

# A unique case of laparoscopically resected gastric adenocarcinoma concurrent with lanthanum deposition

Kosuke Hirose<sup>1</sup>, Shunichi Saito<sup>2</sup>, Yumi Oshiro<sup>3</sup>, Kazuhito Minami<sup>3</sup>, Koji Ikegami<sup>3</sup>, Koichi Kurahara<sup>3</sup>, Takuya Honbo<sup>1</sup>, Noriaki Sadanaga<sup>1</sup>, and Hiroshi Matsuura<sup>1</sup>

<sup>1</sup>Saiseikai Fukuoka General Hospital

<sup>2</sup>Kyushu University

<sup>3</sup>Matsuyama Red Cross Hospital

May 23, 2022

## Abstract

We present a unique case of laparoscopically resected gastric adenocarcinoma with concurrent lanthanum deposition. Lanthanum depositions occasionally appear similar to carcinomas on endoscopy. and surgical resection should be considered for such concurrent carcinoma. Furthermore, more research is needed to clarify the relationship between carcinogenesis and lanthanum deposition.

## Introduction

Lanthanum carbonate is one of the widely used phosphate binders, which are orally taken to reduce serum phosphate levels in dialysis patients with chronic kidney disease.<sup>1</sup>Lanthanum carbonate binds to dietary phosphate and forms insoluble complexes and is excreted in feces, but recently lanthanum carbonate deposition in the gastric and duodenal mucosa has been reported in patients taking them.<sup>2-8</sup> In previous studies, the findings of lanthanum deposition with endoscopy in gastric mucosa, white lesions, elevations, erosions, and ulcerations have been usually described in the gastric mucosa. Pathologically, lanthanum depositions usually appear as subepithelial collections of histocytes or small foreign body granulomas, accompanied by intestinal metaplasia, regenerative changes, and foveolar hyperplasia.<sup>1,9-11</sup>Although some studies have reported that lanthanum deposition and subsequent mucosal changes potentially induce neoplastic lesions, the relationship between lanthanum deposition and carcinogenesis is unknown.<sup>11,12</sup>

There are few reports of gastric cancer concurrent with lanthanum deposition<sup>2,12-14</sup> and surgical resection of gastric cancer concurrent with lanthanum deposition.<sup>2,12</sup>Furthermore, unlike past resected cases, in this case, it was difficult to clearly distinguish gastric adenocarcinoma from mucosal changes because of its confusing appearance following lanthanum deposition.

## Case presentation

A 73-years-old man had been on peritoneal dialysis for 9 years for chronic renal failure due to immunoglobulin A nephropathy and had switched to hemodialysis 3 years before the operations.

He had been taking lanthanum carbonate for seven years. Several months after lanthanum carbonate initiation, regular endoscopy revealed white granular lesions on the gastric mucosa at the gastric body and fundus (Fig.1-A). A biopsy of these lesions revealed chronic active inflammation with regenerative epithelium, intestinal metaplasia, and lanthanum deposition. Regular annual endoscopy revealed that these lesions had grown, changed morphologically, and spread gradually (Fig.1-B), but they showed no malignancy. Two months before the operation, regular endoscopy revealed a gradually growing, reddish, and elevated mucosa

surrounded by white granular mucosa in the gastric antrum (Fig.2-A). Narrow band imaging (NBI) showed no signs of malignancy, such as an irregular microvascular pattern (Fig.2-B), but histological examination revealed well-differentiated adenocarcinoma. The clinical stage was T1bN0M0 stage I based on the TNM classification specified by the International Union Against Cancer (UICC). The boundary between the adenocarcinoma and mucosal changes with lanthanum deposition was unclear by endoscopy with NBI, and neoplastic lesions seemed to be spread around the gastric body. Therefore, we planned to perform a surgical operation to achieve curative resection and laparoscopic distal gastrectomy with lymph node dissection. Histopathological examination revealed a well-differentiated tubular adenocarcinoma, which was limited to the antrum surrounded by lanthanum nodules (Fig.3-A). The tumor was limited to the mucosa at the gastric antrum, and the pathological stage was T1aN0M0 stage I. Lanthanum deposition was observed in the lamina propria of the carcinoma and gastric mucosa (Fig.3-B). Histological alterations, such as glandular atrophy and hyperplasia, were also observed. The resected lymph nodes also included lanthanum deposits eaten by macrophages (Fig.3-C). In the interstitium of cancerous and non-cancerous lesions, lanthanum was mostly eaten by macrophages that expressed CD68 (Fig.4-A, B).

