

Original article

Lanthanum deposition in the gastrointestinal mucosa and regional lymph nodes in dialysis patients: Analysis of surgically excised specimens and review of the literature



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ARTICLE INFO

Article history:

Received 25 April 2016

Received in revised form 22 June 2016

Accepted 31 July 2016

Keywords:

Lanthanum carbonate

Dialysis

Gastrointestinal

Regional lymph node

Deposition

Granuloma

ABSTRACT

Lanthanum carbonate (LC) is one of the most potent phosphate binders currently used to reduce serum phosphate levels in dialysis patients with end-stage renal disease (ESRD). LC forms insoluble complexes with dietary phosphate that pass through the gastrointestinal (GI) tract with little absorption. GI lesions due to lanthanum deposition in biopsy specimens or those in endoscopic submucosal dissection (ESD) in dialysis patients have been recently identified. Here, we describe more detailed histopathological findings in the gastroduodenal mucosa and regional lymph nodes in three patients with gastric cancer. Three patients with ESRD, two elderly women and one man, underwent dialysis and were treated with LC for 3–36 months. The patients underwent laparoscopic distal gastrectomy and lymph node dissection due to gastric cancer. Many subepithelial histiocyte aggregates or small foreign body granulomas, which contained gray or brown pigments or crystal-like structures, were mostly present in non-neoplastic areas of the upper GI. Lanthanum accumulation was noted in the duodenal mucosa and the antral and body mucosae of the gastric lesser curvature. Lanthanum was also deposited in the regional lymph nodes of the three patients. Electron microscopy with energy dispersive X-ray spectroscopy confirmed lanthanum and phosphorus deposits in histiocytes. Long-term prognosis of patients and the excretion or the metabolic pathway of accumulated lanthanum remain unclear.

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1. Introduction

Lanthanum carbonate (LC) is one of the most potent non-calcium and non-aluminum phosphate binders that reduce serum phosphate levels in dialysis patients with end-stage renal disease (ESRD). LC is widely used to effectively control serum phosphate levels [1–5]. Recent reports have described lanthanum deposition in the GI mucosa [6–10] although LC forms insoluble complexes with dietary phosphate that pass through the gastrointestinal (GI) tract where LC is thought to be poorly absorbed [11]. However, the

histopathological assessment of LC status in the GI tract of dialysis patients with ESRD remains limited. Here, we describe detailed histopathological findings of lanthanum deposition in the gastroduodenal mucosa and regional lymph nodes in surgically excised specimens of gastric tumor.

2. Materials and methods

The cases involved three patients with gastric cancer who underwent surgical resection between 2009 and 2015 in the University Hospital of Occupational and Environmental Health, Japan. All patients were treated with dialysis and oral LC administration for ESRD and hyperphosphatemia, respectively (Table 1).

Whole mounts of all surgically excised specimens were formalin-fixed, paraffin-embedded, and routinely processed. The 4- μ m-thick histological sections were stained with hematoxylin and eosin, Berlin blue, and toluidine blue. An immunohistochemical examination was performed using a monoclonal antibody against

Abbreviations: EDS, energy dispersive X-ray spectroscopy; ESD, endoscopic submucosal dissection; ESRD, end-stage renal disease; GI, gastrointestinal tract; LC, lanthanum carbonate; SEM, scanning electron microscopy.

