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An unusual case of IgD Myeloma, a case report

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Abstract

IgD myeloma is a rare subtype of Multiple myeloma characterized by an aggressive disease with a median survival of less than 2 years. Most of the patients with IgD myeloma present with an advanced disease and with extramedullary manifestation. IgD myeloma has a poor overall survival rate, but with the use of novel agents followed by autologous stem cell transplantation the survival rate has improved. However, the overall survival rate is still poor when compared to other subtypes of multiple myeloma. In our case, the patient presented with compression fracture of T8 vertebral body and the biopsy of which came back positive for was positive for kappa plasmacytoma. Eventually, the patient was diagnosed with IgD myeloma.

Keywords

IgD myeloma; stem cell transplantation

Introduction

Multiple myeloma (MM) is a disease which is characterized by the neoplastic proliferation of plasma cells which produces monoclonal immunoglobulin. In one retrospective analysis of 1027 patients [1], various clinical features of multiple myeloma were found and these included bone pain due to lytic lesions in 58 % of cases, renal injury due to deposition of light chains with a bland urinalysis in 48 % of cases but sometimes it can give the picture of nephrotic syndrome when there is concurrent presence of immunoglobulin light chain amyloidosis, anemia in 73 % of cases, hypercalcemia in 28 %, fatigue in 32 % of cases and weight loss in 24 % of cases. These findings were also associated with increased levels of total serum protein and presence of monoclonal proteins in serum or blood which were found in 97 % of cases [1]. Serum protein electrophoresis (SPEP) can be done to identify the presence of monoclonal protein (M protein) followed by serum immunofixation (IFX) to identify the type of monoclonal immunoglobulin. According to the same study mentioned above, IgG was found in 52 % of cases, IgA in 21 %, kappa or lambda light chain in 16 %, bi-clonal in 2 %, IgD in 2 %, IgM 0.5 % of cases and 6.5 % of the cases were found to have non secretory myeloma [1]. IgD myeloma is very rare and we present a case in which a patient with a compression fracture was eventually diagnosed with IgD myeloma.

Case Report

A 50 year old female with past medical history of stage 1 T1bN0M0 non-small cell lung cancer of right upper lobe status post right sided upper lobectomy and pulmonary embolism on Coumadin

presented to oncology outpatient clinic for routine follow up visit because history of lung cancer. The patient underwent CT scan of chest for surveillance of lung cancer and it showed a new anterior wedge compression deformity of the body of T8 vertebrae (Figure1 and 2). The patient also underwent MRI thoracic spine which showed wedge-shaped compression deformity involving body of T8 vertebrae along the superior end plate with decreased signal on T1 consistent with subacute compression fracture and increased signal on T2 images consistent with subacute compression fracture (Figure 3 and 4). The patient underwent kyphoplasty of T8 vertebrae and in order to rule out any metastasis, the patient's neurosurgeon took biopsy of the T8 vertebrae which came back positive for kappa plasmacytoma. Bone marrow spicules in vertebra biopsy were stained with both kappa and lambda (Figure 5 and 6). Inorder to rule out multiple myeloma, serum and urine electrophoresis, serum and urine immunofixation, IgG, IgA, IgM, free light chains and skeletal survey were done. Serum protein electrophoresis showed M protein levels of 0.2 g/L. Urine protein electrophoresis showed that M protein was present and a modest amount of albumin with prominent alpha-2 and beta microglobulin bands which were consistent with tubular proteinuria. Urine immunofixation showed a free Kappa monoclonal (Bence Jones) protein in the urine. IgM levels <5 mg/dl, IgA < 23 mg/dl and IgG 313 mg/dl, free kappa light chain 316 mg/dl, free lambda light chain 0.86 mg/dl and kappa/lambda ratio 367.44. Twenty-four hours urine protein showed total protein at2627mg and monoclonal free kappa light chains at 1842mg. The skeletal survey showed small lytic lesions in the skull and right humerus, consistent with multiple myeloma. Because of abnormal levels of kappa light chains, small spike in M protein and decreased IgA, IgM and IgG levels, serum levels of IgD and IgE were checked. The patient's IgD levels came back elevated at 4700 mg/dL and IgE levels were 6.1 IU/mL. Bone marrow biopsy from iliac crest was also done and it showed that overall bone marrow cellularity was 40% composed of CD138 positive plasma cells occupying 25% of the marrow space in an interstitial and aggregated infiltrate (Figure7, 8 and 9). Serum immunofixation showed the presence of an IgD kappa monoclonal protein. The patient was diagnosed with IgD myeloma and started chemotherapy with lenalidomide, bortezomib and dexamethasone. After 40 days of starting of chemotherapy, patient's IgD levels decreased to 58 mg/L, free kappa light chain decreased to 3.55 mg/dL, free lambda left chain was 3.14 mg/dL and kappa/lambda ratio decreased to 1.13 and there was no detectable M protein. After 60 days of starting of chemotherapy, IgD levels decreased to 9 mg/L, kappa light chain decreased to 1.35 mg/dL, kappa to lambda ratio decreased to 0.82 and M protein was undetectable. The patient underwent four cycles of chemotherapy and as she was not a candidate for bone marrow transplant because of lung cancer, chronic obstructive pulmonary disease and current smoking, it was decided to start the patient on maintenance therapy of lenalidomide.

