



Primary Gastric Histiocytic Sarcoma Reminiscent of Inflammatory Pseudotumor: A Case Report with Review of the Literature

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Histiocytic sarcoma is a malignant proliferation of cells showing similar morphologic and immunophenotypic features to mature tissue histiocytes.¹ It is a very rare neoplasm, and only a limited number of cases have been reported. Although it occurs in lymph nodes, the majority of cases present in extranodal sites, most commonly the intestinal tract, skin, and soft tissues.² In the intestinal tract, primary gastric involvement is exceptional; only a handful of cases have been reported in the English literature.²⁻⁶ In all of these cases, the neoplastic cells were highly atypical, and malignancy was easily suggested based on the morphology. In the case presented here, diagnosis was a challenge due to the lack of a high degree of atypia or pleomorphism of the tumor cells. Herein, we report a case of primary gastric histiocytic sarcoma masquerading as an inflammatory pseudotumor. We also present the clinical characteristics of previously reported gastric histiocytic sarcomas by literature review.

CASE REPORT

A 45-year-old previously healthy woman presented with 40 days history of epigastric pain. Laboratory findings were unremarkable with the exception of mild anemia. Esophagogastroduodenoscopy revealed an irregular ulcerofungating lesion in the gastric antrum. A biopsy report suggested the presence of an inflammatory pseudotumor rather than a malignant lesion.

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However, a positron emission tomography scan showed high fludeoxyglucose uptake in the stomach, perigastric lymph nodes, and right hilar space. The patient underwent palliative distal gastrectomy due to distal gastric obstruction causing difficulties in eating. The resected specimen showed a huge, ulcerofungating mass in the antrum and pylorus of the stomach (Fig. 1A). The duodenal bulb and resection margins were also involved by the tumor. On cut section, the tumor was white-tan, solid, and somewhat rubbery in consistency (Fig. 1B). Microscopically, tumor cells showed band-like infiltration mainly in the mucosa and submucosa, but tumor cells also penetrated into the serosa in some areas (Fig. 2A). Inflammatory cells were intimately admixed with tumor cells (Fig. 2B). Tumor cells mostly had intermediate-sized nuclei with plump, pink cytoplasm (Fig. 2C). Nuclei were ovoid to elongated and frequently showed convoluted or overlapping shapes. The chromatin was fairly vesicular, and one or two micronucleoli were discernible, but they were not prominent. Pleomorphic or multinucleated tumor giant cells were scarcely observed (Fig. 2D). Mitotic figures were found up to 2-3/10 high power fields. The majority of admixed inflammatory cells were mature lymphocytes followed by plasma cells. Some neutrophils and occasional eosinophils were also noted. Metastatic tumor deposits were found in two perigastric lymph nodes (Fig. 2E). Immunohistochemical staining was performed, and the tumor cells were strongly reactive for CD68 (Fig. 3A), CD163 (Fig. 3B), leukocyte common antigen, lysozyme (Fig. 3C), and vimentin. CD4 was weakly stained in the cytoplasm of the tumor cells, and some individual tumor cells were also reactive for CD31. S-100 protein showed patch immunoreactivity for the tumor cytoplasm. Notably, MIB-1 labeling index was about 60% to 70% (Fig. 3D). Tumor cells were negative for epithelial cell markers (cytokeratin [AE1/

