CASE REPORT

Gastric Langerhans cell histiocytosis

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Introduction

Langerhans cell histiocytosis (LCH), formerly known as histiocytosis X, is a disease in which various organs and tissues are infiltrated by proliferating histiocytes phenotypically related to Langerhans cells.\textsuperscript{1,2} The extent of involvement ranges from unifocal to disseminated, and the clinical severity from benign and self-limiting to progressive and sometimes fatal.\textsuperscript{3}

Involvement of the gastrointestinal tract is rare (<5%), but when present it is found mainly in the small and large intestine and is usually asymptomatic.\textsuperscript{3} Gastric involvement is even rarer and only eight cases of gastric LCH have been reported, to our knowledge.\textsuperscript{3–10}

We report a case of multifocal LCH involving stomach, skin and pituitary stalk and discuss the similarities and differences between gastric LCH and other diseases causing diffuse nodularity in the stomach such as low-grade mucosa-associated lymphoid tissue (MALT) lymphoma, reactive lymphoid hyperplasia and \textit{Helicobacter pylori}-related gastritis.

Case report

A 28-year-old man presented with mild epigastric discomfort for 5 months. He also complained of polyuria and polydipsia for 3 months. He visited a local hospital and an upper gastrointestinal series (UGIS) and gastroscopic biopsy of the gastric antrum were performed. The UGIS showed thickened areae gastricae and mucosal irregularity and nodularity extending from the proximal body of the stomach to the gastric antrum (Fig. 1). The distension and movement of the gastric wall were good. On compression study, there was no definite mass or ulcer, but multifocal nodularity in the body and the gastric antrum was confirmed (not shown). There seemed to be no abnormalities in the oesophagus or duodenum.

Endoscopy revealed thickened mucosal folds in the proximal body and mid body of the stomach. The endoscopist’s clinical impression was hypertrophic gastritis. The pathological specimen taken from the greater curvature showed conspicuous infiltration with histiocytes with indented nuclei (Fig. 2). Immunohistochemical study showed positive S-100 (Fig. 3), CD 68 and negative reaction for cytokeratin.

The patient also had multiple erythematous papules on his face detected at the first visit to the local hospital. Skin biopsy was done at the same time as the gastric biopsy revealing LCH. For evaluation of polyuria and polydipsia, a brain magnetic resonance imaging (MRI; Magnetom Expert, Siemens, Germany) was performed, and on gadolinium-enhanced T1-weighted image (TR:590, TE:12), a well-enhancing infundibular mass suggestive of Langerhans cell involvement was detected (Fig. 4). A diagnosis of LCH involving the stomach, skin, and central nervous system was made.

The patient was treated with low-dose radiation therapy for the lesion in pituitary stalk. He was conservatively managed for the lesion in the stomach using oral medication such as famotidine and sucralfate.

Four months after the initial presentation, a follow-up UGIS (Fig. 5) was performed as per routine protocol and the findings were the same as the previous UGIS. Ten months after the initial presentation, he complained of decreased visual acuity. Brain MRI revealed multifocal enhancing lesions in brain parenchyma, brainstem, and basal ganglia (not shown). He has been treated with chemotherapy using etoposide, but without response for the 8 months follow-up period. Eighteen months after the initial presentation, the follow-up endoscopic examination revealed no change (Fig. 6). We have followed up this patient for 1 year after the second endoscopic examination. The third endoscopic examination performed at 30 months after the initial presentation revealed markedly decreased mucosal nodularity in the stomach, and he is now free of gastrointestinal symptoms. The cerebral lesions have also been well controlled by a different chemotherapeutic regimen.

Discussion

Histiocytosis X is a continuum of diseases with variable clinical and pathological expressions, ranging from unifocal eosinophilic granuloma to multifocal eosinophilic granuloma and diffuse histiocytosis X of Letterer-Siwe type.\textsuperscript{11} In case of histiocytosis X, the lung and liver are the most commonly affected internal organs.\textsuperscript{12} Histiocytes have recently been divided into two...
distinct groups: cells of the mononuclear phagocytic system or those of the dendritic cell system, and cells of monocyte-macrophage lineage and those of T-zone histiocytes lineage. Langerhans cells, intermediate cells, interdigitating reticulum cells, and veiled cells belong to the latter group.

