

## Immunoglobulin D Multiple Myeloma-A Rare Case

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### Abstract

#### Introduction

Immunoglobulin D multiple myeloma (IgD MM) accounts for almost 2% of all myeloma cases and has usually an poor prognosis. Due to its rarity, the reports on this disorder in the literature are limited.

#### Case Report

We therefore present a case of Ig D multiple myeloma. The age of the patients was 56 years old and the common presenting symptoms were anorexia, weight loss and bone pain. The patient was also presented with neurological symptoms (peripheral neuropathy), renal impairment and kappa paraproteinemia.

#### Conclusion

The small group of patients who have IgD multiple myeloma is rare and considered to have a poor prognosis compared to other MM isotypes.

The clinical features and prognosis of patients with IgD MM are not the same from those that characterize patients with other immunoglobulin MM subtypes. New treatment strategies that aim to induce high-quality responses before ASCT and after ASCT may be needed to improve the outcomes of such patients.

**Keywords:** Ig D; Multiple Myeloma; Paraproteinemia

### Introduction

Immunglobulin D was first described by Rowe and Fahey [1] in 1960 s. It is associated with an increased frequency of undetectable or small monoclonal (M)-protein levels on electrophoresis; osteolytic lesions; extramedullary involvement; amyloidosis; a lambda light chain predilection; renal failure; hypercalcemia; and, often, advanced disease at diagnosis. It is seen more common in men than in women. The median survival time for this patients is 13–21 months. The responserate to alkylating agents alone or combination chemotherapy regimens has been reported to be 58% [2]. Owing to it is very rare, a little is known about IgD MM. It has appeared in the literature, with most being in the period between 1960s and 1980s, but also latest in 2012. There are only 5 large reviews in the literature of Ig D multiple myeloma cases since the discovery of immunoglobulin D [2-6]. An understanding of this subtype will become when the cases continue to be reported. Over the past 15 years, there have been new treatments of MM, prospective randomized trials have shown the effectivity of high-doses of chemotherapy with autologous stem cell transplantation (Melphalan based HDT/ASCT) against standard therapy (CT) and new drugs, such as immunomodulatory (like lenalidomide) agents and proteasome inhibitors (like bortezomib) [7].

Little is known about the effects of new drugs or the effectiveness of autologous Stem Cell Transplantation (SCT) in patients with IgD MM. Most studies have been not complete datas on different patients and yielding adverse results. For example, one study reported that Overall Survival (OS) time in patients who have autologous SCT was >60 months [8]. Colorable that autologous SCT improved being an independent prognostic factor for poor survival after this therapeutic autologous SCT [9]. A number of clinical and laboratory diverses have been found as prognostic factors in patients with MM. The International Staging System (ISS), based on the serum concentrations of  $\beta$  2 microglobulin and albumin, is considered as the most useful prognostic staging system for patients with this disease [10]. Also, cytogenetic and molecular features are very important as the key of

prognostic determinants outcomes in patients with IgD MM disease [2]. Although prognostic factors in IgD MM can be distinct owing to the unique clinical features of this disease isotype, they have not yet been fined yet. For example, light chain subtype and white blood cell count have been showed as prognostic indicators , but they were not validated and were limited due to the high frequency of lambda light chain type in IgD MM [10].

### Case Report

A 56-year-old man presented in November 2011 with a 2 months' history of low back pain, generalised weakness, anorexia and weight loss. He also represented a short history of bilateral lower costal pain. He was found to have a 5 cm hepatomegaly- 3 cm splenomegaly, peripheral neuropathy and generalize ascites. Renal function impairment and hypercalcemia were present. A lumbar spine CT scan revealed a lateral disc prolapse at L5/S1 with the discmaterial encroachment into the neuroforamina. There was no lytic bone lesions. According to the International Staging System, the patient was in stageII. There wasn't any chromosomal abnormalities by conventional cytogenetics. Blood, serum, urine and bone marrow investigations (Table 1) confirmed the diagnosis of Ig D myeloma. The performed bone marrow biopsy showed 94% plasma cells (Figure 1). Initially, the patient was treated 5 days with intravenous high dose methylprednisolone and 5 days he was subjected on total plasma exchange procedure as asalvege produce for his renal impairment. As a result of that; improvement in his renal

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Blood	Values	Range
Hb (g/dl)	9.5	14-17
ESR (mm/hr)	14	≤ 20
Bone marrow Plasma cells	(%) 94	≤ (%5)
Calcium (mg/dl)	9.9	(8.4-10.20)
Urea (mg/dl)	122	(18-55)
Creatinine (mg/dl)	2.17	(0.72-1.25)
Total protein (g/l)	5.5	(6.4-8.30)
B2-microglobulin (mg/dl) :	2.0	(0.6-2.50)
Urate (mg/dl)	11.2	(3.5-7.2)
Electrophoresis Ig D (mg/L)	560	(0-80)

