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CASE REPORT

Chronic intestinal pseudo-obstruction due to al amyloidosis: a case report and literature review

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Abstract

A 59-year-old woman presented to our hospital with a 6-month history of nausea, weight loss, and abdominal distension. Physical examination revealed abdominal distension without tenderness, and edema, numbness, and multiple peripheral neuropathy in the limbs. Blood test results showed anemia, hypoproteinemia, and hypoalbuminemia. Immunoelectrophoresis detected kappa-type Bence-Jones protein in both the serum and urine. Bone marrow examination did not reveal an increase of plasma cells. Computed tomography showed intestinal distension and retention of intestinal contents. No obstructive intestinal lesions were observed. Lower gastrointestinal endoscopy showed a decrease in the vascular visibility of the rectal mucosa. Histological findings showed amyloid deposition, which was positive for amyloid light-chain (AL) κ. Thus, she was diagnosed with chronic intestinal pseudo-obstruction (CIPO) due to gastrointestinal and neurological involvement of AL amyloidosis. Her abdominal symptoms were gradually improved by the insertion of an ileus tube and medication. Although we recommended chemotherapy for stopping her disease progression, she did not want to receive it. She died 1 year later because of her pneumonia. We should keep in mind that amyloidosis is an important cause of CIPO. Histopathological examination by endoscopic biopsy is required for exact diagnosis and appropriate treatment for CIPO due to amyloidosis.

Keywords Pseudo-obstruction · Ileus · Amyloidosis

Introduction

Intestinal pseudo-obstruction is a clinical syndrome reported by Dudley et al. in 1958 [1]. Intestinal pseudo-obstruction can be classified into chronic intestinal pseudo-obstruction (CIPO), Ogilvie's syndrome, and toxic megacolon, depending on the clinical course. It is required one or more symptoms of ileus onset at least 6 months to diagnose with CIPO. Ogilvie's syndrome and toxic megacolon mainly affect the large bowel, whereas the small intestine is most likely to be involved in CIPO. CIPO involves symptoms of bowel obstruction without gastrointestinal (GI) stenosis owing to severe GI motility disorders [2]. CIPO can be classified into idiopathic CIPO and secondary CIPO, according to the etiology. The causes of secondary CIPO include various diseases, such as metabolic diseases, connective tissue diseases, and infectious diseases. Amyloidosis has been reported to be one of the most important risk factors for secondary CIPO [2, 3].

Amyloidosis is a group of diseases caused by extracellular deposition of amyloid fibrils leading to organ dysfunction. To date, at least 31 different human proteins have been identified as amyloidogenic, causing both systemic and localized disease [4]. The kidney and heart are the most commonly involved organs in patients with systemic amyloidosis, but amyloid also tends to deposit in the GI tract. The GI tract is often the target organ for a pathological diagnostic examination because of its accessibility [5]. Amyloid deposition in the GI tract often causes morphological and functional changes. CIPO due to amyloid deposition is one such change. However, there is limited literature on this subject. Additionally, treatments for this condition have not been established, and the etiology is still mostly unknown. In this case report, we present the case of a patient who was diagnosed with CIPO due to GI and neurological involvement of amyloid light-chain (AL) amyloidosis and review of literature.

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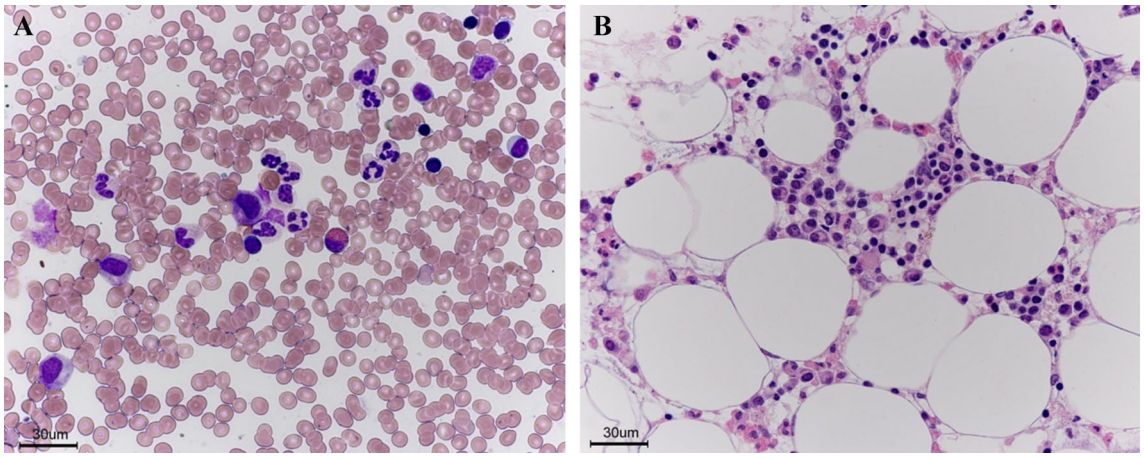

