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Light chain deposition disease presenting with gastrointestinal disorder as primary manifestation: report of two cases and literature review

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Abstract

Light chain deposition disease (LCDD) is an under-recognized condition characterized by deposition of abnormal monoclonal light chains in tissues, leading to organ dysfunction. LCDD involving the gastrointestinal tract is very uncommon, and its diagnosis is challenging. We herein report two cases of LCDD that manifested as inflammatory bowel disease-like symptoms and protein-losing gastroenteropathy. Both patients were women in their early 60s. Tissue biopsies from the gastrointestinal mucosa demonstrated extracellular deposits, which were negative by Congo red staining but positive for κ-light chain by immunohistochemistry. The recent literature on LCDD was reviewed. When patients unexpectedly show extracellular deposits in gastrointestinal biopsy specimens, evaluation of immunoglobulin chains is recommended for diagnosis of LCDD after systemic amyloidosis has been excluded.

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Introduction

Light chain deposition disease (LCDD) is a systemic disorder commonly involving the kidneys, heart, and liver. It is characterized by monoclonal light chain deposition due to clonal plasma cell proliferation (92% κ chain) and was initially described by Randall et al.[1] Unlike the fibrillar nature of the light chain deposits in amyloid light chain amyloidosis, the monoclonal light chains in LCDD are deposited as unorganized, granular punctate to powdery electron-dense deposits as shown by electron microscopy. We herein report two cases of LCDD manifesting as gastrointestinal symptoms and present a review of the recent literature to increase awareness of LCDD with gastrointestinal involvement.

Case report

Case 1

A woman in her early 60s presented with an 11-month history of recurrent abdominal pain and bloody stools. She was diagnosed with ulcerative colitis by colonoscopy at a local hospital and prescribed methylprednisolone and mesalazine. However, her abdominal pain persisted and the symptoms worsened. Finally, she was transferred to our hospital in April 2019 with a hemoglobin concentration of 82 g/L and positive urine protein (1+). Notably, serum immunofixation electrophoresis was positive for κ-light chain of IgG. Esophagogastroduodenoscopy showed multiple erosions scattered throughout the gastric cardia, body, and antrum and the descending part of the duodenum (Figure 1(a–c)). Diffuse mucosal ulcers, erosions, and edema were found by colonoscopy, especially in the left-sided colon (Figure 2(a, b)). Tissue biopsies from the gastric antrum and transverse colon demonstrated extracellular deposits, which were positively stained for κ-light chain but unstained by Congo red and negative for λ-light chain by immunohistochemistry. These pathological findings led to a diagnosis of LCDD with involvement of the gastrointestinal tract (Figures 1(d, e) and 2(c, d)). The patient was treated with bortezomib and lenalidomide in another hospital, and her symptoms of abdominal pain and bloody stools gradually improved.

Case 2

A woman in her early 60s presented with an 8-month history of edema in both lower extremities. The edema was alleviated by diuretic therapy and intravenous transfusion of albumin at a local hospital. However, the edema subsequently became recurrent and more severe and was accompanied by marked hypoalbuminemia of 29.4 g/L (reference range, 35–52 g/L). She was admitted to our hospital in April 2021. The patient was found to have an abnormal elevated urine κ free light chain level and abnormal urine free light chain ratio, but no monoclonal immunoglobulin was found by serum immunofixation electrophoresis. Esophagogastroduodenoscopy indicated chronic inflammation of the antrum and duodenum with bile reflux. Scattered white punctate mucosal changes