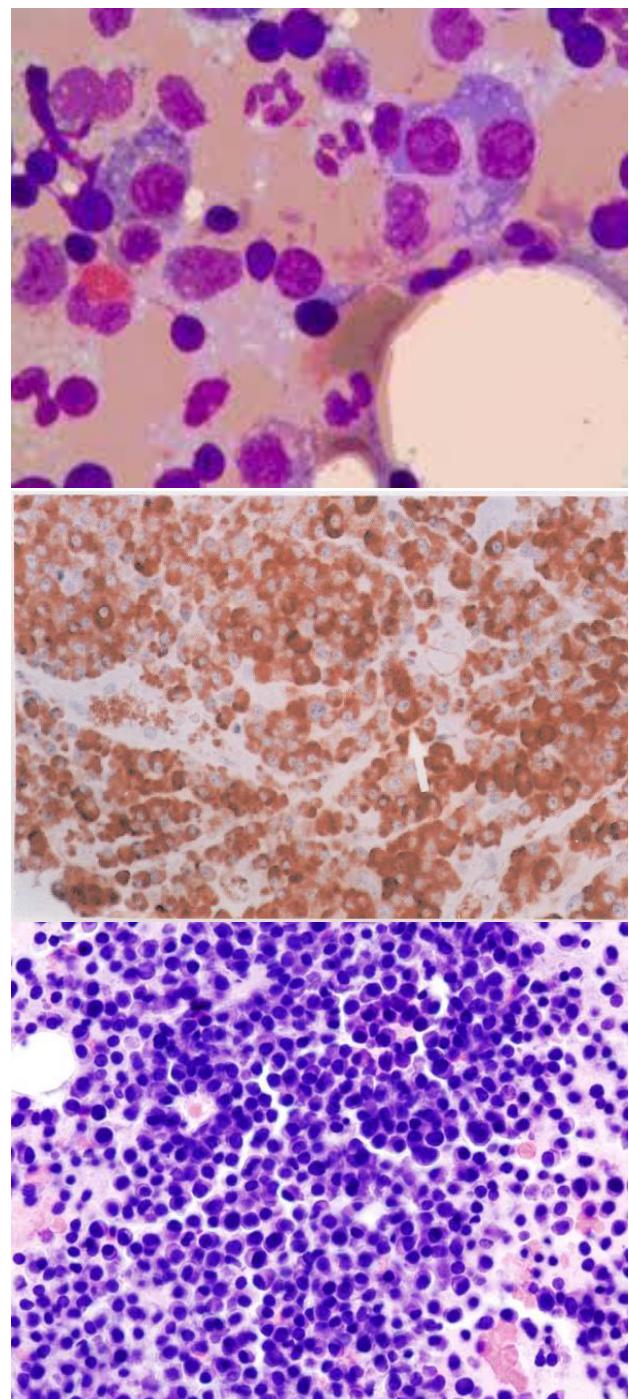
**Table 1:** Laboratory characteristics.

function was marked. One course for each one of them included bortezomib with dexamethasone combination. However, there wasn't any response after the chemotherapy and his family opted for palliative care. Shortly after, he passed away peacefully.

## Discussion

Here we present the clinical features of a 56 years old male patient with IgD MM, we found that IgD MM more likely presented at advanced stage and showed a poor aggressive clinical course and prognoses. In addition, the poor aggressive clinical course, prognoses and survival of the patients with IgD MM may be connected with problems related to delayed diagnosis [6,8]. Patients with renal failure of unknown cause, bone pain, small serum M protein bands, or undefined Ig isotype should keep in mind of having IgD MM. The disease usually presents as an absent spike or a small spike in the gamma or beta zone on serum electrophoresis and an associated heavy Bence Jones proteinuria. The most common subtype is Ig G myeloma. This is followed by Ig A myeloma and light chain disease. Ig D myeloma accounts for only 1-2% of newly diagnosed multiple myeloma cases. Only 5 large reviews of Ig D myeloma are reported in the literature. The first report was from Toronto on 133 cases of Ig D myeloma in 1975 [3]. The next report was almost 20 years later where the Japanese looked at 165 patients in 1991 and established a new risk grouping for Ig D myeloma [4]. The most recent review in 1994 was from a single institution, Mayo Clinic, on 53 patients looking at its clinical presentation, treatment response and survival [2]. A Korean study also shows 75 patients in 2011, and reviews their clinical presentation, treatment response and survival [6]. Due to its rarity of this disorder, case reports on it are invaluable in our future understanding of this subtype of multiple myeloma. Multiple myeloma patients presenting age is in the mid-60s but the age of presentation of the subtype Ig D myeloma is much younger and similar to those with light chain disease [11]. These patients are usually 4 to 9 years younger than those with Ig G or Ig A subtypes [12]. Our patient was 56 years old. Similar to other subtypes of myeloma, the most common presenting symptoms are bone pain, constitutional symptoms and neurological manifestations like our patient [2,12]. Extraosseous involvement is also a common presentation in Ig D myeloma and is reported in 27% to 63% of cases. Amyloidosis is also seen, as high as 44% in a reported study [2]. 50% of the patients with Ig D myeloma are known to have organomegaly and lymphadenopathy [12]. Our patient had a clinically detected hepatomegaly and splenomegaly on ultrasound scanning. Osteolytic lesions are more common in Ig D myeloma and were reported in 75% of the patients [6]. Our patient had not any osteolytic lesions. Related light chain disease is commonly seen among Ig D myeloma patients [13] but it is found in only 16% to 33% of the patients with Ig G or Ig A myeloma [6,8]. About 80-94% of Ig D myeloma patients have lambda light chain subtype [2]. In

