Bortezomib Based Chemotherapy for Light Chain Deposition Disease

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Abstract

Light chain deposition disease (LCDD) is a rare systemic disorder in which monoclonal light chains are abnormally secreted due to clonal proliferation of plasma cells and get deposited in various organs; the kidneys being the common one to be affected leading to renal failure. Advocated therapeutic options include chemotherapy with alkylating agents and steroids, High-Dose Melphalan (HDM) with Autologous Stem Cell Transplantation. Recently, Bortezomib has proven to be a novel therapeutic option in these patients when combined with dexamethasone. Here, we report a patient who presented with acute renal failure, was diagnosed to have LCDD and treated with bortezomib and dexamethasone.

Introduction

Monoclonal Immunoglobulin Deposition Disease (MIDD) is a rare systemic disorder in which monoclonal light and/or heavy chains are deposited in various organs due to clonal proliferation of plasma cells which secrete them. MIDD usually affects the kidneys but involvement of heart, liver, duodenum, brain, cervical lymph nodes, pharynx and peripheral nerves has been reported. Patients present with symptoms based on the site involved. There are three types of MIDD depending on the type of monoclonal immunoglobulins deposited. They are Light Chain Deposition Disease (LCDD) which is the most common one, heavy chain deposition disease, and light and heavy chain deposition disease.¹ The characteristic feature of LCDD is the presence of Periodic Acid-Schiff (PAS) positive, non-Congophilic material seen at the site involved. Here, we describe a patient with LCDD who was treated with bortezomib and dexamethasone.

Case Presentation

A 65-year-old hypertensive female patient, came with complaints of reduced urine output, swelling of both lower limbs, abdominal distension and facial puffiness for 2 days. She was found to have serum creatinine of 1.42 mg/dL, nephrotic range proteinuria and a normal hemogram except for an Erythrocyte Sedimentation Rate (ESR) of 67 mm/hour. Following a renal biopsy, a total of 12 glomeruli were examined under light microscopy (LM) and immunofluorescence microscopy (IM) showing features suggestive of membranous nephropathy with equal staining of glomeruli by kappa and lambda light chains and granular positivity along the capillary walls for IgG (+3) and C3 (+1). Subsequently, her laboratory work up showed blood urea nitrogen 40 mg/dL, serum creatinine 1.61 mg/dL, serum total proteins 3.84 g/dl, serum albumin 2.2 g/dl, serum globulin 3.0 g/dl, spot urine protein creatinine ratio 21.38. Patient was negative for Human Immunodeficiency Virus (HIV) 1 and 2, Hepatitis B surface antigen (HBsAg) and Hepatitis C virus (HCV). Anti-nuclear antibody (ANA) profile and ANA by indirect immunofluorescence was negative. Serum protein electrophoresis pattern indicated significant elevation of alpha-2 globulin and absence of monoclonal band and the serum quantitative immunofixation is shown in the Table 1.

Discussion

MIDD is a rare occurrence affecting middle-aged and elderly patients ranging from 35-76 years with a mean of 56 years. It usually affects men 2.5 times more often than women.² The pathogenesis of LCDD is not yet fully elucidated. However, stimulation of the NFKB signaling pathway of the mesangial cells by the accumulated Light Chains (LCs) results in increased production of transforming growth factor-beta which in turn inhibits degradation of the extracellular matrix (ECM) by decreasing the levels of collagenase and proteinases and promotes the synthesis of collagen.
VI, laminin, fibronectin, tenascin all of which are deposited in the ECM leading to fibrosis and loss of function eventually. Renal involvement is usually a universal finding in MIDD and takes the form of renal insufficiency, microscopic or gross hematuria and non-selective proteinuria. If untreated, the median time taken to progress to end stage renal disease was 2.7 years, and patient survival was 66% at 1 year and 31% at 8 years. The characteristic feature of LCDD on renal biopsy is nodular sclerosing glomerulopathy with variable thickening of the glomerular basement membranes, tubular basement membranes (TBMs), and vascular basement membranes with brightly eosinophilic and strongly PAS positive material which does not stain with Congo Red or Silver stain differentiating it from amyloidosis (Congo Red positive) and diabetic nephropathy (Silver stain positive) respectively and linear deposits of monoclonal light chains along TBMs by immunofluorescence. Hence, immunofixation of serum and/or urine for free light chains along with biopsy of the involved organ showing the characteristic features under LM and IM will help arriving at the diagnosis of LCDD. In our case, the characteristic feature was present on the bone marrow biopsy rather than the renal biopsy probably because of relatively lower levels of free kappa light chains in serum. Advocated therapeutic options include chemotherapy with alkylating agents and steroids, High-Dose Melphalan (HDM) with Autologous Stem Cell Transplantation (ASCT). Recently, Bortezomib, a reversible 26S proteasome inhibitor which acts by down regulation of Transforming Growth Factor-beta through inhibiting the NFkB signaling pathway has proven to be a novel therapeutic option in patients with LCDD when combined with dexamethasone. Trovar et al reported a case series with three patients who were treated for LCDD with Bortezomib/ Dexamethasone as induction treatment followed by HDM and ASCT showing a hematologic complete response in two patients and a very good partial response in the third patient. In patients with benign course who have ended up with ESRD requiring regular maintenance dialysis, it is recommended to achieve a sustained remission before considering renal transplantation. Kaposzta et al demonstrated the efficacy of Bortezomib to treat early recurrence of LCDD in post renal transplant patients without the loss of graft. Bortezomib treatment for LCDD seems to be efficacious but continued follow up for relapse seems warranted as in this patient.

References