Discussion

IgD myeloma is a rare disease and is known to originate from B cells due to hypermutation of IgV regions [2]. Physiologically, IgD immunoglobulin has a serum concentration of only 0-10 mg/dL [3], thus in cases of IgD myeloma, there may only be a small spike in M protein on immunoelectrophoresis. Because of this, there could be diagnostic errors and delay in diagnosis. Most of the patients with IgD myeloma present with an advanced disease (Durie-Salmom stage 3) and extramedullary manifestation. So, patients with only free monoclonal light chain immunoglobulin should be screened for IgD myeloma [3]. IgD myeloma is more commonly found in males, with median age range of 52 years to 60 years at onset and usually presents as extramedullary disease, osteolytic lesions, systemic amyloidosis, anemia,

hypercalcemia, Bence Jones proteinuria oracute renal failure [4-7]. In various case studies, hemoglobin level was found to be less than <10 g/dL, calcium levels >11 mg/dL in 22% to 30% of cases, creatinine levels > 2 mg/dL in 33% to 54% of cases and lambda light chains were elevated when compared to kappa light chains and this could be due to inhibition of IgD kappa chains or rapid intracellular catabolism before IgD kappa chains are secreted in the system [4-7,12,14,16]. In another study, 53 patients with IgD myeloma were studied and it showed 19% of patients had extramedullary manifestation as an initial presentation which included hepatomegaly, lymphadenopathy and splenomegaly, 19% had systemic amyloidosis and 15% of patients had developed extramedullary manifestation later in the course of their disease [4]. Various factors, such as systemic amyloidosis, identification of t (11; 14), del (13) and other cytogenetic abnormalities are associated with poor outcome of the disease and shorter overall survival [4, 8, 9]. In an advanced disease, IgD myeloma may also present as plasma cell leukemia or soft tissue plasmacytoma due to spread of plasma cells into peripheral blood and this is associated with poor prognosis [10,19]. Also, the patients can have elevated serum lactate hydrogenase levels, beta-2 microglobulin and C reactive protein levels, which account for increase in proliferation of tumors and are associated with poor prognosis [11,19]. Various methods other than immunofixation have been described to diagnose IgD myeloma, including Ouchterlony immunoassay [17]. IgD myeloma has a poor overall survival rate, but with the use of newer agents such as thalidomide, lenalidomide, bortezomib and autologous stem cell transplantation, the survival rate has improved, although the overall survival rate is still poor when compared to other subtypes of multiple myeloma, such as IgA, IgG and light chain multiple myeloma [4-7,12,13]. In one study, the median overall survival in patients with IgD myeloma was found to be only 18.5 months when compared with 50.1 months in other myeloma patients [18]. In another study, patients with IgD myeloma who were offered autologous stem cell transplantation after chemotherapy showed progression free survival of 79% at 1 year and 38% at 3 years and the overall survival was 87% at 1 year and 69% at 3 years [7]. In a more recent study, among 34 patients (45%) treated with autologous stem cell transplantation after they received induction therapy had a median overall survival of 30 months (95% CI 17.7-42.3 months) which was significantly longer than that of patients treated with conventional chemotherapy only (16.4 months, P = 0.012) [17]. Recently, a free light chain escape has been described as a unique phenomenon in patients with IgD myeloma with overall survival of only three months in one of the case reports [20]. It is mostly common in patients with IgD myeloma who have clonal heterogeneity [20]. It is found in patients who initially present with intact monoclonal immunoglobulin which can be isolated or associated with free light chains and they relapse after treatment, which is characterized by increased production of free light chain with a stable, missing or decreased intact immunoglobulin [23]. Thus, free light chain levels should be monitored regularly in patients with multiple myeloma and this includes patients who do not have free light chain disease at the time of diagnosis of IgD myeloma because 11% of free light chain escape occurs in patients with intact immunoglobulin and without free light chain disease at the time of diagnosis [21]. Free light chain assay is the diagnostic test of choice to monitor free light chain levels and is more sensitive and reliable when compared to electrophoresis and immunofixation [22]. In our case, the patient presented with kappa IgD myeloma instead of lambda IgD myeloma which is more common but she had excellent response to chemotherapy and thus she has IgD myeloma associated with an extensive production of free light chain.