Fig. 1 Bone marrow examination. **a** On bone marrow puncture, the number of nucleated cells was 54,000/μL, and the bone marrow plasma cell percentage was 3.6%. **b** Although hypoplasia was demonstrated on bone marrow biopsy, plasma cell proliferation was not observed

Case report

A 59-year-old woman presented to our hospital with a 6-month history of nausea, weight loss, and abdominal distension. She had a history of appendectomy but without a notable family history. No abnormality was found in the oral cavity or chest examination. However, on abdominal examination, her intestinal sounds were weak. Although abdominal distension was observed, the abdomen was soft and abdominal tenderness was not observed. Edema, numbness, and multiple peripheral neuropathy was observed in the limbs.

Blood test results indicated anemia (hemoglobin 8.6 g/dL), hypoproteinemia (protein 5.1 g/dL), and hypoalbuminemia (albumin 2.7 g/dL). The results of renal function tests were normal, and serum amyloid A (AA) protein was 6.6 μg/mL (normal). On urine assessment, occult blood was 3+ and urinary protein was 2+. Immunoelectrophoresis detected a kappa-type Bence-Jones protein in the serum and urine. On bone marrow puncture, the number of nucleated cells was 54,000/μL, and the plasma cell percentage was 3.6% (Fig. 1a). Although hypoplasia was demonstrated by bone marrow biopsy, plasma cell proliferation was not observed (Fig. 1b). Primary amyloidosis was suspected at that time.

Abdominal radiography showed minor intestinal gas and niveau. Computed tomography showed distension of the small and large intestine and retention of intestinal contents, indicating GI obstruction. However, the origin of the obstruction was unknown (Fig. 2). As the patient was suspected of having GI amyloidosis, a brief lower GI endoscopy without preparation was performed; this showed reduced vascular visibility of the rectal mucosa (Fig. 3). On biopsy, the muscularis mucosa was visualized

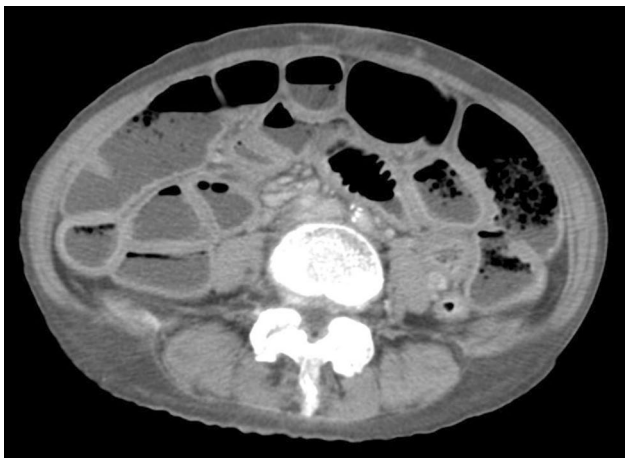

Fig. 2 Contrast-enhanced computed tomography. Computed tomography showed distension of the small and large intestine and retention of intestinal contents, indicating gastrointestinal obstruction. However, the origin of the obstruction is unknown

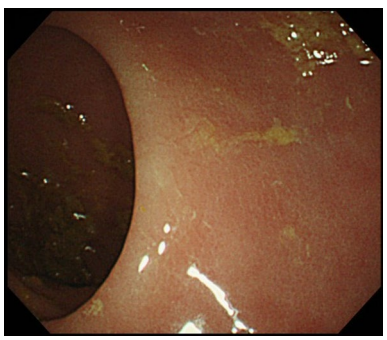

Fig. 3 Endoscopic findings. Lower gastrointestinal endoscopy showed reduced vascular visibility of the rectal mucosa

