of renal failure can be either due to cast nephropathy or direct renal toxicity by intracellular crystals [3]. The diagnosis of IgD MM may be delayed due to the lower prevalence and smaller volume of IgD monoclonal protein in the serum. IgD MM patients were found to have a shorter survival time of 13-18 months [4,6] and a slower response to treatment compared to IgG and IgA MM subtypes.

2. Case Presentation

Here we present a case of a sixty-year-old male with no significant past medical history who presented to our emergency department (ED) for abdominal pain, fatigue, decreased appetite, weight loss, and lower extremity bruising for three weeks. His initial workup revealed that he had anemia (Hemoglobin 5.8 g/dL), thrombocytopenia (Platelet count 22 Thous/uL), proteinuria (urine protein 30 mg/dL), and acute renal failure (serum creatinine 6.99mg/dL). Peripheral blood smear showed pancytopenia with atypical circulating lymphocytes and teardrop cells (Figure 1). Given those results, hematology was consulted due to concern for MM. Serum protein electrophoresis did not reveal an M-spike (Figure 2). However, free light chain analysis revealed a Kappa-Lambda ratio less than 0.01 (Kappa free light chain 1.23 mg/dl, Lambda free light chain 1398 mg/dl – Figure 3). Serum immunofixation demonstrated an IgD monoclonal Lambda gammopathy. The patient then underwent a bone marrow biopsy (Figure 4) which showed 75.9% plasma cells consistent with IgD Multiple Myeloma diagnosis. Flow cytometry of the marrow showed strong positivity for CD38, CD138, and CD56. A small group showed positivity for CD20 (Figure 5). Cytogenetics were positive for amplification of the CKS1B gene and trisomy of IGH and CCND1. However, it was negative for loss of the p53 gene and t (11;14). The patient was started on a CyBorD regimen (Cyclophosamide + Bortezomib + Dexamethasone) and began hemodialysis for his renal failure. However, his clinical course was complicated by methicillin-sensitive Staphylococcus aureus (MSSA) bacteremia, recurrent bleeding, severe anemia and thrombocytopenia requiring multiple transfusions, hypoxic respiratory failure requiring mechanical ventilation, and an acute subdural hematoma. Due to his poor prognosis, his family decided to withdraw care. The patient expired around 6 weeks following his initial presentation to our hospital.

