# Polypoid multifocal ileo-colonic amyloidoma masquerading malignancy - A rare case report

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## ABSTRACT

Amyloidosis is a group of disorders characterized by extracellular deposition of a proteinaceous homogenous eosinophilic hyaline substance known as amyloid. Congo red staining is a specific stain for amyloid which shows an apple-green birefringence on polarized microscopy. Amyloid deposition can be systemic or localized. Primary amyloidosis (also known as AL amyloidosis) is the most common form of amyloidosis characterized by generalized deposition of excess immunoglobulin light chains. It is associated with an underlying plasma cell dyscrasia and has the maximum gastrointestinal (GI) involvement. Secondary amyloidosis is characterized by deposition of acute-phase reactant - serum amyloid A protein (also known as AA amyloidosis) and it is associated with infectious, inflammatory, or less commonly, neoplastic disorders. Renal dysfunction is the most common symptom of AA amyloidosis at diagnosis. Amyloidosis presenting as a localized mass is known as amyloidoma. Amyloidoma of the GI system is a rare finding in the absence of any systemic involvement. We report a rare case of localized multifocal polypoid amyloidoma in the lower GI tract, which masquerades as malignancy.

**Keywords:** *Amyloidoma, Congo red, Ileo-colonic amyloidosis, Polypoid growth.*

An amyloidosis is a group of disorders characterized by extracellular deposition of a non-branching fibrillary proteinaceous substance, known as amyloid. These proteins appear as homogenous eosinophilic hyaline deposition on hematoxylin and eosin (H&E) stained tissue sections and are confirmed by Congo red staining which gives an apple-green birefringence on polarized microscopy. [1] Amyloid deposition can be systemic or localized; [2] systemic amyloidosis is classified as primary amyloidosis, secondary amyloidosis, familial amyloidosis, hemodialysis-associated amyloidosis, and senile amyloidosis. [3,4] Primary amyloidosis (also known as AL amyloidosis) is the most common form of amyloidosis characterized by generalized deposition of excess immunoglobulin light chains. It is associated with an underlying plasma cell dyscrasia and has the maximum gastrointestinal (GI) involvement. [5] Secondary amyloidosis is characterized by deposition of acute-phase reactant - serum amyloid A protein (also known as AA amyloidosis) and associated with infectious, inflammatory, or less commonly, neoplastic disorders. [3] Renal dysfunction is the most common symptom of AA amyloidosis at diagnosis. [3,6] Although amyloidosis can virtually affect any organ in the GI system, the small intestine is the most frequently affected one. [4] Amyloidosis presenting as a localized mass or amyloidoma of the GI system is a rare finding in the absence of any systemic involvement. [7] We report a rare case of localized multifocal polypoid amyloidoma masquerading malignancy in the lower GI tract.

## CASE REPORT

A 45 years old female was presented with a passage of small volume frequent stools for last three years, associated with lower abdomen pain and recurrent episodes of gastrointestinal bleeding in the form of melena and hematochezia for two years. She complained of intermittent exacerbations in stool frequency for 15-20 times a day, which was mixed with blood and mucus. The associated pain was insidious in onset, colicky in nature, poorly localized and subsided on the intake of oral analgesics. At times, the pain was associated with vomiting. She required hospital admission four times over the last three years, in which she was managed conservatively with packed cell transfusion. There was no history of any fever, jaundice, lump abdomen or any perianal discharge or fistula. There was no history of diabetes mellitus, hypothyroidism, hypertension or contact with tuberculosis. There was no family history of similar illness, either.

On clinical examination, a diffused mass was palpable in the right inguinal fossa. The mass had an ill-defined margin, was firm in consistency, and non-tender. Per rectal examination was normal and other systems were within normal limits. Routine blood examination including a complete hemogram, liver function test, renal function test, and serum electrolytes, were within normal limits, except for mildly reduced hemoglobin level. The occult blood test was positive while the ultrasound imaging of the lower abdomen revealed localized adherent bowel loops with

