

Received: 2017.09.09  
Accepted: 2017.10.02  
Published: 2017.11.25

# Diffuse Peritoneal and Bowel Wall Infiltration by Light Chain-AL Amyloidosis with Omental Calcification Mimicking Abdominal Carcinomatosis – An Elderly Female with Incidental Finding of Light Chain Monoclonal Gammopathy of Undetermined Significance (LC-MGUS)

Authors' Contribution:  
Study Design A  
Data Collection B  
Statistical Analysis C  
Data Interpretation D  
Manuscript Preparation E  
Literature Search F  
Funds Collection G

ACDEF 1 **Shoaib Junejo**  
ACDEF 2 **Yasir Ali**  
A 1 **Sandeep Singh Lubana**  
AE 1 **Sandeep S. Tuli**

1 Icahn School of Medicine at Mount Sinai-Queens Hospital Center, Jamaica, NY, U.S.A.  
2 Department of Endocrinology, NYC Health and Queens Hospital Center, Jamaica, NY, U.S.A.

**Corresponding Author:** Shoaib Junejo, e-mail: [shoaibjunejo88@gmail.com](mailto:shoaibjunejo88@gmail.com)  
**Conflict of interest:** None declared

**Patient:** Female, 68  
**Final Diagnosis:** Light chain monoclonal gammopathy of undetermined significance  
**Symptoms:** Abdominal pain  
**Medication:** —  
**Clinical Procedure:** —  
**Specialty:** Oncology

**Objective:** Rare co-existence of disease or pathology  
**Background:** Amyloidosis is the extracellular tissue deposition of plasma proteins, which after conformational changes, forms antiparallel beta pleated sheets of fibrils. Amyloid light-chain (AL) is a type of amyloidosis that is due to deposition of proteins derived from immunoglobulin (Ig) light chains. Gastrointestinal tract (GIT) involvement most often found in amyloid A (AA) amyloidosis type. There have been no reports of obstructive GIT AL amyloid patients having monoclonal gammopathy of undetermined significance (MGUS). Our case is the first case to show two coinciding conditions; one is the association of GIT AL amyloidosis with the incidental finding of a rare type of MGUS (LC-MGUS) and the other is the radiologic presentation of GIT amyloidosis with omental calcification mimicking the GIT malignancy.

**Case Report:** A 68-year-old female presented with symptoms of partial bowel obstruction, including intermittent diffuse abdominal pain and constipation. After computed tomography (CT) abdomen and pelvis, an exploratory laparotomy was needed because of suspicion of abdominal carcinomatosis due to diffuse omental calcification. The tissue sent for biopsy surprisingly showed AL amyloidosis. The patient did not report any systemic symptoms. Further workup was advised to inquire about the plasma cell dyscrasia which eventually turned into a very rare version of MGUS known as light chain MGUS (LC-MGUS). Following adequate resection of the involved structures, the patient was then placed on chemotherapy and successfully went into remission.

**Conclusions:** This case report illustrates that in an era of evidence based medicine, it is important to show through case reports the association of GIT AL amyloidosis with LC-MGUS, as the literature on this topic is lacking. It also points to the importance of timely intervention that can greatly enhance, not only the chances of remission but also prevention of further complications such as malignant transformation.

**MeSH Keywords:** Amyloidosis • Gastrointestinal Neoplasms • Immunoglobulin Light Chains • Monoclonal Gammopathy of Undetermined Significance