## Discussion

We report a rare case of laparoscopically resected gastric adenocarcinoma with concurrent lanthanum deposition. In this case, we chose surgical resection because of the ambiguous boundary between malignant tissue and mucosal changes with lanthanum deposition.

There are a few reports of surgically resected gastric cancer with lanthanum deposition, as summarized in Table 1.<sup>2,12</sup> Yabuki et al. reported a summary of three patients with gastric cancer accompanied by lanthanum deposition who underwent surgical resection.<sup>11</sup> They reported that the duration of lanthanum administration ranged from 3 to 36 months, and the depth of cancer was the entire submucosa (range: 1.5–5 mm). Lanthanum deposition was identified in the regional lymph nodes to some degree in all three cases. These findings support the hypothesis that lanthanum malabsorption in the gastric mucosa leads to other lymph nodes via lymphatic flow. Tonooka et al. reported a case of multiple but early gastric cancers in a patient with lanthanum deposition who underwent subtotal gastrectomy after 7 months of drug use.<sup>12</sup> In this case, many macrophages with lanthanum deposits accumulated in the lamina propria of the gastric wall and tumors, which was confirmed by scanning electron microscopy-energy-dispersive X-ray spectroscopy (SEM-ESD). They also showed intestinal metaplasia associated with lanthanum deposition and considered that altered tight junction proteins may lead to its permeability, possibly resulting in lanthanum deposition. Our case showed mucosal atrophy and metaplasia, including a cancerous lesion at the gastric antrum, with CD68-positive macrophages containing lanthanum deposits, which were also identified in regional lymph nodes.

In gastric adenocarcinoma concurrent with lanthanum deposition, the findings of lanthanum deposition by endoscopy are occasionally similar to carcinoma, and it can be difficult to mark the boundary of the neoplasm and lesions. The findings of lanthanum deposition have been usually described as shiny, bright white, and of varied sizes and shapes, from small and flat to elevated plaques.<sup>9</sup> Gastric carcinoma is also known to show various findings with endoscopy. In previous reports, early gastric cancer with lanthanum deposition was observed as a depressed area surrounded by annular whitish lanthanum-deposited mucosa<sup>8,13</sup> and resected by endoscopy. Yabuki et al. summarized the cases of three patients with concurrent gastric cancer who received laparoscopic distal gastrectomy, but the endoscopic findings showed a clear boundary between malignant tissue and the surrounding mucosa with lanthanum deposition.<sup>11</sup> Tonooka et al. also reported concurrent gastric cancer with lanthanum deposition in patients receiving subtotal gastrectomy, but they did not refer to the endoscopic findings.<sup>12</sup> The usefulness of magnified imaging using NBI was recently reported, and it shows irregular vascular and pit structures of malignant tissues.<sup>13</sup> However, in this case, the carcinoma was detected within multiple reddish granular areas with lanthanum deposition without any specific malignant findings with NBI, and it was difficult to find the boundary between the neoplasm and lanthanum deposition. Therefore, we considered the possibility of non-curative resection with endoscopy and other lurking regions, and the carcinoma was surgically resected. Furthermore, using laparoscopy made it possible to observe the

whole serous membrane of the stomach, nearby lymph nodes, and other organs in detail.

