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A NOVEL APPROACH IN THE MANAGEMENT OF GASTROINTESTINAL AMYLOIDOSIS: A CASE REPORT

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ABSTRACT

Primary amyloidosis is an abnormal deposition of non-branching fibrils extracellularly leading to organ dysfunction. AL amyloidosis primarily affects the heart, kidney and gastrointestinal (GI) system. But amyloid deposition in the GI tract presenting with symptoms is a rare scenario. In this case we present a 58 year old female came with the chief complaints of vomiting, poor appetite and weight loss . After appropriate evaluation of clinical and histological findings she was diagnosed with AL amyloidosis with GI involvement. She underwent a novel chemotherapy regimen for which she responded well. In conclusion even though amyloidosis is an incurable complex disease, early diagnosis and treatment is obligatory to prevent the exacerbation of the disease.

INTRODUCTION

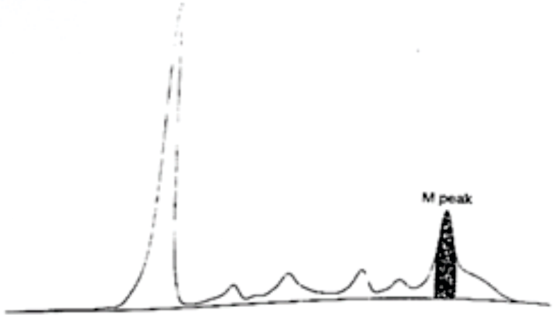
Amyloidosis is a heterogeneous disease and it is caused by the accumulation of toxic, insoluble beta-sheet fibrillar protein aggregates in various tissues.[1] Amyloidosis may be inherited or acquired. The illness may be systemic or localized.[2] The most common types are AL, AA, ATTR (amyloid transport protein transthyretin), and dialysis-related amyloidosis. Primary Amyloidosis is associated with the deposition of immunoglobulin light chain (AL) proteins. It is often associated with plasma cell disorders, such as multiple myeloma. The prevalence rate of primary amyloidosis is thought to be higher, with estimates ranging from 10 to 15 cases per million people.[3] Primary amyloidosis can affect individuals of all ages, but it is more commonly diagnosed in older adults, typically over the age of 60. There may be a slight male predominance, with more men being affected than women. This disease can lead to wide range of symptoms and complications, depending on which organs are involved, and it can result in cardiac failure and renal dysfunction.

CASE STUDY

A 58-year-old female came to the hospital weighing 50.7 kg and height of 152 cm with the chief complaints of nausea, vomiting and dry cough. She had a history of poor appetite History of loss of weight. Routine physicals showed normal vital signs. Evaluation of Upper GI endoscopy and colonoscopy showed amyloid deposits positive. Biopsy from duodenum colon showed Amyloidosis. Bone Marrow biopsy and aspiration suggestive of Primary amyloidosis with or without overt myeloma & Plasma 15%. Serum protein electrophoresis reveals M-peak 0.85 g/dl. Seen by medical oncologist, she has been planned with chemotherapy (CyBorD regimen). Benefits and side effects of treatment were explained to patient and attender in detail. The patient was then admitted for cycle 1 day 1 chemotherapy after adequate pre-medications were given as Inj. CYCLOPHOSPHAMIDE 500 mg iv INFUSION and INJ BORTEZOMIB 1.8 gm subcutaneous. She tolerated the treatment well.

LabValues

Immunofixation - Quantitative Serum		
Parameters	Result	Reference range
Immunoglobulin A, IgA - Serum	112.7 mg/dl	70-400
Immunoglobulin G, IgG - Serum	1,447.7 mg/dl	700-1600
Immunoglobulin M, IgM - Serum	94.2 mg/dl	40-230
Kappa Light Chain Free - Serum	14.5 mg/dl	3.3-19.4
lambda Chain Free	14.5 mg/dl	5.71-26.3
kappa/lambda Ratio	0.1	0.26-1.65
Beta 2 Micro globulin - Serum	1954.00 ng/dl	607-229
Protein Electrophoresis -Serum		
Albumin	3.73 g/dl	3.90-5.10
Alpha 1	0.31 g/dl	0.20-0.40
Alpha 2	0.66 g/dl	0.46-1.38
Beta 1	0.35 g/dl	0.14-0.40
Beta 2	0.26 g/dl	0.16-0.49
Gamma	1.59 g/dl	0.74-1.74
M - Peak	0.85 g/dl	



Interpretation: A sharp M peak value of 0.85 g/dl is indicative of Monoclonal gammopathy

Histopathological Investigation:
Bone Marrow Aspiration: plasma cell constitutes 11.2%

Bone Marrow Trephine Biopsy: gastrointestinal/ systemic

amyloidosis with bone marrow plasma cells of 15%

Other Investigations:
Gastric Biopsy:
Benign hyperplastic polyp.
Duodenum Biopsy:
Consistent with benign submucosal lipoma.
Sigmoid and Ascending Colon Biopsy:
Tubular adenomatous polyp with low grade dysplasia. No evidence of high grade dysplasia / invasion.