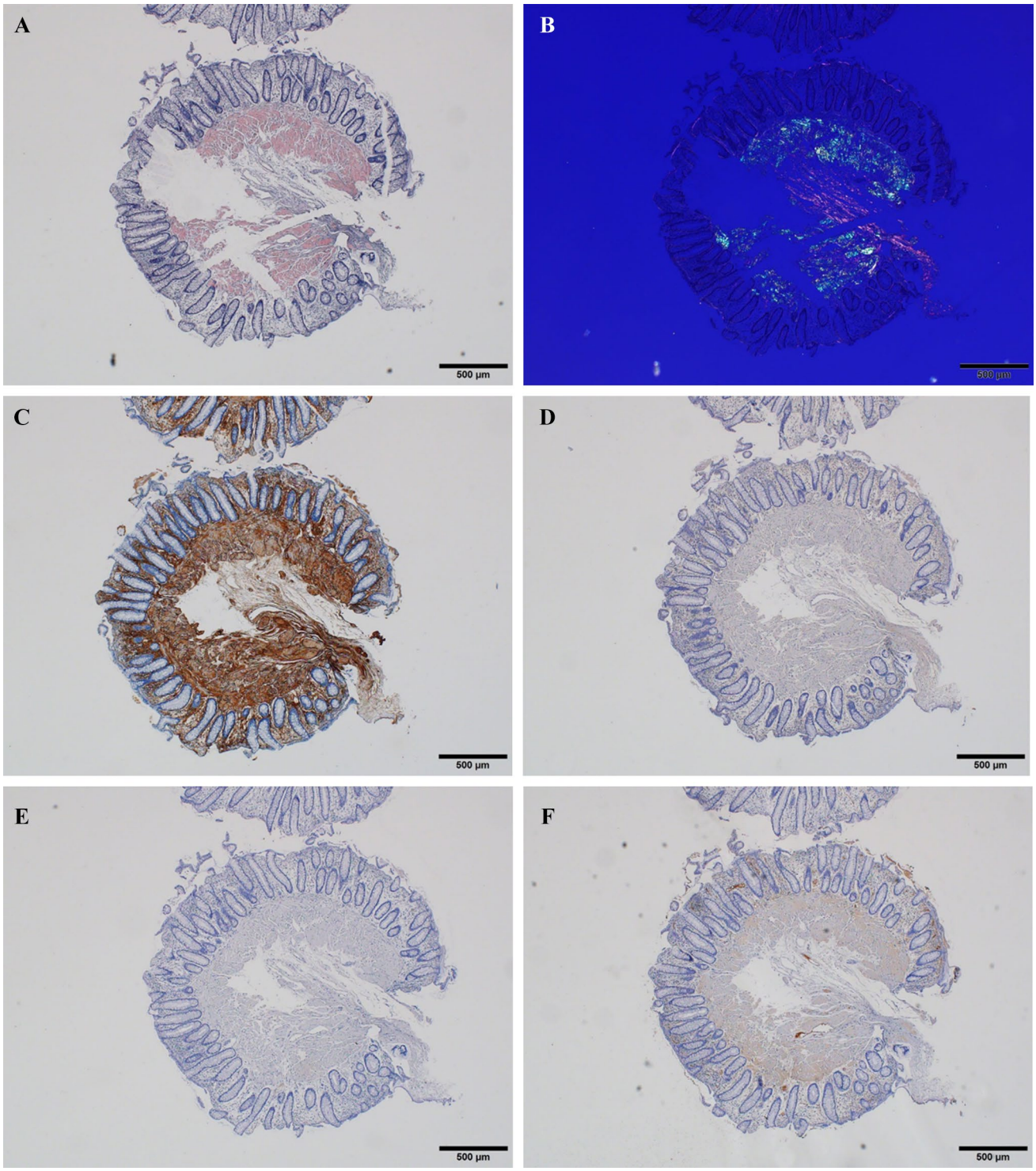

Fig. 4 Gastrointestinal amyloid deposition findings by endoscopic biopsy. **a** The muscularis mucosa was visualized on Congo red staining. **b** Under a polarizing microscope, green birefringent light was observed. **c–f** Immunostaining for biopsy specimens. **c** ALκ. **d** ALλ, **e** AA. **f** TTR

with Congo red staining (Fig. 4a). Under a polarizing microscope, green birefringent light was observed (Fig. 4b), indicating amyloid deposition. On immunostaining, ALκ staining was positive, while ALλ, AA, or transthyretin (TTR) were negative (Fig. 4c–f). Thus, she was diagnosed with CIPO due to GI and neurological involvement of AL amyloidosis.

