

## CASE REPORT

# PRIMARY AMYLOIDOSIS WITH INITIAL GASTROINTESTINAL MANIFESTATION. A CASE REPORT

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### ABSTRACT

**Introduction.** Amyloidosis is a rare disease associated with extracellular accumulation of abnormal protein – amyloid in various organs and systems. This disease can be either acquired or hereditary, systemic or localized. At its core, it represents a grown, tumor-like neoplastic clone of the plasma cells in the bone marrow. Gastrointestinal amyloidosis is manifested by symptoms, such as diarrhea, steatorrhea, constipation, and very rarely – hemorrhages and perforations of the colon.

**Case presentation.** We present a case of primary intestinal amyloidosis with recurrent hematochezia and abdominal pain in a 61-year-old woman. Colonoscopy revealed polyposis of the whole colon and a total colectomy was performed, followed by morphological and paraclinical examinations. Histologically, amyloid deposition, positive for Congo red, was found in the walls of the submucosal blood vessels and in the smooth muscle cells of the muscular layers. The laboratory tests indicated anemia, high erythrocyte sedimentation rate, and Bence-Jones proteins in urine.

**Conclusions.** Our case is a demonstration of primary amyloidosis with intestinal localization that should be

### RÉSUMÉ

**L'amyloïdose primaire avec manifestation gastro-intestinale initiale. Présentation de cas**

**Introduction.** L'amyloïdose est une maladie rare qui est associée à l'accumulation extracellulaire d'une protéine – amyloïde anormale dans différents organes et systèmes. Elle peut être acquise ou héréditaire, systématisée ou localisée. Elle a à la base un type néoplasique des plasmocytes de la moelle osseuse qui s'est agrandie de façon tumorale. L'amyloïdose gastro-intestinale est marquée de symptômes comme la diarrhée, la stéatorrhée, la constipation et, très rarement, d'hémorragie et de perforation du colon.

**Rapport du cas.** Nous présentons un cas d'une femme à l'âge de 61 ans avec une amyloïdose primaire intestinale marquée d'une hématochémie récidivante et une douleur abdominale. La colonoscopie a montré une polypose de l'entier côlon ; on a fait une colectomie totale suivie d'une analyse morphologique et paraclinique. Histologiquement, dans les parois des vaisseaux sanguins sous-muqueux et dans les cellules musculaires lisses des couches musculaires on a trouvé des dépôts amyloïdes positifs au rouge Congo, et

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taken into consideration in the presence of recurrent hematochezia.

**Keywords:** amyloid, colon, hematochezia, histopathology.

## INTRODUCTION

Amyloidosis is a rare disease, which features extracellular accumulation of an abnormal protein in various organs and systems. According to Husby's classification, this disease can be either acquired or hereditary, generalized or localized<sup>1</sup>. Primary amyloidosis is a form of systemic amyloidosis, and is associated, in 10-15% of cases, with immunocyte dyscrasias<sup>2-9</sup>. At its core, it represents a grown, tumor-like neoplastic clone of the plasma cells in the bone marrow. In 70-79% of cases, the gastrointestinal (GI) tract is affected by primary amyloidosis, and in 55% – by secondary amyloidosis<sup>2,10</sup>. The median age of presentation of primary systemic amyloidosis is usually in the sixth to seventh decade of life<sup>11</sup>. Clinically, the accumulation of amyloid in the GI tract can manifest with upper and lower dyspeptic syndrome. However, in 57% of cases, GI amyloidosis initially manifests with GI bleedings<sup>3,10,11</sup>. The endoscopic image of the digestive tract in patients with amyloidosis can show abnormal findings, such as polypoid lesions, erosions, ulcerations, and nodules<sup>12</sup>.