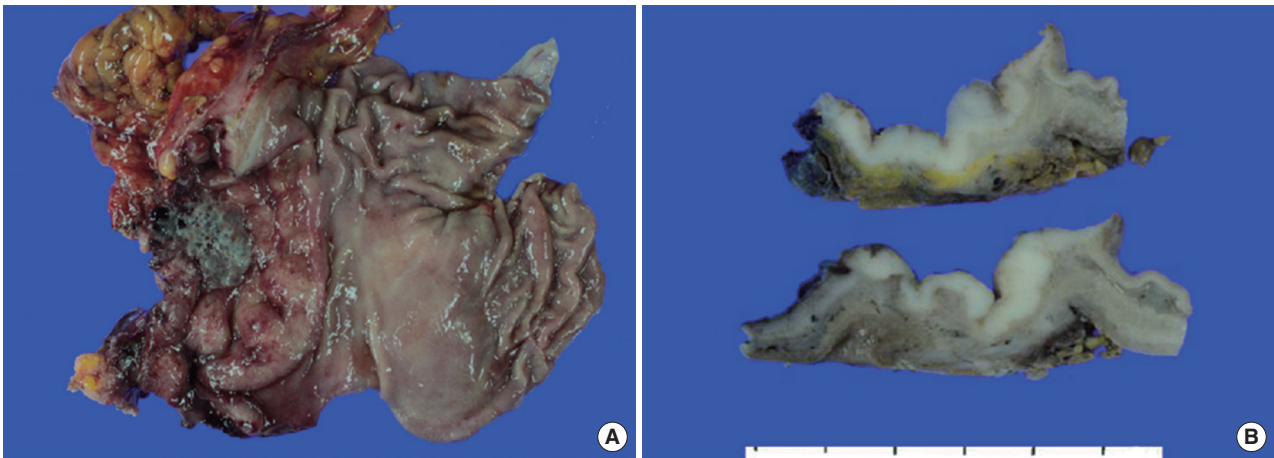


Fig. 1. (A) A huge, ulcerofungating mass involving the antrum and pylorus of the stomach is found. (B) The cut section shows a white-tan, solid lesion that runs mainly along the mucosal surface.