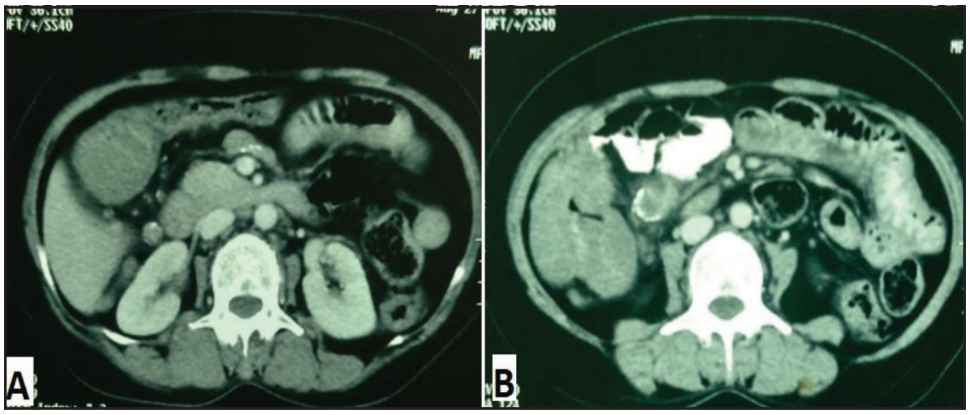


**Figure 1: CT scan of the abdomen showing long segment wall thickening of the right colon with a narrowed lumen (A- without contrast, B- with contrast).**

a mass-like lesion at the right flank, with a clinical impression of intussusception. CT scan of the abdomen showed long segment wall thickening with the narrowed lumen and multifocal nodularity involving terminal ileum, caecum and ascending colon (Fig. 1). The distal colon was collapsed.

Colonoscopy showed multiple areas of mucosal hemorrhage, scattered throughout the entire length in the sigmoid colon, descending colon and transverse colon and the distal part of ascending colon. The proximal part of the ascending colon showed a globular submucosal mass with normal overlying mucosa protruding into the lumen of the ascending colon. The scope could not be passed beyond the mass lesion. Multiple biopsies were taken from the lesion. Histological examination, however, showed only superficial mucosa with preserved crypt architecture and non-specific chronic inflammation in the lamina propria. No submucosal tissue was identified in the sections examined.

In view of persisting symptoms, an exploratory laparotomy was performed. Per-operatively, there was one large polypoid growth at the junction of the caecum and ascending colon with multiple pericolic and mesenteric lymph nodes. The mass was submucosal in origin with normal overlying mucosa. Multiple similar nodular and thickened lesions of varying sizes were also seen in the terminal ileum. Right hemicolectomy with resection of a part of the distal ileum and ileocolonic anastomosis was done and the entire specimen was sent for histopathologic examination.

Macroscopic examination showed multiple submucosal nodular thickenings of varying sizes in the entire hemicolectomy specimen including the ileum, the largest being at the junction of the caecum and ascending colon measuring approximately 6.0 cm x 5.0 cm x 4.2

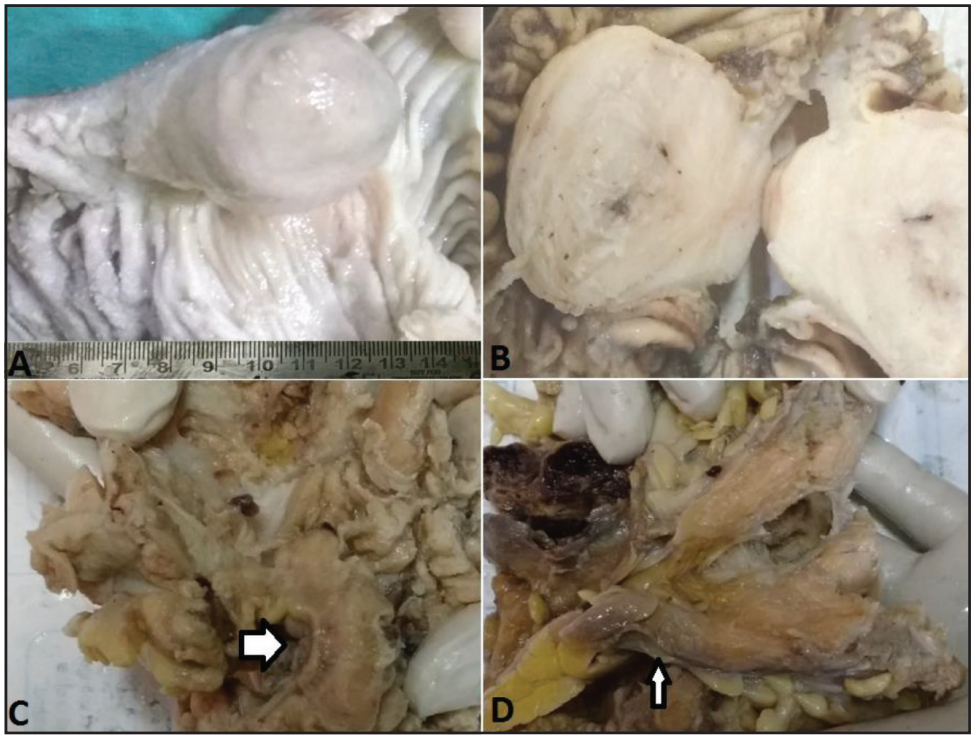


**Figure 2: Gross appearance of the submucosal mass at the junction of caecum & ascending colon (A) which had a smooth homogenous yellowish appearance (B) on cut section; (C) the ileum showed multiple areas of nodularity and thickening (arrow); (D) the appendix had a waxy appearance without any visible lumen (arrow).**

