



Gastric Langerhans Cell Histiocytosis: Case Report and Review of the Literature

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Langerhans cell histiocytosis (LCH) is a rare disease of unknown etiology and is characterized by a clonal proliferation of Langerhans cells.¹ The clinical presentation of LCH is variable, ranging from single organ to multisystem involvement; patients may experience benign to life-threatening outcomes.¹ Localization of LCH to the stomach is extremely rare and is most often found in pediatric patients with systemic disease.² Here we present a case of localized LCH to the stomach in a 64-year-old man who underwent a complete resection of the lesion by endoscopic submucosal dissection (ESD).

CASE REPORT

A 64-year-old man was referred to a gastroenterologist for further evaluation of an abnormality found during an upper gastrointestinal examination. This patient had nothing remarkable in his medical history except medical treatment for hyperthyroidism. Esophagogastroduodenoscopy revealed an elevated mucosal lesion approximately 1 cm in size in the gastric fundus (Fig. 1A). The surface of the lesion was smooth with focal erosion. Microscopic examination of the endoscopic biopsy specimen revealed increased eosinophilia, and a cluster of histiocytic cells infiltrated the lamina propria and were mixed with lymphocytes, neutrophils, and plasma cells (Fig. 1C). The histiocytic cells had elongated nuclei, intranuclear grooves, and irregular nuclear mem-

branes, as well as abundant fine granular eosinophilic to clear cytoplasm. Histiocytic cell clusters showed strong immunoreactivity to S100 and CD1a (Fig. 1D), while they were negative to cytokeratin AE1/AE3 and leukocyte common antigen. Through a combination of morphological and immunohistochemical analyses, a diagnosis of LCH was confirmed. A gastroenterologist performed ESD for complete removal of the lesion. The ESD specimen showed a very focal remnant LCH lesion that had been completely removed (Fig. 1B). Following complete resection of the gastric LCH lesion, a comprehensive evaluation was performed to determine the extent of the disease. No evidence of multisystem involvement was found. The patient's 6-month follow-up visit revealed no local or systemic recurrence, and the patient remained in good health.

DISCUSSION

LCH is a rare disease identified in both children and adults and is characterized by infiltration of histiocytic cells in various organs.³ The pathogenesis and etiology of LCH are not fully understood.¹ A recent hypothesis suggests that LCH cells are derived from bone marrow monocyte precursors that differentiate into antigen-presenting cells (i.e., Langerhans cells or dendritic cells) in the epidermis, respiratory tract, and lymph nodes. The presence of monoclonality itself has been used as evidence that this disease is a clonal neoplastic disorder. Despite the neoplastic nature of the condition, the clinical course of LCH is heterogeneous. Therefore, treatment of LCH depends on the extent and severity of the disease at the time of diagnosis, which includes the number of involved organs and the presence of normal organ function.¹

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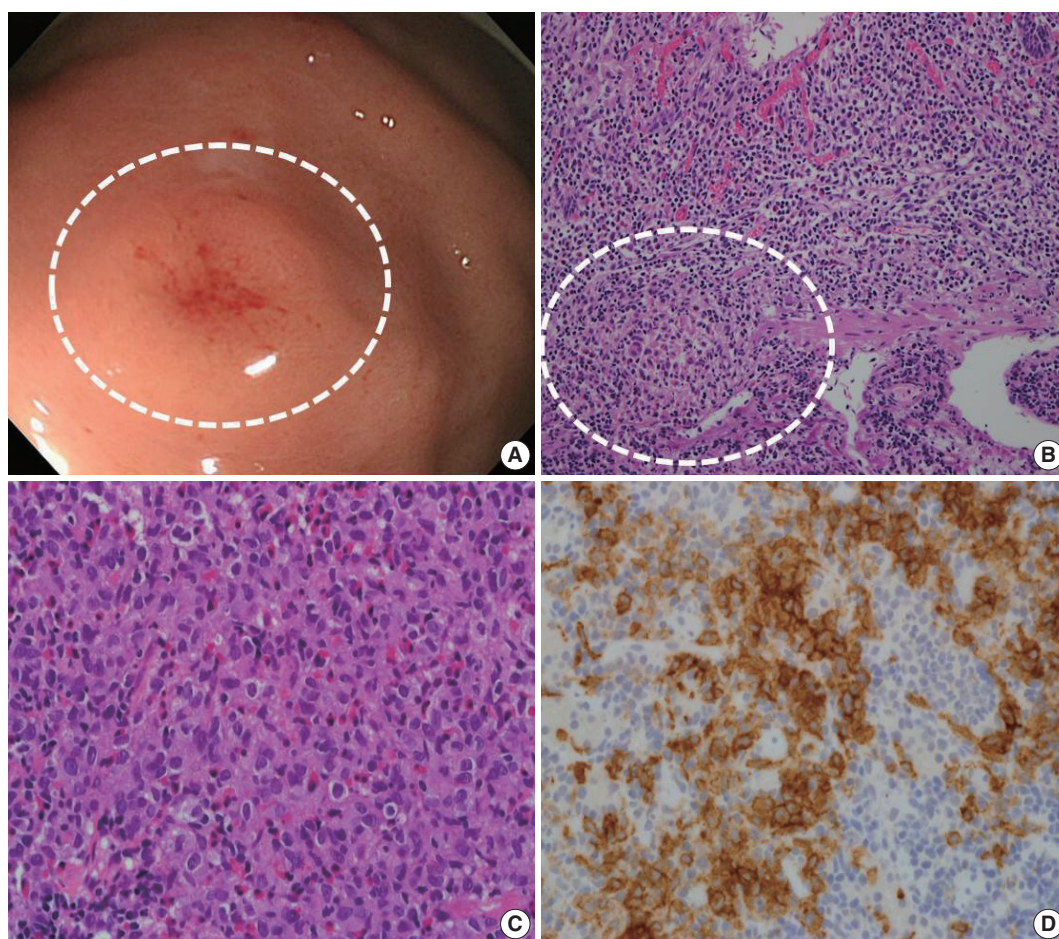