Electrocardiography and echocardiography were performed, and these showed no evidence of cardiac amyloidosis. To further examine the numbness and paresthesia of her limbs, a nerve conduction velocity test was performed and she was subsequently diagnosed with polyneuropathy. The symptoms appeared to be related to peripheral nerve amyloid deposition.

Total parenteral nutrition (TPN) was necessary to improve nutritional condition. After she was treated with the insertion of an ileus tube and intravenous administration of metoclopramide, her abdominal symptoms were gradually improved, and the ileus tube was removed after a week. She did not have a relapse of ileus despite starting diet. We recommended chemotherapy for stopping her disease progression, however, she did not receive it. She was transferred to another hospital because of her and her family intention. She was conservatively treated on each occasion that she complained of abdominal symptoms related to CIPO. Unfortunately, she died 1 year later after transfer because of her pneumonia.

Discussion

This case report describes a patient who was diagnosed with CIPO due to GI and neurological involvement of AL amyloidosis. We should keep in mind that amyloidosis is an important cause of CIPO.

CIPO is classified into idiopathic CIPO and secondary CIPO. The absence/reduction of stromal cells of Cajal was considered to be the cause of idiopathic CIPO, but this finding is not consistent in all cases of idiopathic CIPO. In patients without a histological diagnosis of CIPO, diagnosis is dependent upon a comprehensive evaluation including the assessment of symptoms, imaging test/endoscopy findings, and GI pressure test results [1, 2]. In most cases, the diagnosis is made by the absence of obstructive lesions owing to the scarcity of characteristic signs. On the other hand, in cases of secondary CIPO, it is very important to find the underlying cause and appropriately treat the primary diagnosis to prevent progression to secondary CIPO. In the present case, various tests suggested the presence of secondary CIPO due to GI and neurological involvement of AL amyloidosis, which was diagnosed by endoscopic examination with biopsy.

The positive rate of GI endoscopic biopsy for GI amyloidosis related to systemic AL varies according to the organ involved. It has been reported that the positive rate in rectal and duodenal biopsy is 17–91% and 16–100%, respectively [6–10]. Regarding our data in 36 patients with amyloidosis involving the GI tract, the frequency of amyloid deposition in the biopsy specimens was 86% in the rectum, 85% in the duodenum, 73% in the colon, 65% in stomach, and 38% in the ileum or jejunum [5]. Although the positive rate of biopsy specimens varies by the type of amyloid deposition, rectal and duodenal biopsy is recommended for the diagnosis of CIPO due to GI amyloidosis because of its high diagnostic ability.

The endoscopic manifestations of amyloidosis are variable. Hayman SR et al. [11] reported that among nine patients with GI AL amyloidosis that underwent lower GI endoscopy, polyps were found in two patients, inflammation or colitis in five, and a normal finding in three. Tada et al. [6] reported that among 37 patients with GI amyloidosis (AL 8, AA 29) that underwent upper GI endoscopy, fine granular appearance was found in 26 patients, polypoid protrusions in 2, erosion in 21, ulcers in 5, mucosal friability in 6, and normal findings in 9. Notably, one-fourth to one-third of the endoscopic findings of patients with GI amyloidosis were normal [6, 11]. Thus, biopsy should be performed in the case of suspected amyloidosis, even if no abnormal findings are noted [5].