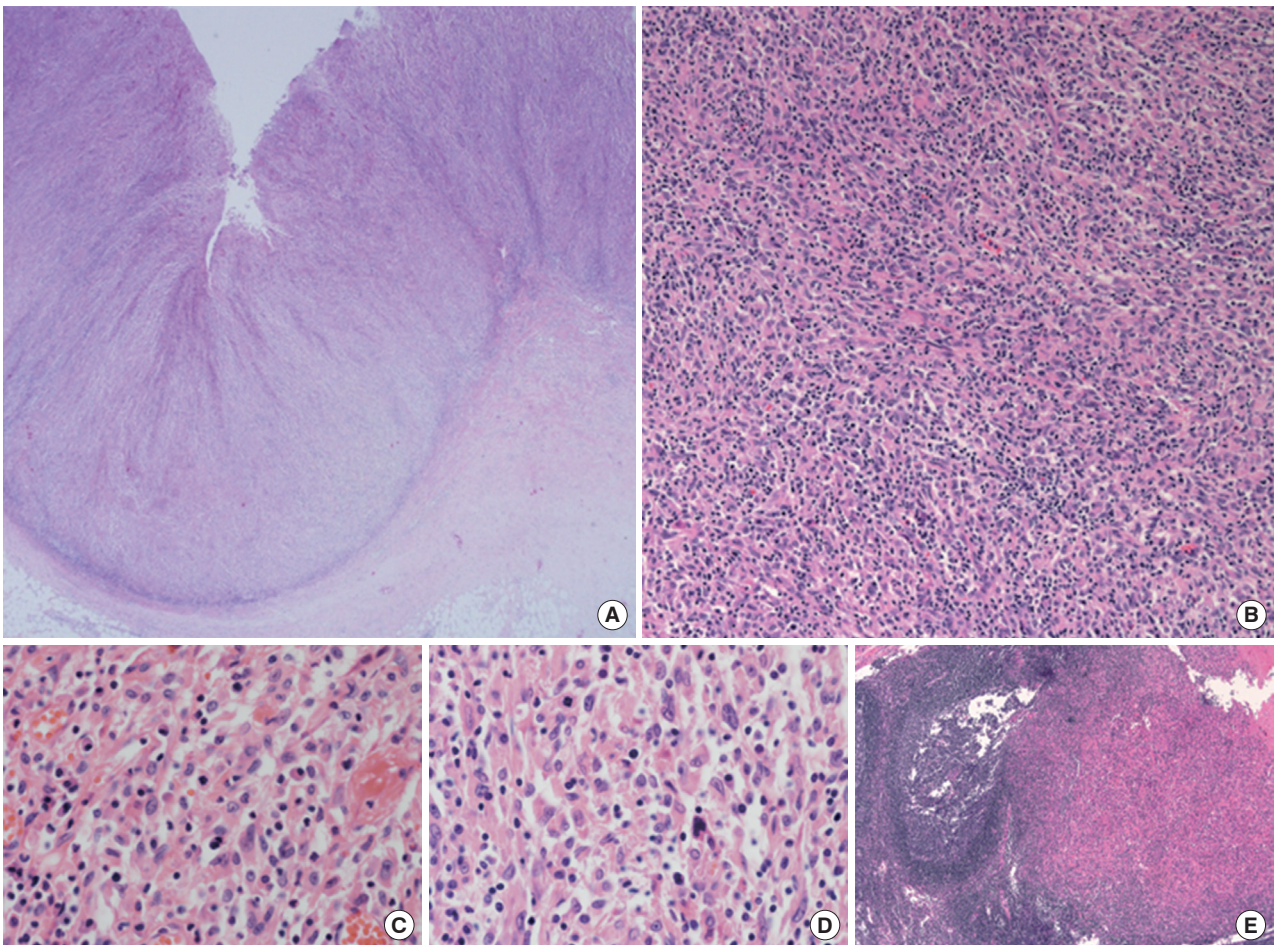


Fig. 2. (A) Microscopic examination of tumor cells reveals a band-like infiltration with a pushing border. (B) Tumor cells are intimately admixed with inflammatory cells. (C) Tumor cells are singly scattered, and have vesicular nuclei with inconspicuous nucleoli. Since the cytological atypia of tumor cells is not evident, the lesion may be misinterpreted as an inflammatory pseudotumor. (D) In some areas, cells with smudged hyperchromatic nuclei or multinucleated tumor cells are observed. Mitotic figures are only occasionally identified. (E) Metastatic tumor deposits are found in two perigastric lymph nodes.