our case, kappa light chain expression was found. The characteristics of kappa and lambda light chain disease do not show any significant difference [2]. In a study [4], Bence Jones proteinuria is detected in 92% of patients. It is felt that IgD myeloma may be considered as a variant of light chain disease as they both have similar characteristics [2]. Renal impairment is reported in 67% of Ig D myeloma patients [8]. In the Nordic myeloma group of 1353 patients, all patients with Ig D myeloma and half of the light chain disease had renal failure [9]. Hypercalcemic



**Figure 1:** Pathology of plasma cells.

patients are more likely to have renal impairment (45%) than those with normocalcaemia (21%) [8]. Our patient had also renal impairment and hypercalcaemia but that therapeutic procedure wasn't effective in him. There is a positive association between Bence Jones proteinuria and renal failure similar to the observed in other myeloma subtypes [14]. The pathogenesis of renal damage in Bence Jones proteinuria is thought to be due to tubular dysfunction and is seen in proteinuria of >1 g/day. Several studies have shown that total plasma exchange (TPE) is more effective than dialysis in removing Bence Jones proteins [12]. Our patient had also TPE as a salvage procedure for his renal impairment but TPE wasn't effective in our patient. Treatment response in Ig D myeloma patients is similar to the observed in other myeloma subtypes [2,12] but the median duration of survival appears to be shorter (12-17 months) [6,12]. Our patient was subjected on chemotherapy with bortezomib combined with dexamethasone. Unfortunately, he had no time to have a new combination. The Durie-Salmon staging of disease does not predict survival in Ig D myeloma patients and response does not appear to correlate with the level of paraprotein and renal function [6,7,12]. With more aggressive and intensive treatment, the median duration of survival can be improved and may be comparable to the other subtypes of myeloma. A longer duration of survival was seen in Japanese patients with associated kappa light chain disease but this was not reported in patients from the Mayo Clinic [12]. According to another study, however, the survival after autologous SCT was only 12 months, with IgD isotype [8].

Several other investigations reported that IgD MM is highly sensitive to novel therapeutic agents such as bortezomib and thalidomide [6-8,13]. The best treatment results for myeloma are obtained with allogeneic bone marrow transplantation, with 35% of patients in complete remission after allografting [10]. This may be due to graft-versus-myeloma effect. However, the transplant-related morbidity and mortality is much higher in allogeneic bone marrow transplantation. The procedure is also limited to a minority of patients, mainly of a younger age group. Autologous bone marrow transplantation may be an option in the achievement of aggregate malignancy reduction, but also improvement of response rate, response duration and disease-free survival. Early transplant-related morbidity and mortality is much less (<5%) and this procedure can be extended to older age patients. Recently, autologous tandem transplantation has been shown to be a feasible procedure and has demonstrated to increase the rate of complete remission [7-8,11]. In summary, Ig D myeloma is a rare disease, accounting for only 2% of newly diagnosed myeloma. It should be considered if only a light chain band, detected on immuno-electrophoresis. These patients should be treated in a similar way as the other subtypes of myeloma with intensive combination chemotherapy [10]. Autologous bone marrow transplantation or stem cell rescue should be performed in suitable patients as this results in which these therapeutic strategies lead to a better disease-free survival. Allogeneic bone marrow transplantation should be considered in long term complete remission. Unfortunately our patients had not the chance to undergo other treatments [15].

## Conclusion

The small group of patients who have IgD multiple myeloma is

rare and considered to have a poor prognosis compared to other MM isotypes. The clinical features and prognosis of patients with IgD MM are not the same from those that characterize patients with other immunoglobulin MM subtypes. New treatment strategies that aim to induce high-quality responses before ASCT and after ASCT may be needed to improve the outcomes of such patients.

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