Full-text PDF: <https://www.amjcaserep.com/abstract/index/idArt/907041>



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## Background

Amyloid light-chain (AL) amyloidosis is caused by the neoplastic proliferation of plasma cells thus it is the only type of amyloidosis that warrants chemotherapy. It is a very rare disorder only 6 to 10.5 cases per million reported in annually in the USA [1]. The presentation of AL amyloidosis depends on the system affected, duration, and amount of amyloid deposited. One comparative study of 423 diagnosed cases of systemic amyloidosis showed no differences in the diagnostic sensitivity of immunoelectron microscopy (IEM) and Congo red staining (75%80%) but the specificity of IEM appears significantly higher (100% versus 80%) [2]. Overall, amyloidosis less commonly involves the gastrointestinal tract (GIT) and it rarely becomes symptomatic. Generally, amyloid A (AA) amyloidosis presents with malabsorption and GI bleed while AL amyloidosis manifests with symptoms of mechanical obstruction [3]. Results of one study of 769 patients with primary systemic AL amyloidosis conducted at the Mayo clinic over a period of 12 years showed only one patient (0.13%) presented with obstructive symptoms of GIT and for that patient they were unable to prove an association with monoclonal gammopathy of undetermined significance (MGUS) [4]. The most common plasma cell proliferative disorder is MGUS [5]. There is a positive linear correlation between MGUS prevalence and age of the patient [6–8]. Studies also report increasing incidence of MGUS, and the overall age-related prevalence of MGUS overtime. Results of one large study published in 2002, showed that MGUS was the diagnosis of 2% of patients with ages  $\geq 50$  years and 3% with ages  $\geq 70$  [6]. Two more large studies published in 2007 and 2010 report a significant rise in this number with 3.2% in patients age  $\geq 50$  versus 5.3% with age  $\geq 70$  years and approximately 9% in patients 85 years or older [7,8]. The conventional MGUS is a pre-malignant asymptomatic disorder which progresses with a rate of around 1% per year, to a relevant malignant disorders including AL amyloidosis, multiple myeloma (MM) or Waldenstrom macroglobulinemia [6–8]. Contrary to conventional MGUS, the prevalence and rate of malignant progression of light chain-MGUS (LC-MGUS) are significantly lower with only 0.8% of patients age  $\geq 50$  years and 0.3% per year, respectively [9].

## Case Report

A 68-year-old female patient presented with recurrent episodes of vomiting, diffuse abdominal pain, and constipation. At presentation, her body temperature was 99.3°F (37.4°C), blood pressure 127/88 mm Hg, heart rate was regular at 96 beats/minute and respiratory rate 18 breaths/minute. Physical examination was significant with an ill-looking older female with diffuse abdominal tenderness, guarding, and rigidity. The bowel sounds were audible but sluggish and no organomegaly appreciated; the rest of the examination was within the normal

limits. The patient was admitted with the initial impression of bowel obstruction. Urgent computed tomography (CT) abdomen and pelvis with oral and IV contrast revealed multiple, diffuse, nodular, ill-defined infiltrating masses with innumerable calcifications in greater omentum filling the peritoneal cavity (Figure 1A–1C). Infiltrative involvement of the mesentery of small bowel and the transverse and sigmoid colon was also seen. These findings were suggestive of calcified peritoneal carcinomatosis due to some primary GI malignancy and small bowel obstruction.