Our literature search using Pubmed identified only 15 cases of secondary CIPO due to amyloidosis (12 case reports and one case series), including our own [12–23] (Table 1). The patients in most cases were in their 40s–70s, except for one case (22 years old). Their chief complaints were appetite loss, weight loss, nausea/vomiting, and abdominal distention. Of the patients with amyloid deposition, ten were AL amyloidosis patients, and of these patients, two had primary AL amyloidosis, seven had multiple myeloma (MM), and one was the case of localized AL amyloidosis. Remaining five patients were AA or/and β2 microgloblin amyloidosis patients. Of 15 patients, four patients received a definitive pathological diagnosis of GI amyloid deposition after surgery. On the contrary, eight patients received a definitive pathological diagnosis of GI amyloid deposition on upper GI endoscopy, and four received it on lower GI endoscopy (including one patient on both upper and lower GI endoscopy). Despite the fact that only a few of the aforementioned cases of CIPO related to amyloidosis, general gastroenterologists should be aware of this diagnosis and the need to perform an endoscopic biopsy to obtain a definitive diagnosis.

Basically, definitive treatment for CIPO due to amyloidosis depends on the primary disease. For AL amyloidosis, including primary amyloidosis or MM, chemotherapy is performed depending on the patient's condition [24]. For AA amyloidosis, anti-inflammatory treatment is performed for various inflammatory disease, which cause deposition of AA amyloid [25]. Main treatment for CIPO is nutritional support, medication, and decompression by ileus tube. Among them, enteral nutrition should be first considered because of the maintenance of intestinal homeostasis with preventing bacterial translocation. However, in severe cases with CIPO, TPN is necessary to improve nutritional condition

Table 1 15 cases of patients with chronic intestinal pseudo-obstruction due to amyloidosis

No.	Author/references	Year	Age	Sex	Type of amyloid	Amyloid deposition	Treatment	Prognosis
1	Our case	2018	59	F	ALκ (primary)	Rectum Peripheral nerve	Decompression Metoclopramide	Died in 1 year
2	Milivojevic et al. [12]	2018	44	F	ALλ (MM)	Duodenum	None	Died prior to treatment
3	Leong et al. [13]	2014	70	M	AL (MM)	Stomach (Ope) Duodenum (Ope)	Steroid Decompression	Improved
4	Kim et al. [14]	2012	44	F	AA	Terminal ileum Ascending colon	Steroid Colchicine	Died in 2 months after admission
5	Liapis et al. [15]	2011	64	M	ALκ (MM)	Jejunum (Ope)	Ope	Died postoperative day 10
6	Fonnesu et al. [16]	2009	64	F	ALλ (primary)	Stomach Duodenum Heart	Chemotherapy	ND
7	Hurlstone [17]	2002	62	M	ALκ (MM)	Duodenum	Decompression	ND
8	Deguchi et al. [18]	2001	47	M	AL (localized)	Duodenum	Ope	Improved
9	Kanai et al. [19]	2000	42	M	β2-MG	Esophagus–rectum (Ope)	Ope	Died in 3 years
10	Hiramatsu et al. [20]	1998	22	F	AA	Stomach Rectum Kidney	Steroid	Improved
11	Borczuk et al. [21]	1995	61	M	β2-MG, AA	Colon (Ope)	Chemotherapy	ND
12	Fraser et al. [22]	1991	62	F	ALκ (MM)	Colon Peripheral nerve	Chemotherapy Cisapride	Improved
13	Tada et al. [23]	1993	77	M	AL (MM)	Jejunum	Cholinergic agents Metoclopramide	Died in 1 month after admission
14	Tada et al. [23]	1993	51	F	AL (MM)	Jejunum	Cholinergic agents Metoclopramide	Died in 2 months after admission
15	Tada et al. [23]	1993	42	M	β2-MG	Jejunum	Cholinergic agents Metoclopramide Cisapride Decompression	Died in 2 years 3 months after admission

F female, *M* male, *AL* amyloid light-chain, *AA* amyloid A, *β2-MG* β2-microglobulin, *Primary* primary amyloidosis, *MM* multiple myeloma, *Ope* operation, *ND* not described

and maintain an adequate level of hydration as well as enteral nutrition. It was reported that a long-term TPN did not seem to be associated with a significant increase in morbidity and mortality in CIPO in comparison with other conditions requiring TPN [26, 27]. Although medication is often not very effective, defecation control is important in CIPO because abdominal symptoms may suddenly worsen due to excessive constipation. In general, it is used metoclopramide [28], erythromycin [29], and various laxatives for patients with CIPO. In addition to these conventional medicine, the efficacy of pyridostigmine (acetylcholinesterase inhibitor) [30] and prucalopride (highly selective 5-HT_4 receptor agonists) [31] has been reported. Regarding decompression therapy which is also performed in the present case, in the short term, a usual nasal ileus tube may be used, but in cases which required hospitalization management frequently, decompression by percutaneous endoscopic gastrostomy (PEG) is useful. Recently, it was reported that a feeding tube insertion to jejunum via PEG (PEG-J) was more effective because the main part of intestinal dilation is the small intestine in CIPO [32].