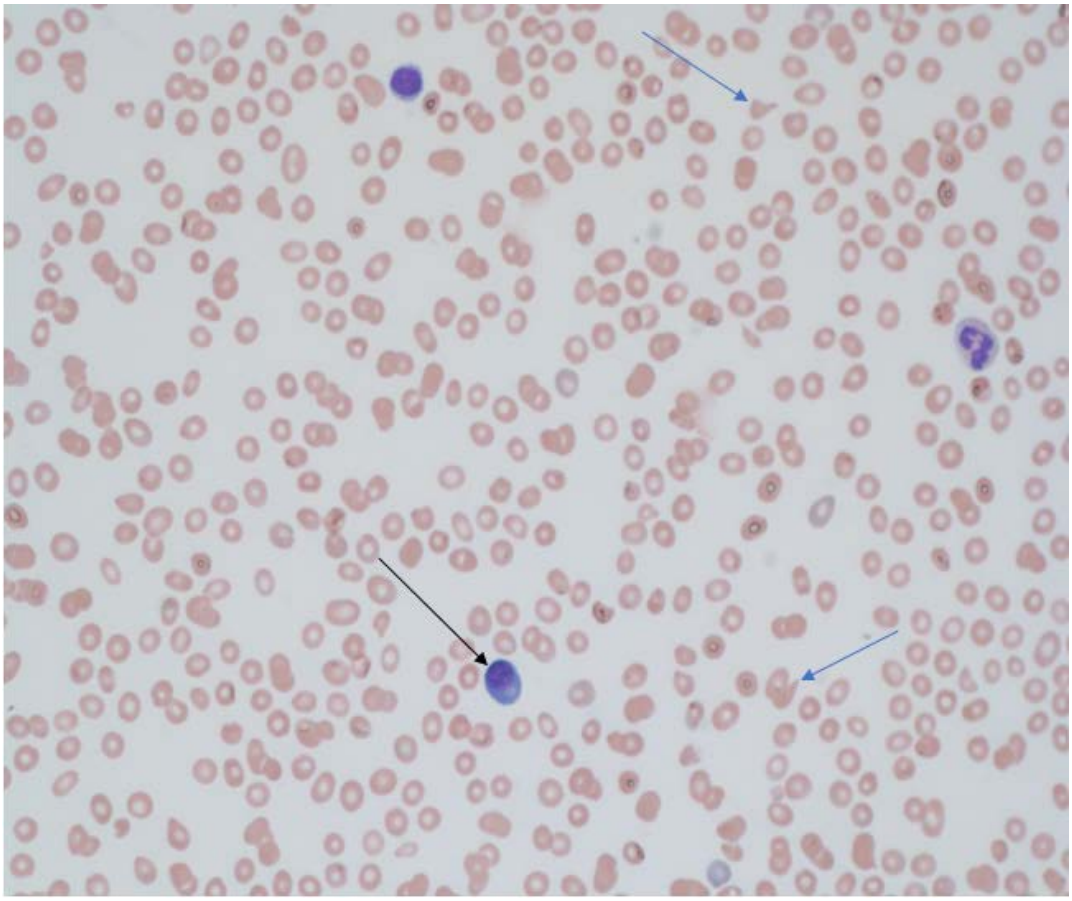

Figure 1. Atypical circulating lymphocytes (black arrow), nucleated red blood cells, and scattered tear drop cells identified (blue arrows)