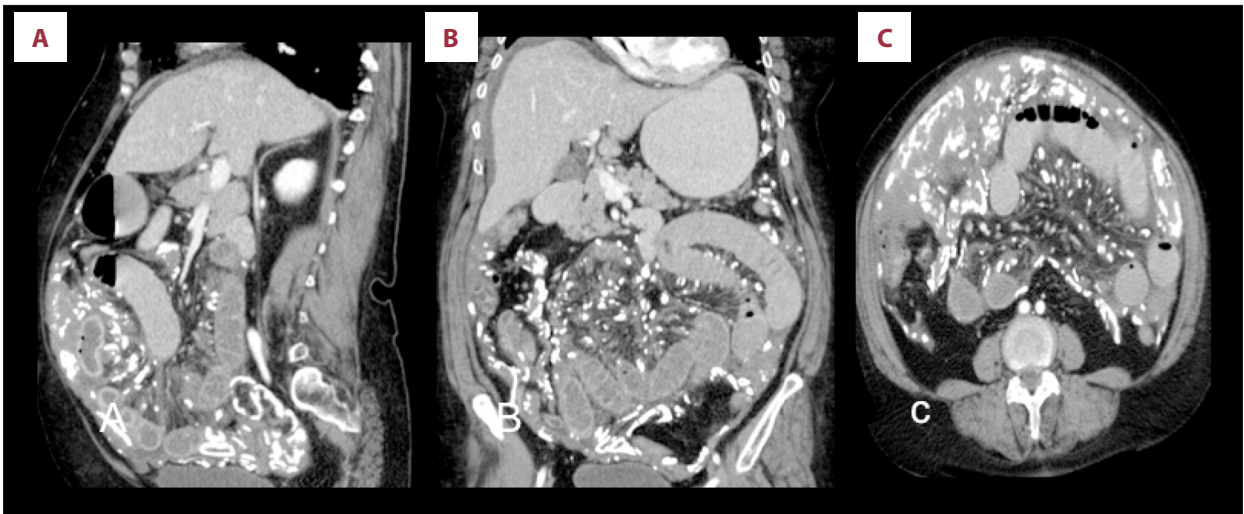
Initial blood workup was done and the patient underwent an immediate exploratory laparotomy that was found to have a large omental cake consisting of multiple solid firm masses. Omenectomy was done along with the resection of the small bowel and a bypass to the transverse colon was performed. The postoperative period remained clinically insignificant and the patient was discharged with further follow-up.

Frozen sections of the omental masses and terminal ileum showed fat necrosis only and surprisingly, no evidence of malignancy was found. Permanent sections sent for additional stains with Congo red revealed marked amyloid deposition in the omentum and mesentery. Immunohistochemical typing followed and the fibrils of light chain-AL amyloid were identified. Subsequently, serum protein electrophoresis (SPEP) with immunofixation was done, followed by the serum free light chain (FLC) assay and the results were consistent with the presence of monoclonal protein (M-protein) without the expression of immunoglobulin (Ig) heavy chain. Additionally, the lambda subset was significantly higher than the kappa and the resultant FLC ratio appeared lower (normal=0.26–1.65). Finally, bone marrow biopsy showed CD 138+ plasma cells comprising only 3% of the overall cellularity.

Upon further inquiry on follow-up visits, the patient reported no systemic symptoms and the results of hemoglobin, serum calcium, and creatinine were within normal limits, both on initial and follow-up labs, and within age-appropriate readings. A thorough skeletal survey was devoid of any bone lesion. Based on the clinical and laboratory findings aforementioned, the diagnosis was consistent with (LC-MGUS). Since the patient was a poor candidate for bone marrow transplant, a bortezomib-based regimen, such as CyBORd (cyclophosphamide-bortezomib-dexamethasone) therapy, was recommended. The patient went into remission as determined by follow-ups at regular intervals.

## Discussion

Amyloidosis, *per se*, is a multisystem disorder with biopsy-proven GIT disease accounting for only 3.2% of cases, out of



**Figure 1.** (A–C) Computed tomography (CT) of the abdomen and pelvis with oral and intravenous contrast revealed a diffuse, nodular, ill-defined infiltrating mass with innumerable calcifications in the greater omentum filling the peritoneal cavity, suggesting peritoneal carcinomatosis.

which 80% presents as a spectrum of systemic amyloidosis with evidence of involvement of other organ(s) [10]. GIT disease is more common in AA than AL amyloidosis [11]. One small study showed the duodenum (100%) and stomach (95%) were almost always involved in the GI amyloidosis, reflecting the significance of upper GI endoscopy and biopsy in suspected cases [12]. The clinical presentation and endoscopic findings depend on the pattern of infiltration, which in turn, depends on the chemical nature of amyloid protein deposits. In AA amyloidosis, the pattern is fine granular deposition spreading widely across the GIT and causing mucosal friability and ulceration that presents mainly with bleeding and symptoms of malabsorption and only less commonly with obstruction [11,12]. Whereas, in AL amyloidosis, the deposits heavily penetrate the mucosa, extend across the submucosa to fill the muscularis layer and thereby causing the formation of multiple finger-like polypoidal projections that obstruct lumen of the bowel [11,12]. Generally, the obstructive symptoms are self-limiting in AA amyloidosis and almost always respond to the medical treatment such as total parenteral nutrition but, with AL amyloidosis, the intestinal obstruction presents as chronic intermittent entity that very often needs surgical intervention [13]. The biopsied section of suspected amyloid deposits can be confirmed by direct electron microscopy to visualize the typical appearance and the ability to bind Congo red or thioflavine-T staining.