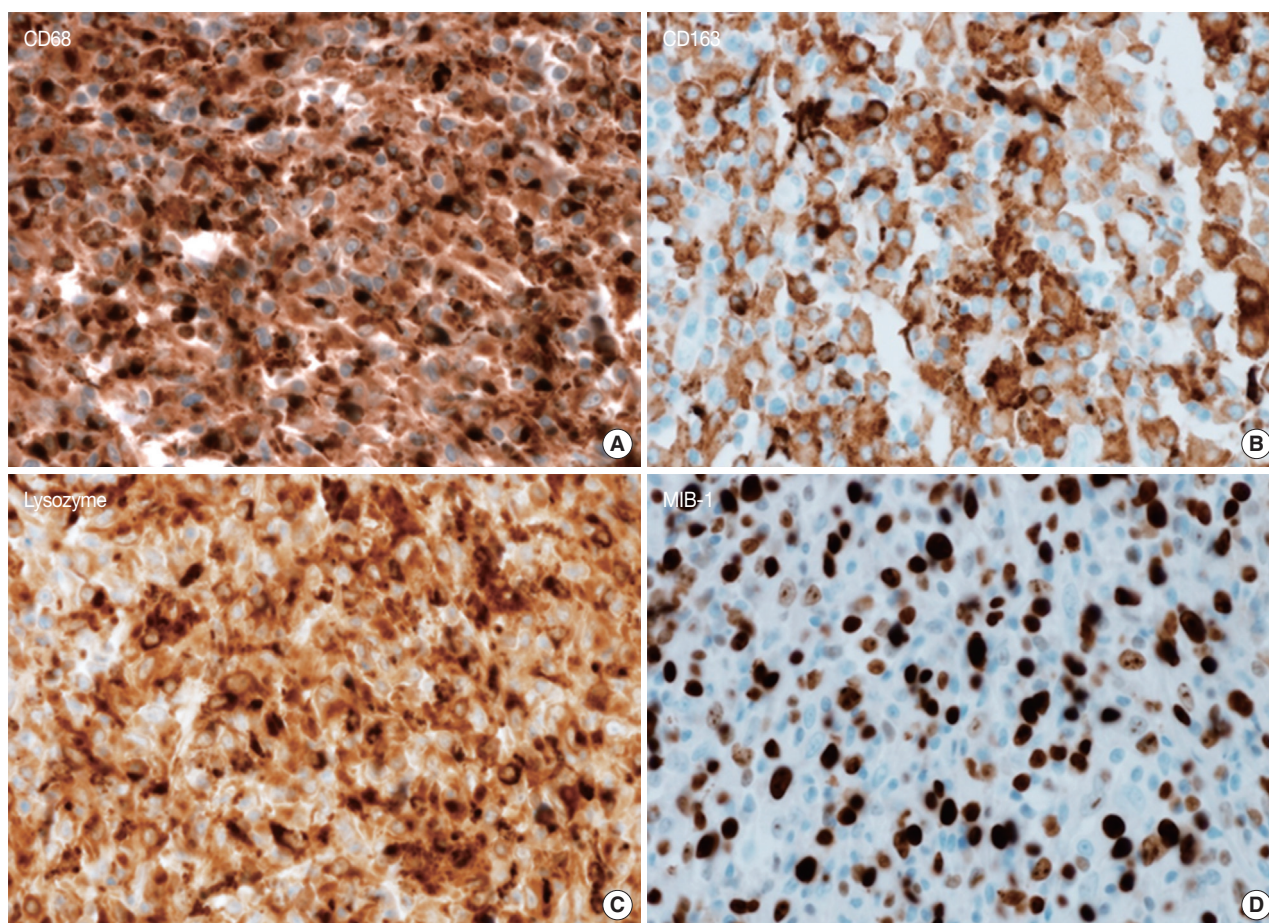


Fig. 3. Immunohistochemical stains for CD68 (A), CD163 (B), and lysozyme (C) demonstrate diffuse cytoplasmic staining of tumor cells. (D) MIB-1 labeling index is approximately 60% to 70%.

AE3], cytokeratin 8&18, epithelial membrane antigen), follicular dendritic cell markers (CD21, CD35), Langerhans cell marker (CD1a), specific myeloid markers (CD34, myeloperoxidase), and other markers including c-kit, smooth muscle actin, and CD30. CD3 and CD20 were not stained in the tumor cells. The infiltrating lymphocytes were predominantly T cells. *In-situ* hybridization for Epstein-Barr virus-encoded RNA was performed, and no apparent positive signal was noted. The deeply infiltrative growth of the tumor and the presence of lymph node metastases indicated the malignant nature of this tumor. Ultimately, a primary gastric histiocytic sarcoma was diagnosed. The postoperative course was uneventful, but the patient is still vulnerable. Bone marrow biopsy was done, and there was no evidence of tumor infiltration. Postoperative adjuvant chemotherapy with cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) is planned.

DISCUSSION

Histiocytic sarcomas usually consist of diffuse, noncohesive proliferation of large cells. These cells are round to oval and are commonly pleomorphic. Large multinucleated nuclei are frequently observed, and single prominent nucleoli are found in most of the tumor cells. Based on morphological similarities, diffuse large B-cell lymphoma or anaplastic large cell lymphoma has long been misdiagnosed as a malignant histiocytic lesion.⁷ Thus, the malignant nature of this lesion is easily detected in general, even though the specific diagnosis is laborious. On the other hand, the tumor cells in the current case were not highly atypical or pleomorphic, and, instead, most of the tumor cells had appearances similar to reactive histiocytes. The diagnosis on a biopsy specimen was even more difficult, and the findings were more suggestive of an inflammatory lesion such as an inflammatory pseudotumor than of a malignant process. However, the resected specimen clearly demonstrated the malignant na-

Table 1. Clinical characteristics of reported cases of primary gastric histiocytic sarcoma

