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Unusual case of amyloidosis presenting as a jejunal mass

Sachin Mohan ,[1,2] Elliot Graziano,[3] James Campbell,[4] Irshad H Jafri[1]

[1]Gastroenterology and Hepatology, Regions Hospital, Saint Paul, Minnesota, USA
[2]Department of Gastroenterology and Hepatology, University of Minnesota System, Minneapolis, Minnesota, USA
[3]Department of Gastroenterology and Hepatology, University of Rochester, Rochester, New York, USA
[4]Gastroenterology and Hepatology, University of Minnesota System, Minneapolis, Minnesota, USA

Correspondence to
Dr Sachin Mohan;
sachinmohan01@gmail.com

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SUMMARY

Amyloidosis constitutes a heterogeneous group of disorders of protein misfolding that can involve different organ systems. The disease can occur either in a systemic or localised manner that is well known to involve the gastrointestinal (GI) tract. GI amyloidosis can present with a wide range of symptoms including diarrhoea, bleeding and obstruction. This case illustrates a patient with localised jejunal amyloid light chain disease that was diagnosed serendipitously during a workup for haematuria. Our patient was otherwise asymptomatic, but this case underscores the importance of considering amyloidosis as a possible cause of isolated masses of the small intestine.

BACKGROUND

Amyloidosis is a condition defined by abnormal protein folding, with the subsequent deposition of β-sheet fibrillar extracellular proteins which then disrupt normal tissue function.[1] The deposition of amyloid varies widely, and can be localised or systemic.

The most common types of systemic amyloidosis include amyloid light chain (AL), which is often associated with a monoclonal plasma cell population and referred to as primary amyloidosis and amyloid associated (AA), which is linked with a variety of systemic inflammatory conditions and known as secondary amyloidosis.[1 2] Other well-characterised types include the form involving the transthyretin protein or due to β_2-microglobulin which occurs in patients on chronic haemodialysis.[1] Localised amyloidosis occurs when amyloid deposits at the site of production, in contrast to systemic amyloidosis where deposition occurs remotely. Clinical symptoms depend on the type of precursor protein, pattern and extent of organ involvement, although the underlying pathophysiology is not entirely understood. Localised gastrointestinal (GI) tract involvement is seen in 3%–8% of cases.[1 3 4] Patients present with a wide array of symptoms, ranging from macroglossia and xerostomia due to deposition in the tongue and salivary glands, respectively, to diarrhoea, constipation and abdominal pain from involvement of the small intestines and colon.[5 6] While the small intestine is the most common GI site affected insystemic amyloidosis, sites of localised GI disease remain difficult to characterise due to non-specific results from endoscopy and imaging modalities.[5] Further, localised GI amyloidosis remains difficult to diagnose as clinical manifestations are dependent on the location and extent of organ involvement.

Here, we describe a case of localised AL amyloidosis, involving the jejunum, identified after an incidental mass was noted in the absence of typical symptoms. This is important to illustrate for several reasons, first that amyloid deposition in the GI tract must be considered in the differential diagnosis of isolated small intestinal masses in the absence of clinical symptoms. Second, it is also important to understand and identify patients with subclinical GI tract involvement to further understand the natural history of the disease, timing of intervention and ongoing surveillance required to limit tissue damage and organ dysfunction.

CASE PRESENTATION

A 62-year-old male patient with medical history of chronic hepatitis C treated successfully with ledipasvir/sofasbuvir therapy, hypertension and type 2 diabetes who developed recurrent haematuria, urinary tract infections, urinary frequency and nausea. Social history was significant for past intravenous drug abuse and 25 pack-year history of smoking (quit 2 years prior). He was treated with several courses of antibiotics for presumed urinary tract infections. Workup included a CT abdomen and pelvis which revealed a 2.3 cm hyperdense mass in the lower pole of the left kidney, multiple subcentimetre renal cysts and wall thickening in the proximal to mid jejunum approximately 2.0×2.2 cm in diameter. Given the incidental jejunal lesion noted on imaging and concern for lymphoma in the context of prior hepatitis C, He was then referred to gastroenterology and subsequently underwent a push enteroscopy for further work-up.