## CASE PRESENTATION

A 61-year-old woman was referred to the Department of Coloproctology and Septic Surgery of our hospital due to recurrent hematochezia and lower abdominal pain. Her medical history included surgery for a bleeding duodenal ulcer, in addition to diarrhea, melena, weight loss and fatigue, all of which dated a year prior to this hospitalization. The surgical approach to the ulcer included a suture and pyloroplasty, followed by conservative therapy with spasmolytics, fluid resuscitation, and medications for the anemic syndrome. As a result, the patient's health status had improved for one year before a hemorrhage from the lower gastrointestinal tract manifested. She was hospitalized at another hospital where colonoscopy was performed, which revealed colonic polyposis. Two months later, a

de l'analyse de laboratoire – des données d'anémie, de vitesse de sédimentation élevée et de protéines Bence-Jones dans l'urine.

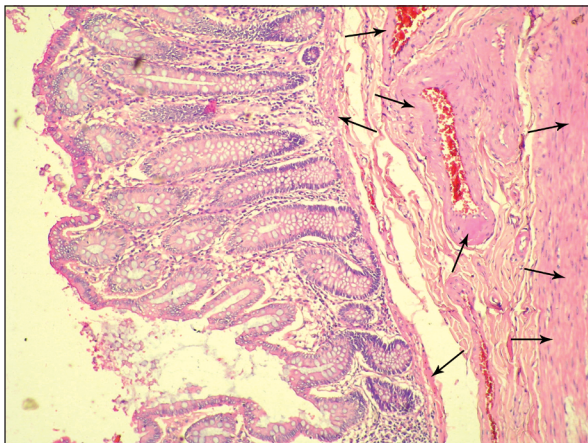
**Conclusions** Notre cas est une démonstration d'amyloïdose primaire avec localisation intestinale qui devrait être pris en considération en présence d'une hématochémie récidivante.

**Mots-clés:** amyloïde, côlon, hématochémie, histopathologie.

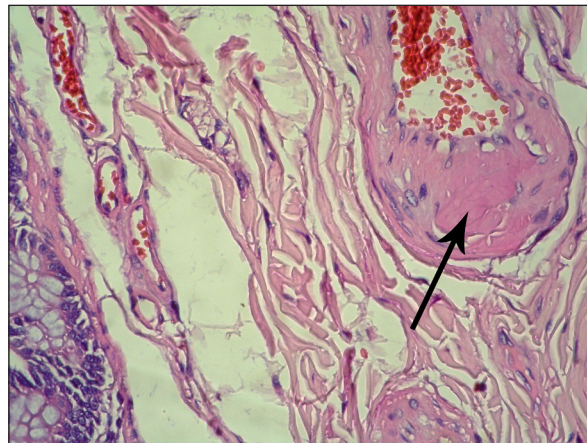
surgical intervention at our hospital was undertaken due to the persisting hematochezia. Preoperatively, laboratory findings indicated anemia – low hemoglobin 8.0-9.0 g/dL (reference range 12.0-16.0 g/dL) and low red blood cell count 3,260,000/mm<sup>3</sup> (reference range 3,700,000-5,300,000/mm<sup>3</sup>); high erythrocyte sedimentation rate – 50 mm/h; serum hypoalbuminemia – 3.24 g/dL (reference range 3.5-5.2 g/dL), and abdominal ultrasound revealed splenomegaly (130/43 mm). A total colectomy was performed and the gastrointestinal passage was recovered through an ileo-recto anastomosis using a stapler. The resected material underwent histological examination (Figure 1). Microscopically, serrated polyps were found as well as homogeneous eosinophilic material located in the walls of the submucosal blood vessels and in the smooth muscle cells of the intestinal wall (Figures 2,3). Congo red staining confirmed that the depositions were amyloid (Figure 4). These findings were relevant to intestinal amyloidosis. Sub-typing of the amyloid deposits was not performed. Following the histological examination, laboratory tests of urine indicated Bence-Jones proteins, which supported the diagnosis of primary systemic amyloidosis. The patient was redirected to a hematological department for additional laboratory tests and treatment of the disease.