CT findings for GIT amyloidosis are non-specific, ranging from the normal bowel (most common) to the wall thickening and/or dilation, mesenteric infiltration, and rarely mesenteric adenopathy [14,15]. Amyloidoma of the GIT is a very rare condition caused by the patchy accumulation of amyloid deposits, and presents with obstructive symptoms and gives the

impression of abdominal carcinomatosis on CT scan [15]. No case of obstructive AL amyloid GI disease associated with MGUS has been reported in literature until now. Our case uniquely shows this association.

By definition, MGUS is an asymptomatic pre-malignant disorder with serum monoclonal protein (M-protein) <3 g/dL, clonal bone marrow plasma cells <10% and notably no evidence of end organ damage including hypercalcemia, renal insufficiency, anemia, or lytic bone lesions (CRAB features) [7,8,16]. Conventional MGUS includes IgM and non-IgM types, whereas the LC-MGUS is the new, unique entity. Rajkumar et al. published a large study conducted by the International Myeloma Working Group (IMWG) in 2014 [16], which clearly updates the diagnostic criteria for LC-MGUS: 1) abnormal free light chain (FLC) ratio (<0.26 or >1.65); 2) increased level of the appropriate involved light chain (increased kappa- $\kappa$  gives ratio >1.65 and increased lambda- $\lambda$  gives ratio <0.26); 3) no expression of immunoglobulin heavy chain; 4) clonal bone marrow plasma cells <10%; 5) absence of features of end organ damage (CRAB); and 6) urinary M-protein <500 mg/day.

Generally, the rate of progression of conventional MGUS to malignant disorder (AL-Amyloidosis, MM, WM) is 1% per year, whereas, that of LC-MGUS is only 0.3% [9,16]. Results of many large studies show evidence of preceding MGUS in patients diagnosed with AL amyloidosis [17] and MM [18]. Essentially, factors which may significantly speed up the malignant progression to make it high risk-MGUS are 1) size of the M-protein ( $\geq 1.5$  g/dL), 2) abnormal FLC ratio, and 3) non-immunoglobulin-G (Ig-G) MGUS [7,8,16,19]. The FLC ratio (kappa-lambda ratio, normal=0.26 to 1.65) is a significant and independent risk factor for MGUS progression [19]. A simplified risk-stratification

model constructed to estimate the malignant progression of MGUS at 20 years is 58% when all three risk factors are found, 37% when any two of the three are found, versus 21% when a single risk factor is identified and only 5% when MGUS is free of all risk factors [19]. As we discussed, because MGUS is an asymptomatic disorder, there is no role for chemotherapy approved. Drugs like lenalidomide and bisphosphonates are under continuous trials as they might halt the progression into malignant disorders. Since AL amyloidosis is one of the plasma cell proliferative disorders, the definitive treatment is hematopoietic cell transplantation (HCT). Patients who are poor surgical candidates are best treated with bortezomib-based regimens such as cyclophosphamide-bortezomib-dexamethasone (CyBorD).

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## Conclusions

This case underscores the significance of the association of LC-MGUS with GIT AL amyloidosis that presents with intestinal obstruction. Physicians should be aware of this possibility so they may efficiently identify the diagnosis after relevant investigations and start appropriate management. Timely intervention is key to treating an acute presentation and to preventing the further malignant possibilities.

## Acknowledgements

Deborah Goss, MLS (Director, Health Sciences Library, Queens Hospital Center) reviewed and edited the manuscript.