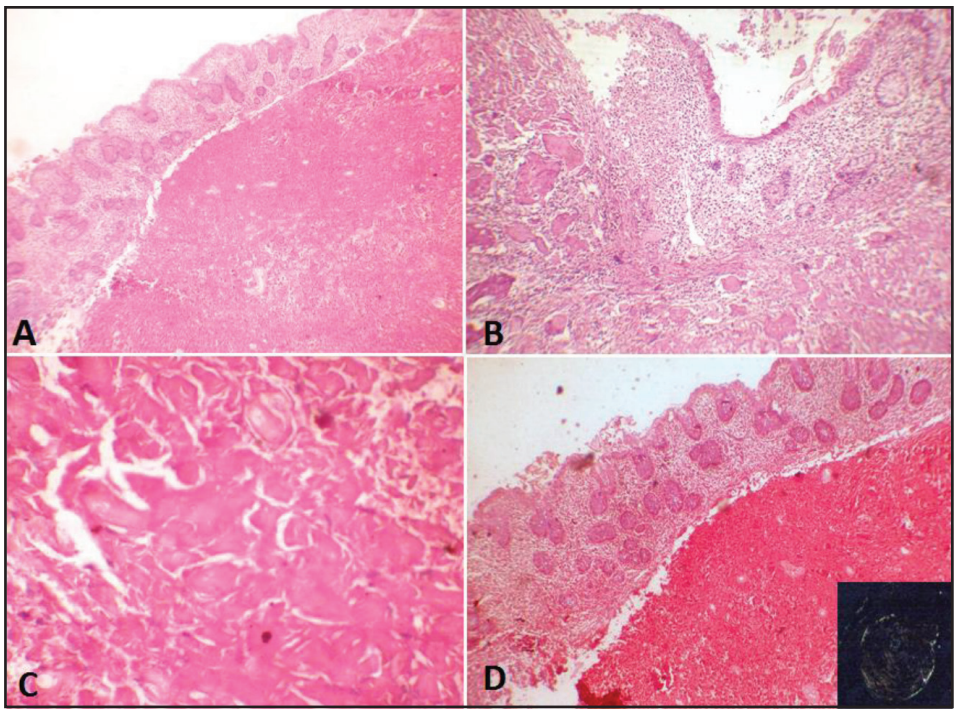


**Figure 3: Photomicrograph of the colonic mass showing submucosal deposition of a eosinophilic homogenous amorphous material (H&E stain; A-4x, B-10x) with overlying mucosa showing focal ulceration; C -high power view of the material in H&E stain(40X); On congo red staining, the material had a salmon-red appearance, which showed apple green birefringence on polarized microscopy (inset).**

cm. The mass was polypoid and on cut sections, was pale yellowish with a homogenous waxy appearance. The ileal thickening and nodules had a similar appearance. The entire appendix had a pale waxy appearance without any visible lumen (Fig. 2). Multiple sections were taken from the mass lesions in the colon, ileum, and appendix. Eighteen lymph nodes identified grossly were sampled and submitted in-toto.

Microscopic examination of the mass lesions showed extensive deposition of amorphous eosinophilic extracellular hyaline material in the submucosa of the ileum and the colon (Fig. 3). The material had a salmon-red appearance on congo red staining which showed apple-green birefringence on polarized microscopy, thus confirming amyloid deposits. The submucosal blood vessels showed homogenous thickening by circumferential amyloid deposition as well. The overlying colonic & ileal mucosa was normal. The appendix showed extensive amyloid deposition in the wall with complete obliteration of the lumen. Ten out of the eighteen lymph nodes showed partial to complete effacement of the lymph node architecture by amyloid deposition. Hence, a diagnosis of ileo-colonic amyloidosis was suggested. The patient was then investigated for any underlying plasma cell dyscrasias. She underwent a bone marrow examination which did not reveal any significant rise in plasma cells. Serum protein electrophoresis was also negative for any monoclonal gammopathy. Autoantibodies for rheumatic factor, anti-nuclear antibody, and anti-neutrophil cytoplasmic antibody were all negative. Immunohistochemistry was carried out for AL and AA amyloid, which was inconclusive as well. Post-operative recovery of the patient was uneventful and she is being closely followed-up and currently is doing well.