**Figure 1.** Macroscopic view of the colon after total colectomy



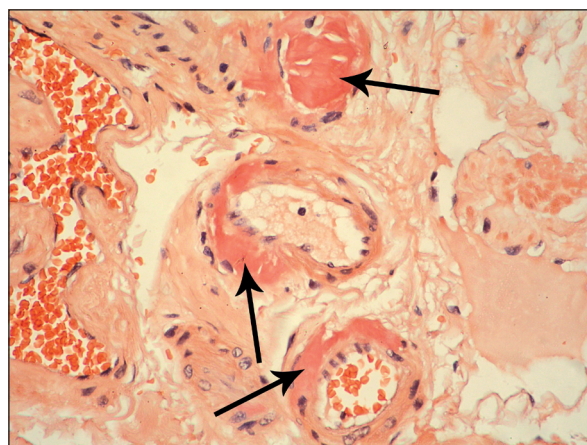
**Figure 2.** Microscopic view of amyloid deposits (arrows) in the walls of submucosal blood vessels and in the smooth muscle cells of muscularis mucosae and muscularis propria of the colon, hematoxylin-eosin, magnification x200



**Figure 3.** Amyloid deposits (arrow) in the wall of a submucosal blood vessel, hematoxylin-eosin, magnification x400

## DISCUSSION

Primary amyloidosis with initial involvement in the GI tract has an unusual presentation and in most of the cases specific clinical symptoms lack when organs and systems are being affected. Initially, the disease can manifest with complications, such as hemorrhages from the upper and lower parts of the digestive tract, as it was in our case as well<sup>1,2,7,12</sup>. According to Spier et al, gastrointestinal hemorrhages may appear in 5% of patients with amyloidosis, however, Gaduputi et al have reported an incidence of up to 45%<sup>3,11</sup>. Several mechanisms have been described in the literature, explaining GI hemorrhages caused by accumulation of amyloid protein. The best established mechanism is that abnormalities in the coagulation status, such as acquired deficiency of factor X, increase the risk of intestinal hemorrhages in patients with amyloidosis<sup>3,10-12</sup>. Another mechanism that was also observed in our case and contributed to bleedings is the deposition of amyloid in the vascular walls and in muscularis mucosae, leading to ischemia, hemochezia and perforations<sup>11,12</sup>. In this regard, one year prior to colectomy, our patient had a bleeding duodenal ulcer, most likely as a sign of progression of amyloidosis. In 98% of the autopsy cases, the GI tract is affected by amyloidosis and only 5 cases are reported to have had initial hemorrhage from the digestive tract<sup>3,8,12</sup>. According to Dustin et al analyses of the autopsy cases, amyloid deposits in the GI tract are common among patients older than the age of 80<sup>9,13</sup>. Despite the sigmoid colon and the recto-sigmoid region being the most common amyloid localizations, rectal hemorrhages manifest only in 25-45% of cases with intestinal amyloidosis<sup>7,14</sup>. Amyloidosis has a variable clinical presentation that



**Figure 4.** Amyloid deposits (arrows) in the walls of submucosal blood vessels, Congo red, magnification x400

ranges from cases without symptoms to fatal ones. Most commonly the disease manifests with upper dyspeptic syndrome along with symptoms, such as pseudo-obstruction, gastric malformations, ulcers, and, although rarely encountered, hematoma<sup>14,15</sup>. This clinical presentation may mimic neoplasms or non-specific chronic colitis, as well as ischemic and microscopic colitis<sup>4,7,15</sup>. Anemia is not a prominent feature of primary amyloidosis but when present, it is most commonly due to multiple myeloma, or renal insufficiency, or hemorrhages in the digestive tract<sup>14,15</sup>. Endoscopy and imaging can display the following atypical findings: erosions, ulcerations, granular appearances, mucosal friability, and multiple polypoid lesions, all of which, in the setting of a GI bleeding, should raise suspicion of the disease. Gastrointestinal amyloidosis should be taken into consideration when manifestations of dysmotility, bloody diarrhea, and astheno-dynamic syndrome are present, as in our