Figures

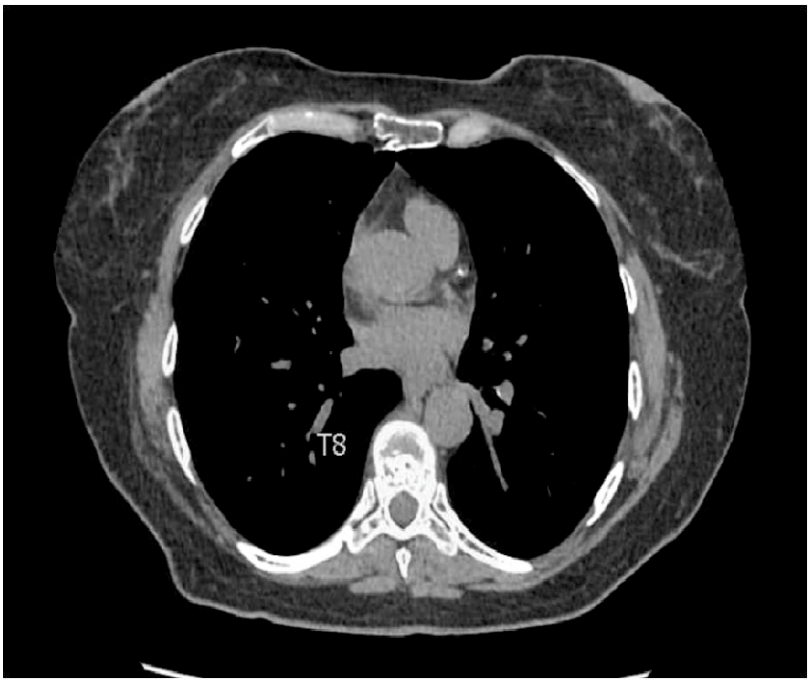

Figure 1: CT chest without contrast showing anterior wedge compression deformity of the body of T8.

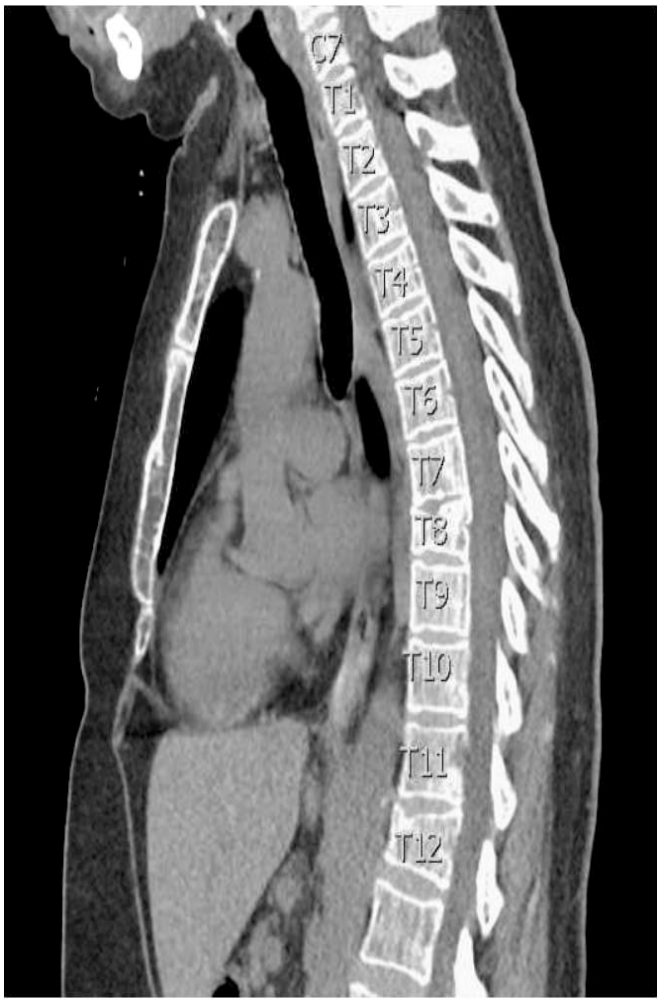

Figure 2: CT chest without contrast (sagittal view) showing anterior wedge compression deformity of the body of T8.