The relationship between malignancy and lanthanum deposition in gastric cancer concurrent with lanthanum deposition is unknown. Yabuki et al. examined the effect of oral administration of lanthanum carbonate on gastric mucosa in a rat model.<sup>11</sup> They showed that it caused various histologic alterations such as glandular atrophy, the proliferation of mucous neck cells, and intestinal metaplasia, and concluded that these mucosal injuries, named lanthanum gastropathy, could potentially induce abnormal cell proliferation or neoplastic lesions. In sequential changes of the gastric epithelium due to lanthanum gastropathy, it becomes difficult to identify the boundary between the neoplasm and mucosal changes without malignancy, and surgical resection is recommended in such cases.

We present a rare case of gastric adenocarcinoma concurrent with lanthanum deposition in a patient who underwent laparoscopic distal gastrectomy due to ambiguous borders. In our case, it is difficult to mark the border between the neoplasm and lesions due to lanthanum deposition, and we performed surgical resection to secure a curative margin. The clinical significance and relationship between neoplasm and lanthanum deposition have been suggested, but enough evidence has not been reported. Our results add to this growing body of data and will aid in clarifying this relationship.

Table.1 Summary of surgically resected gastric cancer with lanthanum deposition, including this case

case	age/sex	location	histology	differentiation	T	pN	dose of LC (mg/day)	duration of LC administration (months)	H.pylori infection	PPI	Laparoscopic surgery	resected range	prognosis
1	81/F	multiple	Adeno.	well	T1a	0	750	7	NA	NA	no	subtotal	3y alive no recu
2	77/F	antrum	Adeno.	well	T1b	0	1500	36	negative	use	yes	distal	unkn
3	68/F	body	Adeno.	poor/sig	T1b	0	750	3	NA	use	yes	distal	unkn
4	77/M	antrum	Adeno.	well	T1b	1	750	12	NA	not use	yes	distal	unkn
5	73/M	antrum	Adeno.	well	T1a	0	750	84	negative	use	yes	distal	8m alive no recu

LC, lanthanum carbonate; PPI, proton pump inhibitor; Adeno, adenocarcinoma; NA, not available

### Authors' contributions

KH operated on and followed the patients, selected the associated data and edited the manuscript accordingly. SS also operated on and took care of the patients. YO analyzed the specimens and supervised the pathology.

KM performed the surgery on the patient as a supervisor. KI and KK participated in the treatment of the patient as gastroenterologists. TH, NS, TN and HM supervised and revised the article. All the authors have read and approved the final manuscript.

## Acknowledgments

We would like to thank Editage (<https://www.editage.jp/>) for the English language editing of this manuscript.