Regarding the prognosis of CIPO due to amyloidosis, Tada et al. [23] reported that symptoms of bowel obstruction were more refractory to nutrition therapy and other therapies in patients with AL amyloidosis than in patients with AA amyloidosis. The authors speculated the differences in therapeutic response to the fact that (1) in patients with AA amyloidosis, amyloid deposits in the submucosal plexus, but not in the muscular layer; whereas (2) in patients with AL amyloidosis, amyloid deposition in the muscular layer causes irreversible GI motility disorders. However, the number of patients with CIPO included in this study was only three of 16 and the remaining 13 were cases less than 6 months after onset. Furthermore, there have been patients with AL amyloidosis responding to medical treatments in the previous reports [13, 18, 22]. Therefore, we cannot conclude that the prognosis varies depending on the type of amyloid deposition.

In conclusion, we herein report a patient with CIPO due to AL amyloidosis. Rectal biopsy was a convenient and useful approach to demonstrate GI amyloid deposition in this case. Further accumulation of data regarding the clinical outcome of patients with AL amyloidosis accompanied with bowel obstruction is required to improve the diagnosis and management.

Compliance with ethical standards

Conflict of interest Tomoya Iida, Daisuke Hirayama, Gota Sudo, Kei Mitsuhashi, Hisayoshi Igarashi, Kentaro Yamashita, Hiroo Yamano, and Hiroshi Nakase declare that they have no conflict of interest.

Research involving human and/or animal participants All procedures followed have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Informed consent Informed consent was obtained from this patient for being described in this case report.