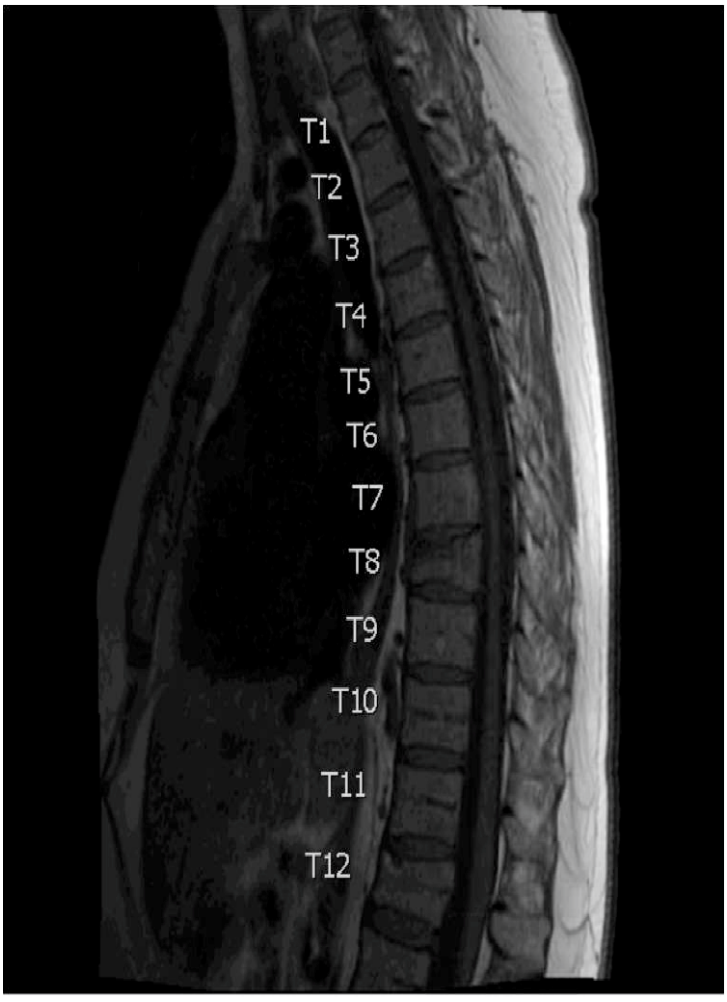

Figure 3: MRI thoracic spine showing mild wedge-shaped compression deformity involving body of T8 vertebrae along the superior endplate with decreased signal on T1 consistent with subacute compression fracture.

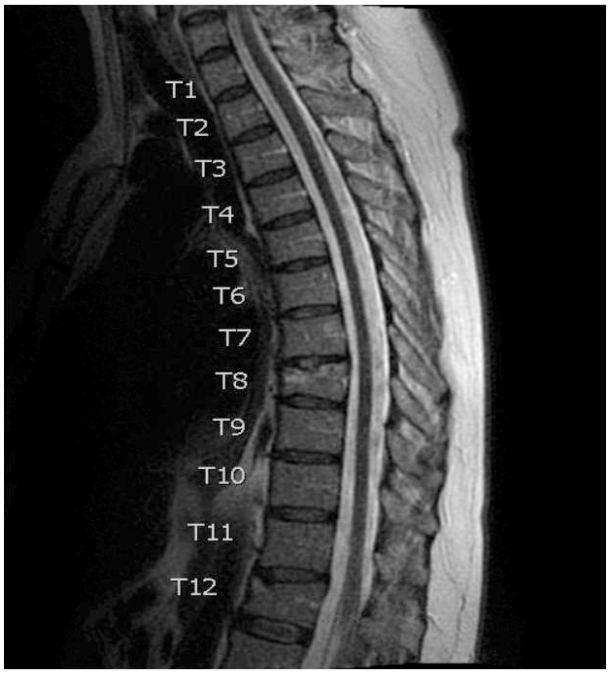

Figure 4: RI thoracic spine showing mild wedge-shaped compression deformity involving body of T8 along the superior end plate with increased signal on T2 images consistent with subacute compression fracture.