Fig. 1. Endoscopic and histologic finding of gastric Langerhans cell histiocytosis. (A) A mild elevated mucosal lesion (1 cm in size) with central erosion is observed upon gastroenteroscopy (circle). The lesion is located in the fundus of the stomach. (B) Microscopic analysis of the endoscopic submucosal dissection specimen. Focal histiocytic cell aggregates are present in the lamina propria and muscularis mucosa, with abundant eosinophils and other inflammatory cells. (C) Microscopic analysis of the endoscopic biopsy specimen reveals histiocytic cell aggregates in the lamina propria of the mucosa, with abundant eosinophil infiltration. Lymphocytes and plasma cells are also observed. The histiocytic cells show an irregular nuclear membrane and groove. These cells have abundant and granular eosinophilic to clear cytoplasm. (D) Immunohistochemistry for CD1a. The histiocytic cells show positive staining for CD1a.

Involvement of the gastrointestinal tract is very rare and has been associated with systemic involvement and poor prognosis.⁴ In pediatric patients, LCH in the gastrointestinal tract produces symptoms such as vomiting, loose stool, and abdominal pain and is related to a poor prognosis in the majority of neonatal cases; in these patients, skin lesions usually precede gastrointestinal LCH.^{4,5} In contrast to children, adult patients are asymptomatic and present with solitary polypoids or elevated lesions.⁴ Only six cases in adult of gastric LCH have been reported in the literature.^{4,6-10} In contrast to pediatric LCH, adult gastric LCH appears as a unifocal disease without recurrence or progression, in a similar manner to our case (Table 1). Like many other gastric LCH cases, an elevated mucosal lesion was noted in our patient by the gastroenterologist, whose initial impression was a sub-

mucosal tumor. Endoscopic findings of gastric LCH mucosa are sometimes confused with gastric tumors presenting as polypoids and ulcerative mucosa.^{2,4} Despite the absence of clinical features, gastric LCH shows the typical histological characteristics of LCH in other organs.^{3,4} Histologically, histiocytic cells resemble Langerhans cells of the epidermis. Langerhans cells form a sheet of islands with indistinct cell borders and abundant eosinophilic cytoplasm. Their nuclei are elongated and irregular, exhibiting vesicular chromatin with a nuclear groove and often presenting with a single prominent nucleoli.^{3,4} Langerhans cells are usually mixed with other inflammatory cells such as eosinophils, lymphocytes, plasma cells, and neutrophils. In the literature, predominant eosinophil infiltration has been reported in 50% of cases with gastric LCH.⁴ In a similar manner to a previous re-

Table 1. Comparison of reported cases and presented case

Case no.	Reference	Age (yr)/ Sex	Symptom	Endoscopic finding	Site	Multiplicity	Specimen	Multisystem ^a	Outcomes	Follow-up
1	Singhi and Montgomery ⁴	68/M	Dysphasia	Polyp	Antrum	Solitary	Biopsy	Absent	Remission	22 mo
2	Iwafuchi <i>et al.</i> ⁶	49/F	Asymptomatic	Sessile elevation	Throughout the stomach	Multiple	Biopsy	Absent	Remission	5.6 yr
3	Nihei <i>et al.</i> ⁷	47/F	R/O cancer	Flat	Body	Solitary	Resection	Absent	Remission	20 mo
4	Vazquez and Ayestaran ⁸	59/F	Epigastric pain	Ulcer	Lesser curvature	Solitary	Resection	N/A	N/A	N/A
5	Lee <i>et al.</i> ⁹	51/M	Asymptomatic	Elevated	Antrum	Solitary	Biopsy, ESD	Absent	Remission	12 mo
6	Wada <i>et al.</i> ¹⁰	53/F	Abdominal discomfort	Polypoid	Throughout the stomach	Multiple	Biopsy	Absent	Alive/skin lesion developed	2 yr
7	Present case	64/M	Asymptomatic	Elevated	Fundus	Solitary	Biopsy, ESD	Absent	Remission	6 mo

M, male; F, female; R/O, rule out; N/A, not applicable; ESD, endoscopic submucosal dissection.

^aMultisystem involvement at diagnosis.

port,⁴ our case showed aggregates of histiocytic cells with Langerhans cell nuclear features, which were mixed with inflammatory cells, mainly eosinophils. Immunohistochemical analysis is helpful to confirm the diagnosis, and Langerhans cells show diffuse immunoreactivity for S100 and CD1a.^{1,4} In such cases, we suggest that stomach LCH could appear as a submucosal tumor upon endoscopy. Pathologists should consider the possibility of LCH if microscopic observation of biopsy specimens reveals increased eosinophilia or histiocytic cells. In these cases, immunohistochemical staining for S100 and CD1a is needed.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

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