Perivascular pale amorphous eosinophil deposits which are congophilic and show a green birefringence under polarizer noted in gastric, duodenal and colonic biopsy consistent with gastrointestinal amyloidosis.

Final Diagnosis:
Primary amyloidosis with or without overt myeloma, involving gastrointestinal with Bone marrow plasma cells of 15%.

Treatment
Treatment of primary amyloidosis involves chemotherapy; it involves reduction of the amyloidogenic light chains accumulation on the damaged amyloidotic organs. By targeting the underlying clonal plasma cell dyscrasia that causes primary amyloidosis. The standard chemotherapy regimen involves the use of Cyclophosphamide– thalidomide–dexamethasone, which showed 74% (21% complete response & 27% organ response) in a Randomized control trial (RCT) that included 75 patients.[4] Novel chemotherapy combinations include Cyclophosphamide– bort-ezomib-dexamethasone (CyBorD) regimen, this showed about 81% response (65% complete response and 46% organ response).[4] Here, the patient was given (CyBorD)regimen that constitute TAB CYCLOPHOSPHAMIDE 50 mg OD, INJ BORTEZOMIB (s/c) 1.8 gm on days 1, 4, 8,11 and TAB DEXA 4 mg TID, the plan was to complete cycle 1 day 8 chemotherapy. Other adjuvant medications include TAB EMESET 4mg 1-0-1x 3 days TAB PAN 40mg 1-0-1x 3 DAYS TAB GANATON 50MG 1-0-1 daily.

Outcome & Followup
After completing cycle 1 day 6 chemotherapy, the patient showed good clinical response with no specific complaints has gained roughly 2 kgs and was decided to undergo two more cycles of chemotherapy. But this time Inj.Bortezomib was replaced with Inj.Myzomib 2 mg (s/c) on days 1,8,4,11.

DISCUSSION
Amyloidosis are a rare group of diseases that result from extracellular deposition of amyloid, a fibrillar material derived from various precursor proteins that self-assemble with highly ordered abnormal cross β-sheet conformation. More than 30 proteins have been identified to form amyloid in human but recent use of mass spectrometry to identify amyloid suggests that many more proteins might be amyloidogenic [4]. In AL amyloidosis there is immoderate production of monoclonal immunoglobulin (Ig) light chain which are deposited in multiple organs such as kidney, heart and the gastrointestinal tract [6]. A study reported that in AL amyloidosis the peptides of the proteins represent the N-terminal of the variable region of the kappa or lambda Ig light chains. The amyloid fibrils are non-branching and shows a twisted, antiparallel β-pleated sheet configuration which renders them resistant to proteolytic digestion resulting in amyloid accumulation [5]. In the GI tract the amyloids are mainly deposited in the muscularis mucosae which increases the frailty of blood vessels, decreases the compliance of gut wall, restricts the intrinsic peristalsis, these factors together contribute to the symptoms observed in gastrointestinal (GI) amyloidosis [7]. The clinical manifestations include nausea, vomiting, abdominal pain, diarrhea and weight loss. The symptoms the patient presented were found to be relevant to GI amyloidosis.

The diagnosis of amyloidosis relies on clinical, laboratory and histological findings. For the diagnosis of amyloidosis presence of monoclonal gammopathy with urine and serum electrophoresis and measurements of kappa (k) and lambda (λ) light chain levels are the initial laboratory tests but for confirmation histological findings are necessary. This is because tissue biopsy with Congo red stain showing green birefringence under polarized light is considered the golden standard for amyloidosis diagnosis [5,6,7]. Here in this patient green birefringence under polarizer was noted in gastric, duodenal and colonic biopsy conforming the diagnosis of gastrointestinal amyloidosis and was managed with novel chemotherapy combination CyBorD regimen, which has a median progression free survival (at 2 years) by 53% and an overall survival (at 2 years) by 98%.[4]

CONCLUSION
Overall, Amyloidosis is a complex disease affecting multiple organs with varying symptoms. Here, we report a rare case of primary amyloidosis with or without overt myeloma, involving gastrointestinal system and symptoms related to it. Early suspicion and management with appropriate chemotherapy regimen is important for improving the prognosis and better life time survival of the patient. Thus, timely diagnosis enables treatable amyloidosis and promising rapid organ recovery.

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