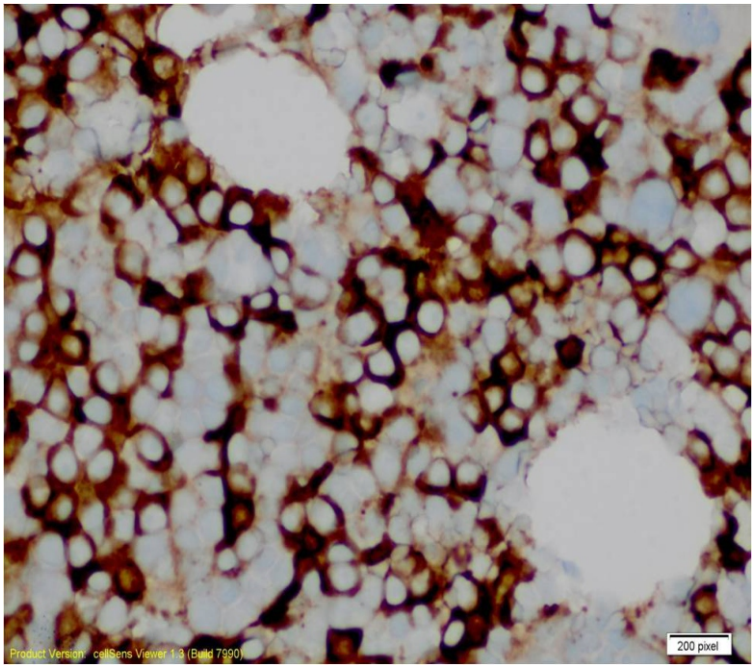

Figure 5: 400x immunohistochemical staining of bone marrow spicules in vertebra biopsy with kappa.

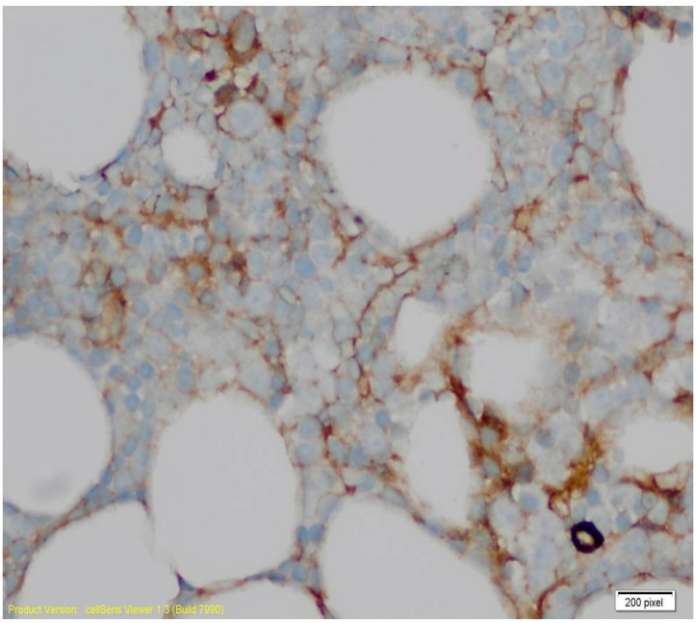

Figure 6: 400x immunohistochemical staining of bone marrow spicules in vertebra biopsy with lambda.