patient. Due to the non-specificity of the symptoms, the diagnosis of amyloidosis usually takes a long time. The histological examination of the biopsy material along with conducting specific histochemical methods, such as Congo red, methyl-violet or gentian-violet staining (under white light microscope), immunofluorescent and immunohistochemical methods (with monoclonal antibodies), and the apple-green birefringence when viewed with crossed polarized light are important for visualizing and typing of amyloidosis<sup>14,16</sup>. Amyloid deposits that are found in the walls of blood vessels in the mucosa, submucosa, and muscularis mucosae layers of the GI tract, lead to vascular insufficiency and a tendency for hemorrhages<sup>7,13,17</sup>. Tissue samples with diagnostic value for amyloidosis can be: abdominal periumbilical adipose tissue, minor salivary glands, gingiva, and renal/skin tissue taken with fine-needle aspiration or surgical incision. The frequencies of amyloid accumulation in the GI tract are as follow: duodenal mucosa (100%), stomach (95%), rectum/sigmoid colon (91%), and esophagus (72%)<sup>1-4</sup>. Iida et al have reported other frequencies of amyloid deposition: 38% in the colon, 23% in the stomach, 17% in the rectum, 16% in the duodenum, and 6% in the jejunum and ileum<sup>12</sup>. Nevertheless, the most common material used for diagnosis is abdominal adipose tissue, which is positive in 70% of cases with amyloidosis<sup>4</sup>. The duodenum might also be an appropriate site for endoscopic biopsy since it has been determined that the positivity of amyloid deposition was the highest in duodenal mucosa<sup>11,12</sup>. The presence of monoclonal immunoglobulins (light chains) in serum/urine or a pathologic clone of the plasma cells in the bone marrow is at the basis of the diagnosis of amyloidosis. These light chains in urine, also known as Bence-Jones proteins, have been found in our case as well and supported the histological diagnosis. In 84% of patients with GI amyloidosis, AL-amyloid is detected<sup>12-18</sup>. According to Petre et al and James et al, the median survival for patients with untreated primary systemic amyloidosis is less than 2 years and the mortality rate is approximately 50%<sup>1,9</sup>. Kidney and congestive heart insufficiency are common causes for the fatal outcome<sup>10,19,20</sup>. The therapeutic approach aims to slow the amyloid synthesis, reduce the amyloidogenic proteins, as well as control the clinical symptoms. The treatment of amyloidosis is complex and includes transplantation of stem cells, dexamethasone, and chemotherapeutic medicaments. Correction of the coagulation status, reduction of portal hypertension, and a surgical resection are necessary in cases with intestinal bleeding determined by amyloidosis<sup>18-20</sup>. The surgical approach can also act as a method of treatment. Splenectomy is suggested to stop the amyloidosis-related GI bleeding,

based on the mechanism of decreasing the amyloid burden and normalization of factor X. Colectomy, on the other hand, should only be performed in cases with localized amyloidosis due to an existing risk of decompensation of the affected organs or, in other cases such as our, due to recurrent hemorrhages<sup>16-20</sup>.

## CONCLUSIONS

The presented case is a demonstration of primary amyloidosis with initial intestinal localization, which should be taken into consideration in cases with recurrent hematochezia. This disease should be suspected in cases with endoscopic detection of multiple polypoid lesions in the setting of a GI bleeding. The morphological examination of amyloid accumulations in the anatomical structures of the GI tract and laboratory tests are necessary for the accurate diagnosis of GI amyloidosis and the adequate approach to the patient's therapy.

## COMPLIANCE WITH ETHICS REQUIREMENTS:

„The authors declare no conflict of interest regarding this article“

„The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from the patient included in the study“

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