## References

1. Zhang C, Wen J, Li Z, Fan J. Efficacy and safety of lanthanum carbonate on chronic kidney disease-mineral and bone disorder in dialysis patients: a systematic review. *BMC Nephrol* . 2013;14:226. doi: 10.1186/1471-2369-14-226.
2. Yabuki K, Shiba E, Harada H, et al. Lanthanum deposition in the gastrointestinal mucosa and regional lymph nodes in dialysis patients: analysis of surgically excised specimens and review of the literature. *Pathol Res Pract* . 2016;212(10):919-926. doi: 10.1016/j.prp.2016.07.017.
3. Tatsuta T, Mikami T, Chinda D, et al. Case report of lanthanum deposition in the esophagus. *Clin J Gastroenterol* . 2020;13(5):683-687. doi: 10.1007/s12328-019-01085-4.
4. Goto K, Ogawa K. Lanthanum deposition is frequently observed in the gastric mucosa of dialysis patients with lanthanum carbonate therapy: A Clinicopathologic Study of 13 Cases, Including 1 Case of lanthanum granuloma in the Colon and 2 nongranulomatous Gastric Cases. *Int J Surg Pathol* . 2016;24(1):89-92. doi: 10.1177/1066896915613434.
5. Makino M, Kawaguchi K, Shimojo H, Nakamura H, Nagasawa M, Kodama R. Extensive lanthanum deposition in the gastric mucosa: the first histopathological report. *Pathol Int* . 2015;65(1):33-37. doi: 10.1111/pin.12227.
6. Haratake J, Yasunaga C, Ootani A, Shimajiri S, Matsuyama A, Hisaoka M. Peculiar histiocytic lesions with massive lanthanum deposition in dialysis patients treated with lanthanum carbonate. *Am J Surg Pathol* . 2015;39(6):767-771. doi: 10.1097/PAS.0000000000000385.
7. Hattori K, Maeda T, Nishida S, et al. Correlation of lanthanum dosage with lanthanum deposition in the gastroduodenal mucosa of dialysis patients. *Pathol Int* . 2017;67(9):447-452. doi: 10.1111/pin.12564.
8. Yamada T, Oyama T, Tomori A, et al. Distribution of lanthanum carbonate in the gastric mucosa confirmed by electron microscopy with a magnified endoscopy: a case report and literature review. *Clin J Gastroenterol* . 2020;13(3):365-371. doi: 10.1007/s12328-019-01076-5.
9. Shitomi Y, Nishida H, Kusaba T, et al. Gastric lanthanosis (lanthanum deposition) in dialysis patients treated with lanthanum carbonate. *Pathol Int* . 2017;67(8):389-397. doi: 10.1111/pin.12558.
10. Ban S, Suzuki S, Kubota K, et al. Gastric mucosal status susceptible to lanthanum deposition in patients treated with dialysis and lanthanum carbonate. *Ann Diagn Pathol* . 2017;26:6-9. doi: 10.1016/j.anndiagpath.2016.10.001.
11. Yabuki K, Haratake J, Tsuda Y, et al. Lanthanum-induced mucosal alterations in the stomach (lanthanum gastropathy): a comparative study using an animal model. *Biol Trace Elem Res* . 2018;185(1):36-47. doi: 10.1007/s12011-017-1235-4.
12. Tonooka A, Uda S, Tanaka H, Yao A, Uekusa T. Possibility of lanthanum absorption in the stomach. *Clin Kidney J* . 2015;8(5):572-575. doi: 10.1093/ckj/sfv062.
13. Takatsuna M, Takeuchi M, Usuda H, Terai S. Case of early-stage gastric cancer identified in the gastric mucosa with lanthanum phosphate deposition. *Endosc Int Open* . 2019;7(7):E893-E895. doi: 10.1055/a-0918-5804.

14. Tabuchi M, Takeshima F, Akazawa Y, Nakao K. Early gastric cancer with diffuse lanthanum deposition. *Intern Med* . 2019;58(3):447-448. doi: 10.2169/internalmedicine.1543-18.

### Figure legends

#### Figure 1.

- (A) The endoscopic image of lanthanum deposition on stomach few months after drug initiation.
- (B) Follow-up endoscopic image of lanthanum deposition at the same lesions

#### Figure 2.

- (A) The endoscopic images of grown lanthanum deposition and gastric cancer at antrum (arrowhead).
- (B) Narrow band imaging of cancer showing no irregular microvascular pattern.

#### Figure 3.

- (A) Resected specimen and mapping of the malignant region (yellow line)
- (B) Histological image of gastric adenocarcinoma with hematoxylin and eosin staining. Arrowheads indicate lanthanum carbonate eaten by histiocytes.
- (C) Histological image of a resected lymph node. It also includes histiocytes eating lanthanum carbonate (arrowhead).

#### Figure 4.

The histological images indicate the distribution of CD68-positive macrophages eating lanthanum carbonate with hematoxylin and eosin staining (A). Immunohistochemical staining with CD68 monoclonal antibody at almost the same specimen (B)

#### Hosted file

figure\_0517.pptx available at <https://authorea.com/users/484335/articles/570193-a-unique-case-of-laparoscopically-resected-gastric-adenocarcinoma-concurrent-with-lanthanum-deposition>