Langerhans cells differ from the other three cell types only in the possession of Birbeck granules. Iwafuchi et al. suggest that histiocytosis X of the stomach may derive from Langerhans cells or interdigitating reticulum cells appearing in the T-zone near the lymphoid follicles of the gastric mucosa.

Eight cases of gastric LCH have been reported. Among them, macroscopic appearances were polypoid in three, ulcerated in two, and flat and spherical in one case, respectively. One case was not described macroscopically. The present case shows numerous polypoid lesions in the stomach and these macroscopic appearances were similar to those of three cases previously reported.

An impressive histological feature of the present case was the granulomatous pattern displayed by
the LCH cells. The differential diagnosis of granulomatous gastritis includes foreign body reactions, infectious disorders, such as tuberculosis or late syphilis, and idiopathic disorders such as Crohn’s disease, sarcoidosis, and isolated granulomatous gastritis.\textsuperscript{3} Granulomas have also been described in association with vasculitis, gastric and extragastric carcinoma, and isolated cases of malignant lymphoma, and Whipple’s disease.\textsuperscript{15–17} The previously reported cases and present case suggests that gastric LCH can be added to the list of differential diagnosis of granulomatous gastritis.

Dhillon and Sawyer\textsuperscript{18} reported three cases of granulomatous gastritis associated with \textit{H. pylori} infection. An et al.\textsuperscript{19} reported focal or diffuse mucosal nodularity was found in seven cases of 22 patients with low-grade MALT lymphoma, and multiplicity of lesions in MALT lymphoma was closely associated with \textit{H. pylori} infection. Gastric MALT lymphoma is the major consideration in the differential diagnosis of a nodular antral mucosa in patients with \textit{H. pylori} gastritis. In a previous study, gastric MALT lymphoma showed multiple, round, variably sized (2–7 mm in diameter) nodules with poorly defined borders. In contrast, the nodules of gastric lymphoid hyperplasia have more discrete borders, a more uniform size, and not infrequently, central umbilications. Furthermore, MALT lymphoma may be associated with other radiographic findings of lymphoma, including malignant-appearing gastric ulcers, thickened lobulated folds, and polypoid mass lesions.\textsuperscript{20} Torigian et al.\textsuperscript{21} reported the radiological findings of biopsy-proven lymphoid hyperplasia of the stomach in five adult patients. They found innumerable tiny nodules in the antrum of the stomach in four patients, and in the antrum and body in one. In all patients, the lesions were relatively uniform in size (1–3 mm), appearing radiographically as smooth round discrete nodules with central umbilications manifested by punctate collections of barium. No other features of gastritis (including thickened folds, mucosal erosions, or luminal narrowing) and no ulcers or masses were detected in any of these patients.\textsuperscript{21} In the present case, the patient did not have \textit{H. pylori} colonization in stomach and the radiological and endoscopic examinations showed diffuse nodularity with relatively discrete margins, and no umbilication was detected within nodules. However, in practice, these suggested differentiating radiological signs have a limited role because of the lack of specificity of the imaging findings, and the rarity of gastric LCH.

Four of eight reported cases of gastric LCH were treated by gastrectomy as there was a suspicion of malignancy. Three patients had gastric polyposis and the diagnosis of LCH was established by biopsy.\textsuperscript{3,6,10} One report suggested that the infiltrating histiocytes may be neoplastic.\textsuperscript{4} If the histiocytes in the stomach were neoplastic, multifocal involvement might indicate progression and

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**Figure 5** Supine double contrast study in supine position in June 2000 shows grossly the same finding as in Fig. 1.

**Figure 6** At endoscopy in August 2001, there were innumerable nodular lesions in the gastric antrum.
aggressive chemotherapy would be the choice of treatment.\textsuperscript{10}

The prognosis of LCH depends not only on the age of the patient, but also the number of organs involved and the rate of tumour progression.\textsuperscript{22}

Absence of organ dysfunction, lack of progression of the disease, and older age of the patient are good prognostic factors. Some cases may be mistaken for malignant disease, but precise pathological examination will prevent unnecessary surgical resection.\textsuperscript{10}

There have been too few reported cases to permit generalization regarding the spectrum of endoscopic appearances and radiological findings in gastric LCH. Nonetheless, striking mucosal nodularity was encountered in the present case and described in three previous cases. Clinically, the distinction from various other forms of gastric polyposis must be based on histological evaluation.

In conclusion, when a patient presents with diffuse nodularity of the gastric mucosa, although extremely rare, gastric LCH should be considered.

References