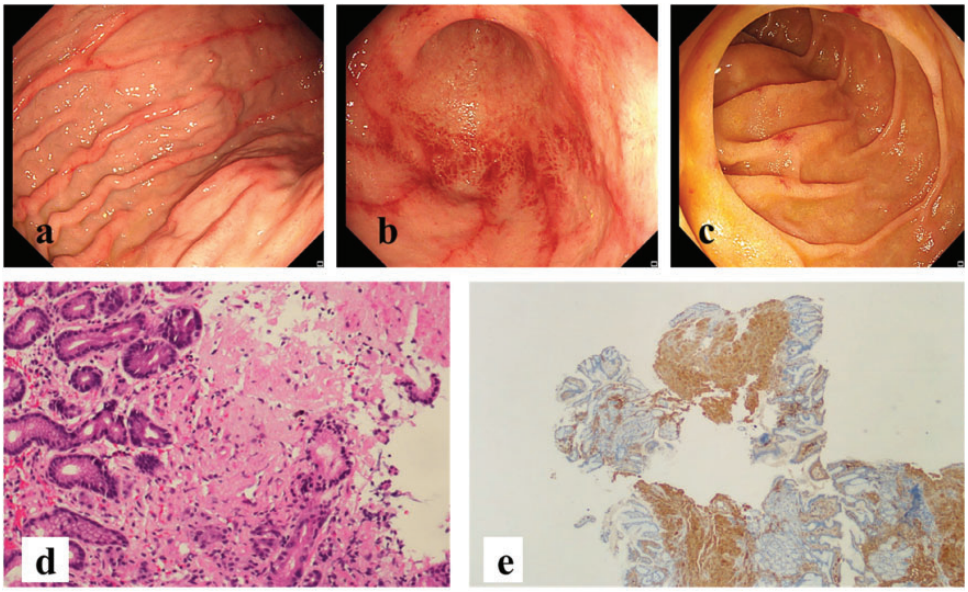

Figure 1. (a, b) Multiple erosions with erythema were observed in the gastric body along crests of gastric body folds without ulceration. (c) Scattered hyperemic foci were observed in the descending segment. (d) Biopsy specimens of the gastric antrum demonstrated nodular amorphous eosinophilic deposits in the lamina propria (hematoxylin and eosin stain, 200×) and (e) The eosinophilic deposits and vessel walls were positive for immunoglobulin κ-light chains (40×) on immunohistochemical studies with no significant λ-light chain staining (images not shown).

were present in the descending duodenum (Figure 3(a, b)). Colonoscopy revealed multiple polyps in the colon (images not shown). The deposits in the gastric antrum were positive for κ-light chain (Figure 3(d)) with no staining for λ-light chain. The material stained weakly with Congo red but was negative for the characteristic green birefringence of amyloid (images not shown). No metachromasia was observed with crystal violet stain (images not shown). Therefore, a pathological diagnosis of LCDD was made by histopathologic examination of tissues from the gastric antrum (Figure 3(c, d)). The patient was discharged and transferred to another hospital for further confirmation by tissue mass spectrometry analysis.

This study was conducted in accordance with the principles of the Declaration of Helsinki. Our hospital is a high-level teaching hospital, and all patients' information is preserved electronically and can be used for teaching and research purposes if anonymized. Thus, the need for ethics approval and written informed consent for publication of this case report was waived. The reporting of this study conforms to the CARE guidelines.[2]

Discussion

LCDD is a systemic disease characterized by monoclonal immunoglobulin light chain deposition in tissue and organs. The kidneys are the predominantly involved organ. Diagnosis of LCDD is based on histopathological detection, which is the most dependable standard for diagnosis. To our knowledge, LCDD mainly affects men of