Reference	Age (yr)	Sex	Tumor location	Tumor size (cm)	Accompanying lesion	Regional LN involvement	Surgical treatment	Adjuvant chemotherapy	Distant metastasis	Survival
Hornick <i>et al.</i> ² (2004)	89	Male	Stomach+colon	12	No	Yes	Gastrectomy ^a	No	Sternum	Died (5 mo)
Yoo <i>et al.</i> ⁶ (2010)	71	Male	Stomach (F & B)	3, 1 (2 distinct masses)	No	No	Total gastrectomy	No	Spleen and intra-abdominal LNs	Alive with disease (9 mo)
Congyang <i>et al.</i> ³ (2011)	62	Female	Stomach (B & A)	20	DLBCL	Yes	Total gastrectomy	No	No	Died (7 mo)
Sundersingh <i>et al.</i> ⁵ (2012)	28	Female	Stomach (A & P)+ jejunum	9	No	Yes	Distal gastrectomy+ jejunal resection	Yes (CHOP, 4 cycles)	No	Alive without disease (3 yr)
Shen <i>et al.</i> ⁴ (2013)	52	Female	Stomach (F)	7	No	No	Total gastrectomy	Yes	No	Alive without disease (4 mo)
Present case	45	Female	Stomach (A & P)	7.5	No	Yes	Distal gastrectomy	Not yet	No	Alive with residual disease (1 mo)

LN, lymph node; F, fundus; B, body; A, antrum; DLBCL, diffuse large B cell lymphoma; P, pylorus; CHOP, cyclophosphamide, doxorubicin, vincristine, and prednisolone.
^aThe surgical treatment for the colonic mass is not described in the paper.

ture of this tumor. The cellular atypia of histiocytic sarcoma has been reported to be variable, but its diagnostic confusion with a benign reactive lesion is exceptional.⁸ In line with this, sometimes the neoplastic cells in histiocytic sarcomas involving the central nervous system are obscured by a heavy inflammatory infiltrate including neutrophils and lymphocytes, thereby mimicking an inflammatory lesion.⁹ Therefore, histiocytic sarcoma also should be included in the differential diagnoses of lesions with even bland-looking histiocytic proliferation, and clinicopathologic correlation is mandatory for the diagnosis.

Histiocytic sarcoma rarely occurs in the stomach; we found only 5 such cases through our Pubmed search. The clinical characteristics of primary gastric histiocytic sarcomas including ours are summarized in Table 1. Initially, we found two more single case reports in the literature, but these were not included in our analysis because they were written in Chinese, and even the abstracts were not available online. Among the 6 patients including ours, there were 2 men and 4 women. There is a wide age range, from 28 to 89 years old (average, 57.8 years), but most cases occurred in the middle-aged or elderly. Two cases showed multiple tumor involvement (colon and jejunum), while the rest presented with a solitary gastric mass. Tumor size ranged from 2 to 20 cm, and most cases presented with a large, ulcerofungating mass, which, preoperatively, had been suspected as an advanced gastric cancer. All patients underwent a gastrectomy, and 4 of 6 (66.7%) patients had regional lymph node metastases at the time of surgery. Two patients succumbed to the disease during the follow-up period. The remaining four patients were alive at the last follow-up, but the follow-up periods were all short. Histiocytic sarcoma is usually aggressive, and the clinical course is grim due to the poor response to conventional chemotherapy.² With regard to gastric histiocytic sarcomas, one previous case showed a relatively long survival (3 years) after surgery and adjuvant chemotherapy.⁵ On the other hand, a different case with small tumor size (2 cm) and no initial regional lymph node involvement developed multiple distant metastases before long, and this patient had not received chemotherapy.⁶ These examples suggest that adjuvant chemotherapy may be effective and prolong the survival of patients with gastric histiocytic sarcoma.

In summary, histiocytic sarcoma rarely occurs in the stomach, and it usually presents with a large, ulcerofungating mass with an advanced clinical stage. Histologically, since the cellular atypia of this tumor is variable and may be minimal, clinical correlation is warranted before a definite diagnosis is made. Like other extranodal histiocytic sarcomas, primary gastric histiocyt-

ic sarcoma appears to be an aggressive neoplasm, but adjuvant chemotherapy may be effective in some cases.

Conflicts of Interest

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

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