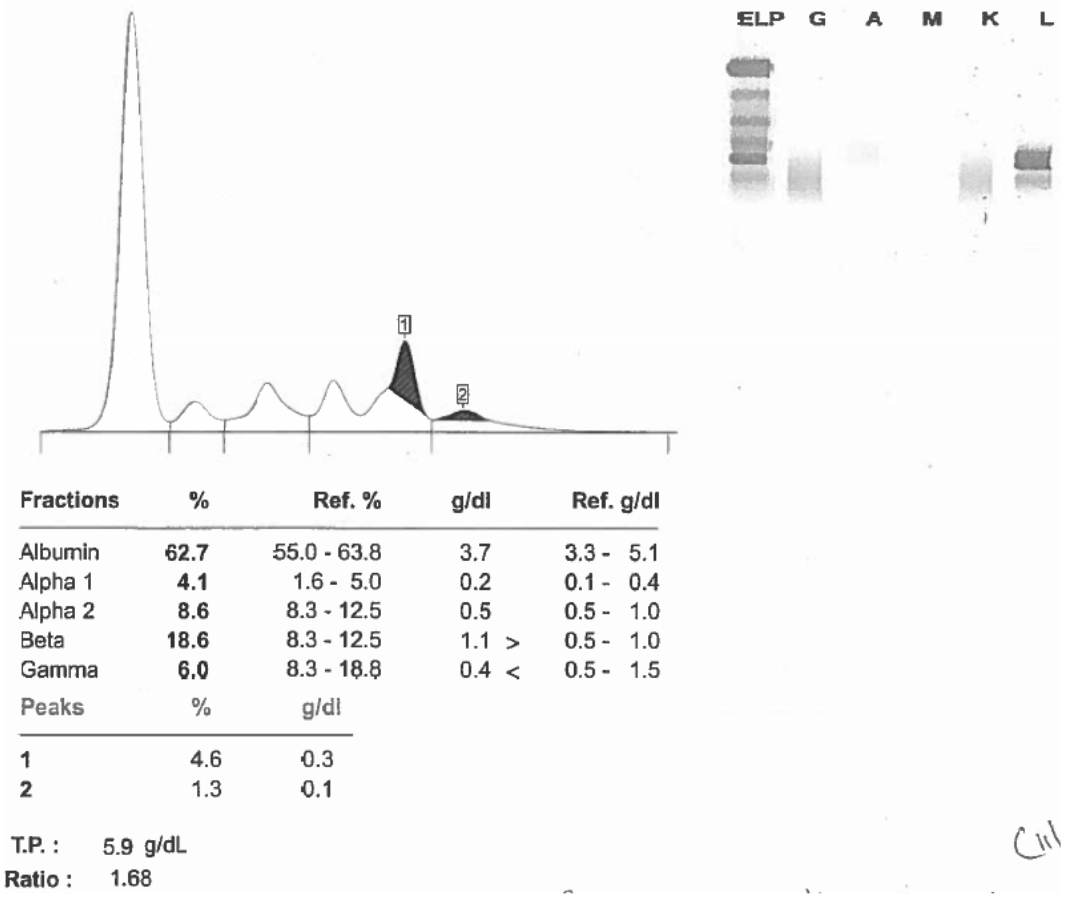

Figure 2. Serum protein electrophoresis showing no M spike

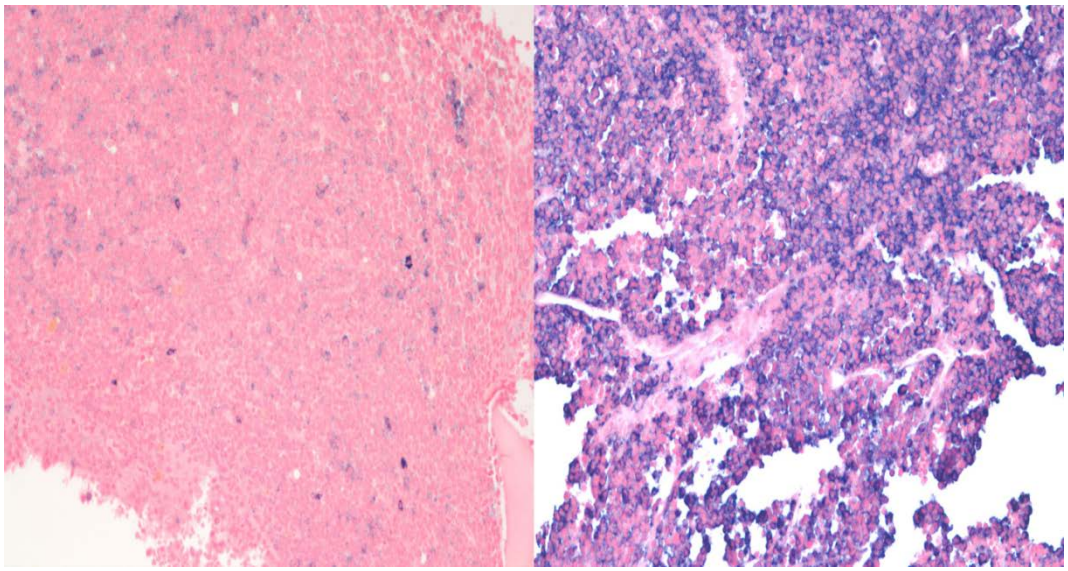

Figure 3. In situ hybridization stains for kappa and lambda showing predominant lambda light chain restriction