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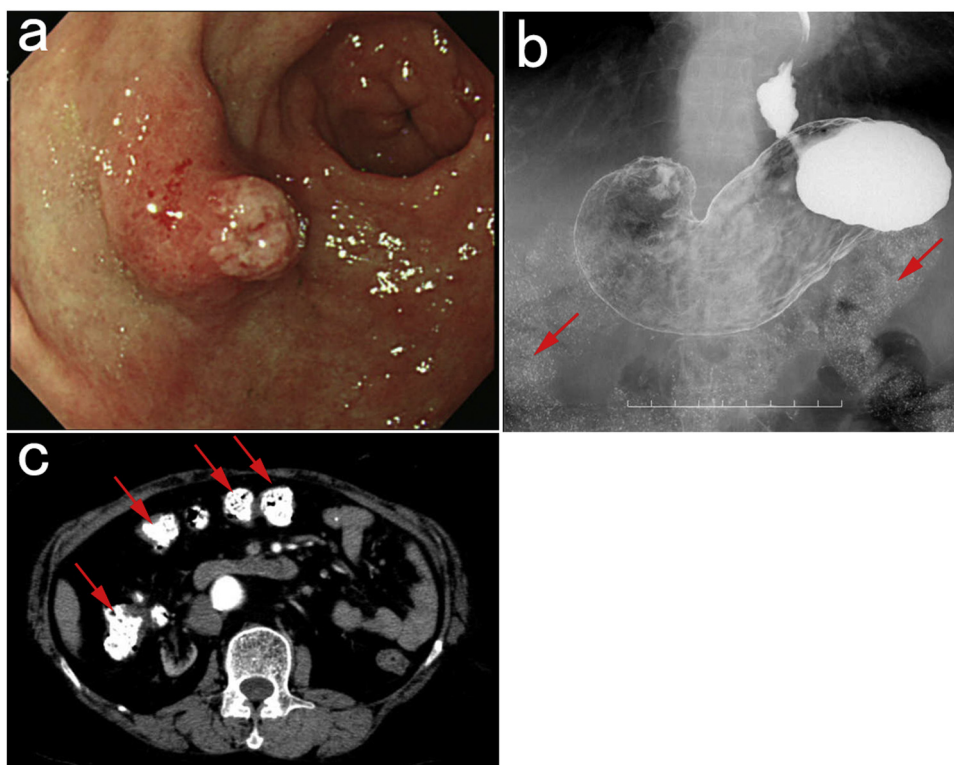


Fig. 1. Endoscopic findings of case 1, which shows a protruding lesion with atrophic gastritis in the antrum of the stomach (a). In gastrointestinal series (b) and computed tomography (c), numerous radio-opaque microparticles or positive contrast (arrows) are seen in the intestine.

Table 1
Case summary.

	Case 1	Case 2	Case 3
Sex	Female	Female	Male
Age (years)	77	68	77
Cause of renal failure	Nephrosclerosis	Diabetic nephropathy	Unknown
Duration of dialysis (years)	17	8	5
Mode of dialysis	Hemodialysis	Peritoneal 4 years Hemodialysis 4 years	Hemodialysis
Duration of LC administration (months)	36	3	12
Dose of LC (mg/day)	1500	750	750
Clinical presentation	None	Anemia	Anemia
Site of gastric cancer	Antrum	Body	Antrum
Depth of cancer	SM (5 mm)	SM (1.5 mm)	SM (2 mm)
Deposition area	Duodenum, antrum, body	Duodenum, antrum, body	Body
Total numbers of deposited lymph nodes	24/33	4/22	1/27
Lesser curvature (station 1, 3, 5, 7)	10/13	1/6	0/11
Greater curvature (station 2, 4, 6)	12/12	3/12	1/7
Suprapancreatic (station 8a, 9, 11p)	2/8	0/4	0/9

CD68. The sections were deparaffinized in xylene, dehydrated in graded ethanol series, and examined using scanning electron microscopy (SEM) (Miniscope TM3000, Hitachi, Japan) and energy dispersive X-ray spectroscopy (EDS) (Quantax 70, Bruker Nano GmbH, Germany).

3. Results

3.1. Case 1

A 77-year-old woman with chronic renal failure caused by nephrosclerosis, who underwent hemodialysis for 17 years, was admitted in our hospital for gastric cancer treatment. Her past medical history included hypertension, atrial fibrillation, and hyperparathyroidism. She received LC (1500 mg/day) for three years together with vitamin D, calcium channel blocker, proton

pump inhibitor, and warfarin, an anticoagulant. Screening upper GI endoscopy revealed a protruding lesion in the antrum of the stomach, which was otherwise atrophic (Fig. 1a). The biopsy of the protruding lesion was performed and revealed well-differentiated tubular adenocarcinoma. Numerous radio-opaque microparticles in the intestine, which were suggestive of LC binding to dietary phosphate, were seen in the GI series and computed tomography (Fig. 1b,c). She underwent laparoscopic distal gastrectomy and regional lymph node dissection. The macroscopic finding of the resected stomach showed an elevated gastric lesion in the antrum, measuring approximately 2 cm in diameter. Tubular adenocarcinoma was confined microscopically to the gastric mucosa and submucosa (depth, 5 mm) without vascular invasion or lymphatic permeation. All 33 regional lymph nodes examined were free of the carcinoma cells. Many subepithelial histiocyte aggregates or small foreign body granulomas contain gray or brown pigments or

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