## DISCUSSION

Amyloidosis is a disorder characterized by extracellular deposition of proteinaceous fibrillary hyaline material in various tissues and organs, the material is known as amyloid. [8] Gastrointestinal system involvement can occur at all levels and is associated with primary AL amyloidosis in about 70% of the cases, while the association with secondary amyloidosis is only 5%. [9] Localized amyloidosis is the form of amyloidosis which is limited to a particular organ or organ system and does not become systemic. These patients do not have a circulating monoclonal protein in the serum or urine, nor do they have clonal plasmacytosis in the bone marrow. Distinguishing patients with amyloidosis localized to the colon, from the patients with primary systemic AL amyloidosis, is essential because the overall survival in the latter is short. [10] Most localized amyloidosis occurs in the respiratory tract, lower genitourinary tract, and skin. [11,12] Within the gastrointestinal tract, the descending and recto-sigmoid colon are the most frequently involved sites [10].

The symptoms of amyloidosis involving GI tract are varied and include malabsorption, pseudo-obstruction, hemorrhage, abdominal distension, pain, diarrhea, constipation, weight loss or dysphagia depending on the part of the GI tract involved. [7] Our case presented mainly with signs of GI tract bleeding in the form of melena, hematochezia and poorly localized abdominal pain for two years. The colonoscopic examination may reveal varied findings, which includes polypoid lesions, ulcerations, nodularity, petechial mucosal suggillations, and stricture formation. [4] Our case showed a globular mass lesion protruding into the lumen in the proximal ascending colon with a normal overlying mucosa with significant luminal narrowing. Rest of the colon showed multiple areas of

mucosal hemorrhages. Amyloid deposition in the submucosal blood vessels results in thickening of the vessel wall with narrowing of the lumen, which eventually may completely occlude, resulting in ischemia and infarction of the area supplied by them. [4] Lower GI bleeding in the form of submucosal hemorrhage, melena and hematochezia, in our case, can be explained by the ischemia and infarction caused by extensive deposition of amyloid in the submucosa as well as submucosal blood vessels.

Considering the submucosal localization of amyloid deposition, colonoscopic biopsies are often inconclusive and shows non-specific changes, [4] which was observed in our case too. On laparotomic exploration, the pre-operative findings were suggestive of malignant growth in the proximal ascending colon. Chen *et al* [13] also described a similar case in which colonic amyloidosis mimicked carcinoma of the colon, macroscopically. In these cases, a histopathological examination is the only reliable tool to differentiate between a localized amyloidoma and a neoplasm. Diaz Del Arco *et al*. [14] in their case report described globular AL amyloidosis within the lamina propria of the left colon in a 74-year-old man. The patient was presented with anemia and multiple ulcerative lesions were found on colonoscopic examination. His disease was localized without any systemic involvement and had been doing well on conservative management. They concluded that systemic therapy can be avoided in localized gastrointestinal amyloidosis and patients may be followed up periodically. Willson *et al* [15] described a case of systemic pseudo-tumoral amyloidosis in an 82-year-old man presenting as an extraluminal mass in the pelvic cavity in relation to recto-sigmoid, ureters and iliac vessels. The mass was inoperable on exploratory laparotomy and hence not resected. The patient died after two months of surgery. In addition to colonic as well as ileal submucosal amyloid nodules, our case is unique in a sense that there was extensive amyloid deposition in the appendix and in most of the lymph nodes. In spite of the extensive literature search, only a few cases reports documented amyloid deposition in the appendix or lymph nodes, associated with AL or AA amyloidosis [16,17].

Once the histopathological confirmation of amyloid is done using congo red staining, it is essential to distinguish patients with amyloidosis localized to the colon from patients with primary systemic AL amyloidosis because overall survival in AL amyloidosis is short. [10] Bone marrow examination, along with immunofixation electrophoresis of serum and urine, is required to detect monoclonal immunoglobulins or light chains and hence exclude any underlying plasma cell dyscrasia. [7,18] In our case, there was no evidence of any underlying plasma cell dyscrasia. The aim of therapy in amyloidosis is to slow amyloid formation by reducing production of the amyloidogenic protein and to control the clinical symptoms. Primary AL amyloidosis is treated by immunosuppressants like alkylating agents whereas AA amyloidosis is managed by treatment of the underlying systemic disorder. [10] Nevertheless, in cases of localized amyloidosis with symptomatic disease, surgical intervention is the mainstay of treatment to prevent organ decompensation [18].

## CONCLUSIONS

In our case report, apart from the extensive submucosal amyloid deposition in the colon and ileum, there was involvement of the appendix and lymph nodes as well, which is a rare finding. Identification of this localized form of amyloidosis is important because the overall prognosis is better than GI involvement by systemic amyloidosis.

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