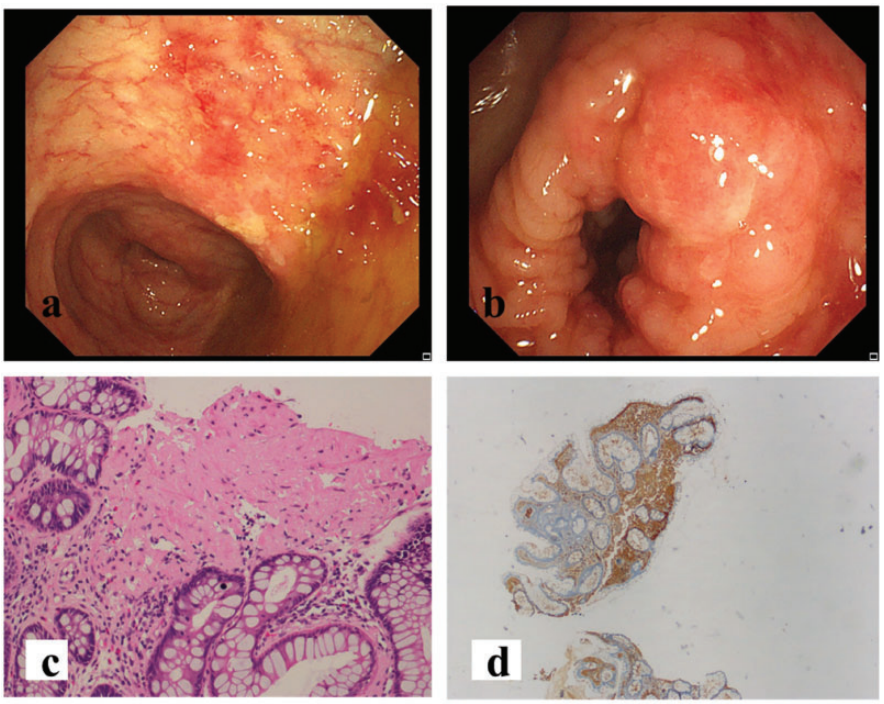

Figure 2. Colonoscopy. The mucosa of the (a) descending and (b) sigmoid colon showed scattered patchy hyperemia and ulceration. (c) Transverse colon histopathology (hematoxylin and eosin stain, 200×) and (d) biopsy tissue from the transverse colon was κ-light chain positive on immunohistochemical studies (40×), while the tissue was λ-light chain negative (images not shown). These findings supported the pathologic diagnosis of light chain deposition disease.

approximately 50 years old,[3] and it is usually accompanied by multiple myeloma or other low-grade lymphoproliferative disorders.[4,5] However, the exact incidence of LCDD is still unclear.

We reviewed all cases of LCDD reported in PubMed (https://pubmed.ncbi.nlm.nih.gov/) within the past 5 years and found only one case in which the gastrointestinal tract was affected.[4] Considering the rarity of LCDD, we then reviewed the publications within the past 20 years. Among these, a case of LCDD with gastrointestinal involvement was reported by Jiménez-Zepeda et al.[6] This was the first case of LCDD with symptomatic gastrointestinal involvement, and the diagnosis was established by intestinal biopsies. The clinical manifestations of LCDD involving the gastrointestinal tract include watery diarrhea,[1] acute pancreatitis, and gastrointestinal bleeding.[7] This is consistent with Case 1 in the present report; this patient's clinical features and endoscopic images were similar to those of ulcerative colitis. Gastrointestinal lymphoma must be carefully excluded before LCDD is diagnosed because these conditions share the same symptoms of abdominal pain (78%–93%) and gastrointestinal bleeding (19%).[8]

LCDD-related protein-losing gastroenteropathy, as occurred in Case 2 of our report, is rare. Patients with protein-losing gastroenteropathy may commonly have allergic enteritis or eosinophilic gastroenteritis; these conditions impair the mucosal

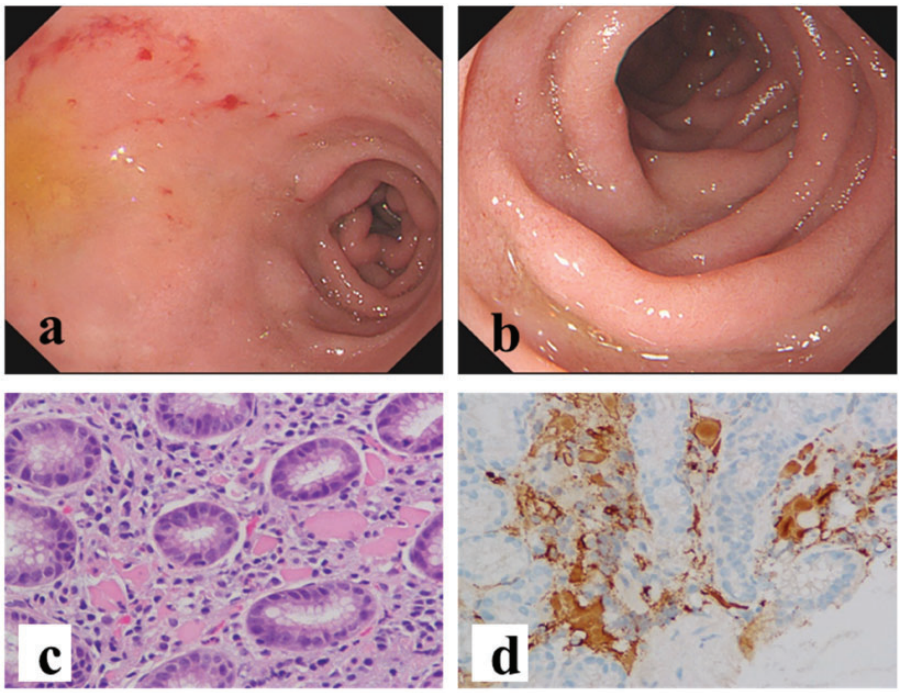

Figure 3. (a) The mucosa of the duodenal bulb was slightly congested with edema, and the villi were thickened. (b) Scattered white punctate mucosal changes were present in the descending duodenum. (c) Histopathology of tissues from the gastric antrum showed microscopic nodular aggregates of pink amorphous material in the lamina propria (hematoxylin and eosin stain 400×) and (d) these were stained positively for κ-light chain (400×) but negatively for λ-light chain (images not shown).