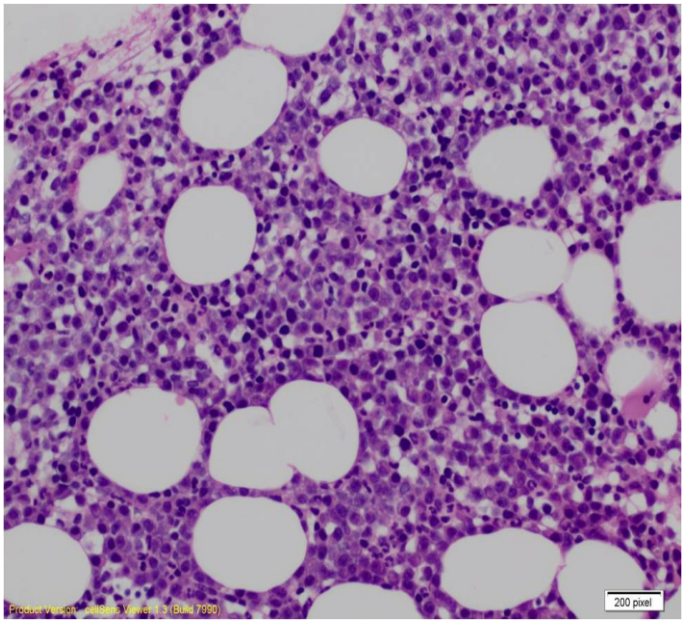

Figure 7: 200x magnification Hematoxylin and Eosin stain of bone marrow biopsy from iliac crest showing bone marrow cellularity was 40%.

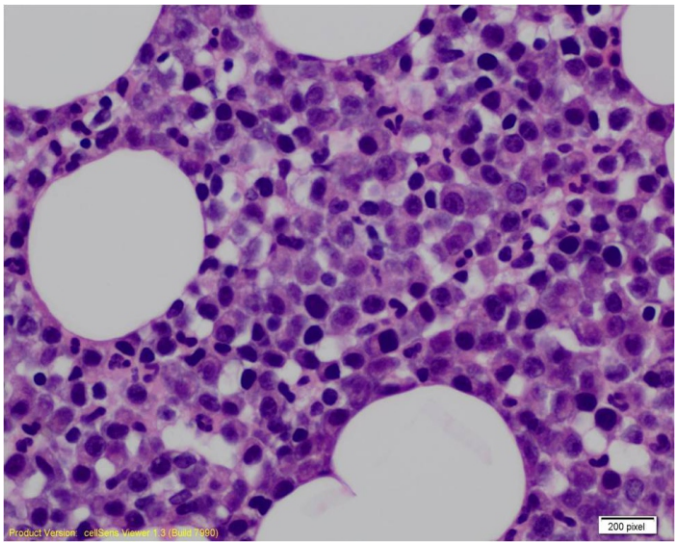

Figure 8: 400x magnification Hematoxylin and Eosin stain of bone marrow biopsy from iliac crest showing bone marrow cellularity was 40%.

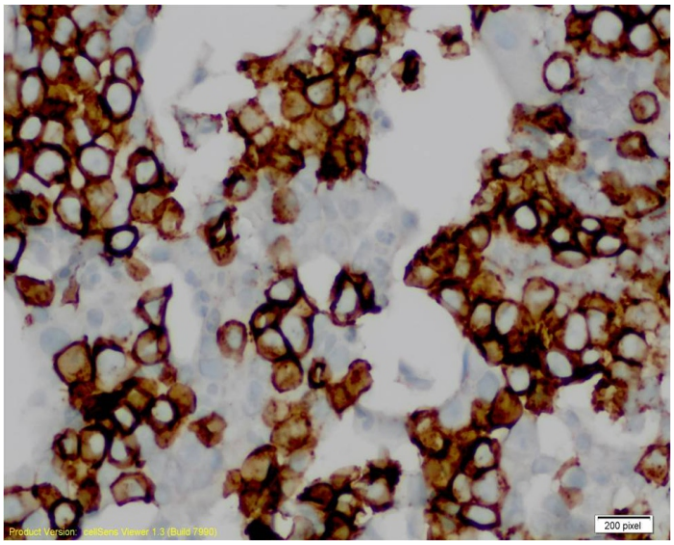

Figure 9: Bone marrow biopsy from iliac crest showing CD138 positive plasma cells occupying 25% of the marrow space in an interstitial and aggregated infiltrate.

Conclusion

IgD myeloma is a rare and an aggressive disease with the median survival of less than 2 years, but the survival is improved with the use of new novel agents and autologous stem cell transplantation. The cure of IgD myeloma is rare and so far only one patient with IgD multiple myeloma was considered to have been cured and was found to be disease free after 21 years of treatment [15]. A very high level of suspicion is required to diagnose IgD myeloma and it should be considered in patients with normal and decreased levels of IgG, IgM and IgA and in the presence of free light chain monoclonal gammopathy. Early recognition can help in preventing the spread of disease and thus can improve overall survival. Our patient had a good response to medical therapy and she will be maintained on maintenance therapy of lenalidomide.

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