INVESTIGATIONS

Push enteroscopy identified multiple medium-sized submucosal masses in the proximal to mid jejunum (figures 1 and 2). Biopsies revealed Congo red positive deposits consistent with amyloid protein (figure 3). Liquid chromatography tandem mass spectrometry demonstrated a peptide profile consistent with AL (lambda) type amyloid protein. Further investigations included a serum protein electrophoresis (SPEP) that was negative for a monoclonal spike, and negative cryoglobulins along with a normal complement profile (C1q, C4 and C3). Bone marrow was normocellular with a <5% polyclonal plasma cell population and negative for amyloid. A 24-hour urine protein electrophoresis was positive for proteinuria (24 hours total protein=79 mg) and immunofixation revealed free lambda light chains. Echocardiogram was notable for an ejection fraction of 55%–60%, and grade 1

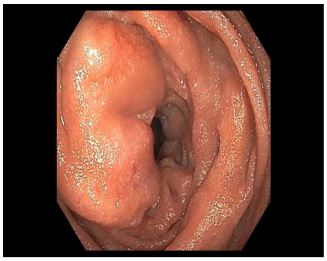

Figure 1 Mid-jejunal submucosal mass.

diastolic dysfunction. Additional workup included a complete blood cell count with differential, troponin, N-terminal pro b type natriuretic peptide (NT pro-BNP), hepatic panel and international normalized ratio/ activated partial thromboplastin time (INR/aPTT) which were normal.

OUTCOME AND FOLLOW-UP

At a 2-week follow-up, he was again treated for a urinary tract infection and had a normal cystoscopy. At a subsequent 3-month visit, he reported haematochezia that prompted a colonoscopy which revealed internal haemorrhoids, diverticulosis and three <4 mm hyperplastic polyps in the sigmoid colon. Haematochezia was attributed to haemorrhoids, and addressed with supportive care. Blood work revealed an elevated creatinine (1.21 mg/dL), calcium (10.6 mg/dL) and uric acid (9.8 mg/mL) levels. Minimally elevated Kappa free light chains (1.98 mg/L), normal lambda free light chains (1.76 mg/L) with a normal ratio (1.13) were noted. Elevated IgA (421 mg/d)L with normal IgG and IgM was noted. Repeat SPEP, fat aspirate and echocardiogram were unremarkable. A diagnosis of localised AL amyloidosis involving the jejunum was suspected, with annual follow-ups recommended and close monitoring of symptoms. He continues to be stable with no GI or systemic symptoms after 3 years.

DISCUSSION

In summary, we describe a patient with localised AL amyloidosis, involving only the jejunum, identified fortuitously on a workup for haematuria. Our patient was evaluated and ruled out for lymphoma, given past medical history of hepatitis C. Further, a normal complement profile along with the absence of cryoglobulinaemia was also noted in our patient.

While systemic amyloidosis is a heterogeneous disease, with varying clinical manifestations, localised amyloidosis remains a challenging diagnosis to prove.[1 3 5] The presence of GI symptoms, along with direct biopsy evidence of involvement remains the gold standard for defining GI disease in amyloidosis. Pragmatically, that is much less common. Amyloidosis of the GI tract is usually systemic. All organs of the GI tract may be impacted in AL amyloidosis. Symptoms vary depending on organ and

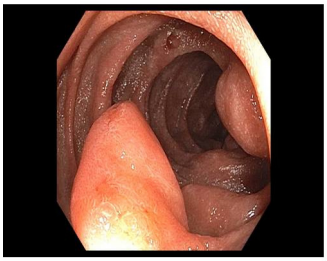

Figure 2 Mid-jejunal submucosal mass.