References

1. Dudley HA, Sinclair IS, McLaren IF, et al. Intestinal pseudo-obstruction. J R Coll Surg Edinb. 1958;3:206–17.
2. Stanghellini V, Cogliandro RF, de Giorgio R, et al. Chronic intestinal pseudo-obstruction; manifestations, natural history and management. Neurogastroenterol Motil. 2007;19:440–52.
3. Connor FL, Di Lorenzo C. Chronic intestinal pseudo-obstruction: assessment and management. Gastroenterology. 2006;130:29–36.
4. Sipe JD, Benson MD, Buxbaum JN, et al. Nomenclature 2014: amyloid fibril proteins and clinical classification of the amyloidosis. Amyloid. 2014;21:221–4.
5. Iida T, Yamano H, Nakase H. Systemic amyloidosis with gastrointestinal involvement: diagnosis from endoscopic and histological views. J Gastroenterol Hepatol. 2018;33:583–90.
6. Tada S, Iida M, Iwashita A, et al. Endoscopic and biopsy findings of the upper digestive tract in patients with amyloidosis. Gastrointest Endosc. 1990;36:10–4.
7. Lim AY, Lee JH, Jung KS, et al. Clinical features and outcomes of systemic amyloidosis with gastrointestinal involvement: a single-center experience. Korean J Intern Med. 2015;30:496–505.
8. Freudenthaler S, Hegenbart U, Schönland S, et al. Amyloid in biopsies of the gastrointestinal tract—a retrospective observational study on 542 patients. Virchows Arch. 2016;468:569–77.
9. Briggs GW. Amyloidosis. Ann Intern Med. 1961;55:943–57.
10. Yilmaz M, Unsal A, Sokmen M, et al. Duodenal biopsy for diagnosis of renal involvement in amyloidosis. Clin Nephrol. 2012;77:114–8.
11. Hayman SR, Lacy MQ, Kyle RA, et al. Primary systemic amyloidosis: a cause of malabsorption syndrome. Am J Med. 2001;111:535–40.
12. Milivojevic V, Stojanovic M, Rankovic I, et al. Multiple myeloma associated intestinal amyloidosis: intestinal pseudoobstruction falsely considered as an ascites. Rev Recent Clin Trials. 2018;13:79–81.
13. Leong RY, Nio K, Plumley L, et al. Systemic amyloidosis causing intestinal hemorrhage and pseudo-obstruction. J Surg Case Rep. 2014. https://doi.org/10.1093/jscr/rju087
14. Kim YJ, Kim HS, Park SY, et al. Intestinal amyloidosis with intractable diarrhea and intestinal pseudo-obstruction. Korean J Gastroenterol. 2012;60:172–6.
15. Liapis K, Michelis FV, Delimpasi S, et al. Intestinal pseudo-obstruction associated with amyloidosis. Amyloid. 2011;18:76–8.
16. Fonnesu C, Giovinale M, Verrecchia E, et al. Gastrointestinal amyloidosis: a case of chronic diarrhoea. Eur Rev Med Pharmacol Sci. 2009;13:45–50.
17. Hurlstone DP. Iron-deficiency anemia complicating AL amyloidosis with recurrent small bowel pseudo-obstruction and hindgut sparing. J Gastroenterol Hepatol. 2002;17:623–4.
18. Deguchi M, Shiraki K, Okano H, et al. Primary localized amyloidosis of the small intestine presenting as an intestinal pseudo-obstruction: report of a case. Surg Today. 2001;31:1091–3.
19. Kanai H, Kashiwagi M, Hirakata H, et al. Chronic intestinal pseudo-obstruction due to dialysis-related amyloid deposition in the propria muscularis in a hemodialysis patient. Clin Nephrol. 2000;53:394–9.
20. Hiramatsu K, Kaneko S, Shirota Y, et al. Gastrointestinal amyloidosis secondary to hypersensitivity vasculitis presenting with intestinal pseudoobstruction. Dig Dis Sci. 1998;43:1824–30.
21. Borczuk A, Mannion C, Dickson D, et al. Intestinal pseudo-obstruction and ischemia secondary to both beta 2-microglobulin and serum A amyloid deposition. Mod Pathol. 1995;8:577–82.
22. Fraser AG, Arthur JF, Hamilton I. Intestinal pseudoobstruction secondary to amyloidosis responsive to cisapride. Dig Dis Sci. 1991;36:532–5.
23. Tada S, Iida M, Yao T, et al. Intestinal pseudo-obstruction in patients with amyloidosis: clinicopathologic differences between chemical types of amyloid protein. Gut. 1993;34:1412–7.
24. Gertz MA. Immunoglobulin light chain amyloidosis diagnosis and treatment algorithm 2018. Blood Cancer J. 2018;8:44.
25. Westermark GT, Fändrich M, Westermark P. AA amyloidosis: pathogenesis and targeted therapy. Annu Rev Pathol. 2015;10:321–44.
26. Amiot A, Jolly F, Alves A, et al. Long-term outcome of chronic intestinal pseudo-obstruction adult patients requiring home parenteral nutrition. Am J Gastroenterol. 2009;104:1262–70.
27. Pironi L, Joly F, Forbes A, et al. Long-term follow-up of patients on home parenteral nutrition in Europe: implication for intestinal transplantation. Gut. 2011;60:17–25.
28. Rao AS, Camilleri M. Metoclopramide and tardive dyskinesia. Aliment Pharmacol Ther. 2010;31:11–9.
29. Emmanuel AV, Shand AG, Kamm MA. Erythromycin for the treatment of chronic intestinal pseudo-obstruction: description of six cases with a positive response. Aliment Pharmacol Ther. 2004;19:687–94.
30. O'Dea CJ, Brookes JH, Wattchow DA. The efficacy of treatment of patients with severe constipation or recurrent pseudo-obstruction with pyridostigmine. Colorectal Dis. 2010;12:540–8.
31. Emmanuel AV, Kamm MA, Roy AJ, et al. Randomised clinical trial: the efficacy of prucalopride in patients with chronic intestinal pseudo-obstruction—a double-blind, placebo-controlled, cross-over, multiple n = 1 study. Aliment Pharmacol Ther. 2012;35:48–55.
32. Ohkubo H, Fuyuki A, Arimoto J, et al. Efficacy of percutaneous endoscopic gastro-jejunostomy (PEG-J) decompression therapy for patients with chronic intestinal pseudo-obstruction (CIPO). Neurogastroenterol Motil. 2017. https://doi.org/10.1111/nmo.13127.