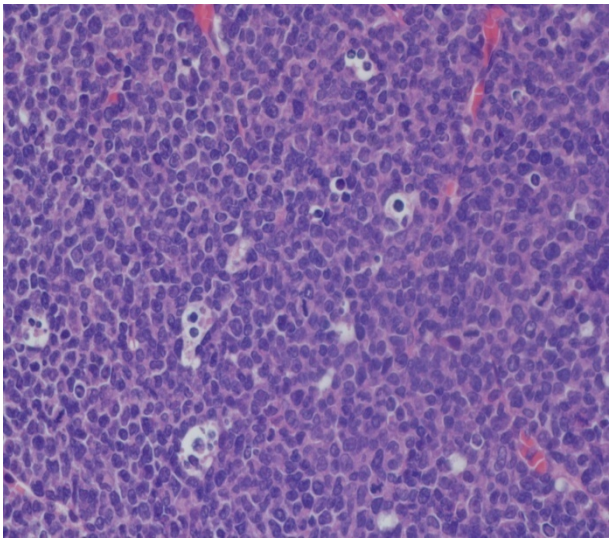

Figure 4. Bone marrow biopsy showing sheets of neoplastic plasmocytic cells

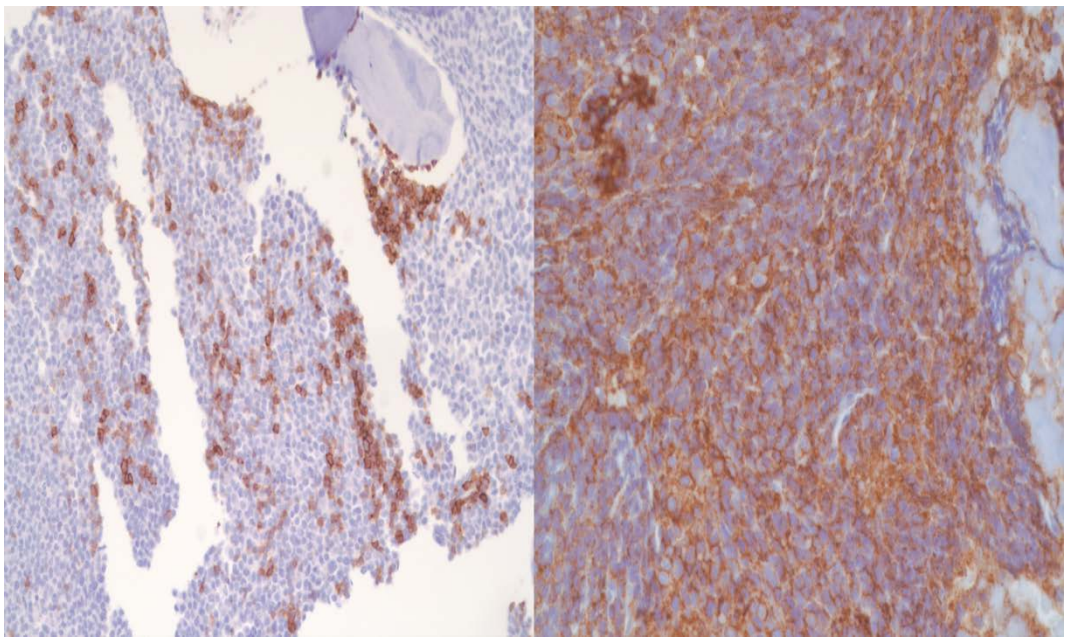

Figure 5. Positive immunohistochemical stains showing positivity for CD20 (left) and CD138 (right)

3. Discussion

IgD MM is a rare subtype of multiple myeloma that accounts for approximately 2% of all MM cases. It is more aggressive than other MM subtypes and can occur at a younger age (median age 52 to 60 years old). It also presents more often with significant renal dysfunction that may require renal replacement on presentation and extensive bone marrow disease as evidence by our case {1-7}.

Patients with IgD MM are found to have a predominant lambda over kappa (k) chain which leads to a significant abnormal serum free light chain ratio (sFLC) <0.01 mg/dl [1,3,5] and a smaller or absent M spike on serum protein electrophoresis (SPEP) similar to our case.

IgD MM patients have higher risk chromosomal anomalies including 1q21 amplification, t(4,14), t(11,14), del 17, and del p53 compared to other MM subtypes. Our patient's cytogenetics were positive for amplification of the CKS1B gene which is associated with a poorer prognosis.

The rarity of this disease makes treatment very challenging. Studies showed that combination therapy with either high doses of chemotherapy (HDT) or immunotherapy (as lenalidomide or thalidomide)or protease inhibitor (as bortezomib) with autologous stem cell transplant (ASTC) are superior to Melphalan based regimens that were frequently used in the past (Melphalan, Vincristine, Adriamycin, and dexamethasone) [3,7,8].

Our patient was a sixty-year-old man with no comorbidities. He presented with extensive bone marrow disease and renal failure requiring hemodialysis. There was no delay in his diagnosis. Unfortunately, he was not able to complete even his first cycle of CyBord due to multiple complications directly related to the myeloma itself, including bleeding complications from thrombocytopenia and MSSA bacteremia related to immunosuppression. Ultimately, he continued to experience further decline that lead to a de-escalation of care per the family's request and expiration six weeks following his initial diagnosis.

4. Conclusion

IgD MM is a highly aggressive subtype of Multiple Myeloma that tends to occur at a younger age. It is associated with a highly aggressive disease at the time of presentation and has consistently shown poorer outcomes compared with other MM subtypes. Given the poor prognosis associated with the disease and difficulty in effectively managing it, more studies are needed to improve patient outcomes.

Conflict of Interest

None of the authors have any conflicts of interest to declare.

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