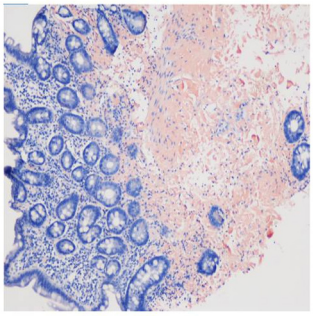

Figure 3 Mucosa with glands and underlying salmon coloured amyloid (Congo red stain).

extent of involvement. Hepatic involvement may be present in up to 70% of patients with systemic amyloidosis, with either subtle manifestations like an isolated elevation in alkaline phosphatase to fulminate hepatic failure.[5 7] Pancreatic involvement is much less common but can manifest as exocrine or endocrine dysfunction.[5]

The small intestine is the most common GI site affected by systemic amyloidosis and presentation is often dependent on the pattern of protein deposition. Symptoms typically differ based on the type of amyloid deposition. AA amyloid is more often defined by symptoms of diarrhoea and malabsorption likely due to its mucosal predominance of protein deposition.[6] However, AL generally is more predominant in the muscular layer and can present with obstructive symptoms.[6 8] Endoscopic AL amyloid involvement of the GI tract is more characterised by polypoid protruding masses as opposed to AA amyloid which is usually characterised by friable mucosa and ulcerations.[8–10] There are previous cases of AL amyloidosis diagnosed following the presentation of life-threatening GI bleeding.[3 11] Proven GI tract involvement in AL amyloidosis is rare; in one review of 2300 amyloid cases, just 3.2% (76 patients) had biopsy-proven GI involvement.[4] The majority of these cases were identified due to symptomatic involvement of the GI tract, with the most common symptoms including early satiety, GI bleeding and diarrhoea.[4] Management of small bowel amyloidosis is generally aimed at treating the underlying process which in the case of AL amyloid often involves chemotherapy targeted at controlling the production of the precursor protein. However, symptomatic management which can range from antinausea, dysmotility and antidiarrhoeal agents are all important treatment modalities.[6 7]

Localised GI amyloidosis without evidence of other organ involvement or an associated plasma cell dyscrasia is rare. A retrospective review of 2300 patients identified only 16 with localised amyloidosis of the GI tract.[4] Symptoms included GI bleeding in eight (50%), heartburn in eight (50%) and constipation in three patients (19%).[4] Biopsy sites included the stomach in 8 (50%), colon in 7 (44%) and small bowel in 3 patients (19%) and 11 of the 16 cases had AL type disease. Supportive care without treatment was recommended for all patients. All were alive at a median 39 months follow-up mark.[4] However, case reports with fatal GI bleeds as manifestations of localised amyloidosis have been described, suggesting that the complete spectrum of the disease remains unknown.[11]

Our patient with localised AL amyloidosis, involving the jejunum, is interesting as localised jejunal involvement in amyloidosis is very rare. To our knowledge, only one other case of jejunal amyloidosis has been reported to date.[11] In contrast to our patient who was asymptomatic, the previously described

Learning points

- While small intestinal involvement of amyloid light chain amyloidosis is well established, isolated jejunal involvement with the absence of typical symptoms or other organ involvement is unusual and demonstrates amyloidosis should be considered in the differential diagnosis of isolated submucosal masses of the small intestine.
- Localised amyloidosis to the gastrointestinal (GI) tract is rare and an extensive evaluation for end-organ involvement is essential in order to determine appropriate treatment and surveillance.
- Early recognition of the disease is important to limit tissue damage, organ dysfunction and prevent GI complications like mucosal ulcerations, GI bleeding, diarrhoea, weight loss and malabsorption.

patient presented with pain and fatal GI bleeding. Clinically, our patient continues to be asymptomatic 3 years after diagnosis, without any need for intervention or additional therapies. While our case underscores the importance of considering localised GI amyloid deposits in the differential diagnosis of unexplained small intestinal submucosal masses or ulcerations, it also emphasises the importance of recognising subclinical localised GI involvement in amyloidosis. It highlights the need to outline the natural history of the disease to better define when to, initiate appropriate treatment and in turn, limit tissue damage.

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ORCID iD
Sachin Mohan http://orcid.org/0000-0002-6798-4767

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