barrier integrity, allowing protein to leak into the gastrointestinal lumen.[9] The diagnosis of protein-losing enteropathy is based on determining the fecal α1-antitrypsin concentration and clearance and performing 51Cr-labeled or 99mTc-labeled human serum albumin scintigraphy.[10,11] The endoscopic findings are not specific.

Although LCDD is a well-known monoclonal gammopathy of renal significance, cardiac[12] or gastrointestinal manifestations are also clinically very important. We analyzed our two patients based on the assessment of organ involvement in amyloid light chain amyloidosis.[13] In Case 1, the kidneys and gastrointestinal tract were likely affected as indicated by proteinuria, positive serum IgG-κ monoclonal immunoglobulin, and typical results of tissue immunohistochemistry. However, heart involvement could not be confirmed on the basis of only the slightly elevated troponin T concentration (0.053 ng/mL) without cardiac magnetic resonance imaging. In Case 2, we considered isolated LCDD of the gastrointestinal tract because the urine protein test was negative, the serum myocardial enzymes and liver and renal function tests were normal, and color Doppler ultrasonography of the heart, kidneys, and liver indicated normality. Nevertheless, the diagnosis of LCDD in both cases had some limitations because cardiac magnetic resonance imaging, renal biopsy, and bone marrow examination could not be performed without the consent of the patients and their

families. Moreover, it is very important to perform electron microscopy to exclude the presence of amyloid deposits. The negative Congo red staining and the absence of apple-green birefringence, characteristic of amyloid deposits, together with the positivity of deposits for κ-light chain (or λ-light chain) in the immunofluorescence examination, may be sufficient to support the diagnosis of LCDD. However, cases of amyloidosis with inconclusive Congo red staining have been reported in the literature.[14,15]

Basic scientific studies have shown that amino acid chains in the variable region of monoclonal light chains are closely related to organ involvement of LCDD.[16,17] Mass spectrometry can accurately identify and classify serum M proteins via high-resolution molecular weight detection, which is currently considered the optimal technique for LCDD workup.[18]

A bortezomib-based regimen is recommended as the first-line treatment.[19] The patient in Case 1 gradually achieved remission after treatment with bortezomib and lenalidomide. Daratumumab, an anti-CD38 monoclonal antibody, is used to treat refractory LCDD as a single agent or in combination with rapid induction of the hematological response.[20] Doxycycline was recently approved for clinical use as an adjunct to systemic chemotherapy[21]; however, whether doxycycline has a therapeutic effect on LCDD remains unknown. Research has recently revealed the concept of monoclonal gammopathy of clinical significance, a newly recognized clinical entity encompassing various pathological conditions associated with monoclonal gammopathy of undetermined significance.[22] Further research is warranted to bridge the gap in understanding this emerging clinical category.

Age and serum creatinine are the main risk factors associated with the prognosis of LCDD.[23] Older age is positively correlated with the severity of LCDD. A markedly decreased estimated glomerular filtration rate is an independent predictor of overall survival.[24] The estimated glomerular filtration rate was normal in both of our patients, with may have contributed to the good clinical outcome. A telephone follow-up in September 2022 revealed that their symptoms were stable.

Conclusion

LCDD was diagnosed on the basis of pathological evaluation and clinical manifestations in two patients. Early diagnosis and treatment of LCDD will benefit organ protection and prolong patient survival.

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Author contributions

Wei CX and Yang DY designed the study, analyzed the data, wrote the manuscript, and approved the final manuscript. Wei CX, Tong SW, Wang M, Huang J, Li JM, and Su JJ collected the data, read the manuscript, and approved the final manuscript.

Data availability statement

All data generated or analyzed during this study are included in this article.

Declaration of conflicting interests

The authors declare that there is no conflict of interest.

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