

## Hodgkin's Lymphoma of the Stomach: A Rare Entity

### Introduction

Lymphomatous involvement of the gastrointestinal (GI) tract is usually seen in the setting of disseminated disease. Primary GI involvement is usually seen in non-Hodgkin's lymphoma. Primary Hodgkin's lymphoma of the stomach is a rare entity with data from the NCI reporting just six cases of Hodgkin's lymphoma of the GI tract between 1953 and 1990.<sup>[1]</sup> Herein, we report a case of Hodgkin's lymphoma of the stomach.

### Case Report

A 48-year-old woman presented to our department with a history of epigastric pain, early satiety, loss of appetite, and weight loss of 10 kg in the preceding 6 months. She had taken a course of proton pump inhibitors as prescribed by her family physician with no improvement in symptoms. No history of any nausea, vomiting, hematemesis, or melena was noted. On examination, she had good performance status, vitals were normal, and there was no peripheral lymphadenopathy. Examination of the abdomen did not reveal any mass, hepatosplenomegaly, or ascites. Complete blood counts and renal and liver functions were normal. Lactate dehydrogenase was elevated (350 U/L).

### Question 1

What are the most common malignant causes of such presentation?

Answer: (1) Carcinoma of the stomach; (2) lymphoma of the stomach; and (3) GI stromal tumor.

She underwent upper GI (UGI) endoscopy which revealed multiple ulcers in the fundus along the lesser curvature of

the stomach [Figure 1a]. Biopsy from the lesion showed gastric mucosa with ulceration and infiltration by large atypical lymphoid cells admixed with inflammatory cells.

### Question 2

What are the most common types of lymphoma of the stomach?

Answer: (1) Diffuse large B-cell lymphoma; (2) marginal zone lymphoma.

Immunohistochemistry (IHC) was done and these cells expressed PAX5, CD30, and MUM1. They were negative for CK, LCA, CD15, ALK, CD20, CD3, and LMP1 [Figure 1b-f]. *In situ* hybridization for EBER was negative in the atypical cells. In view of the above findings, a diagnosis of Hodgkin's lymphoma was made.

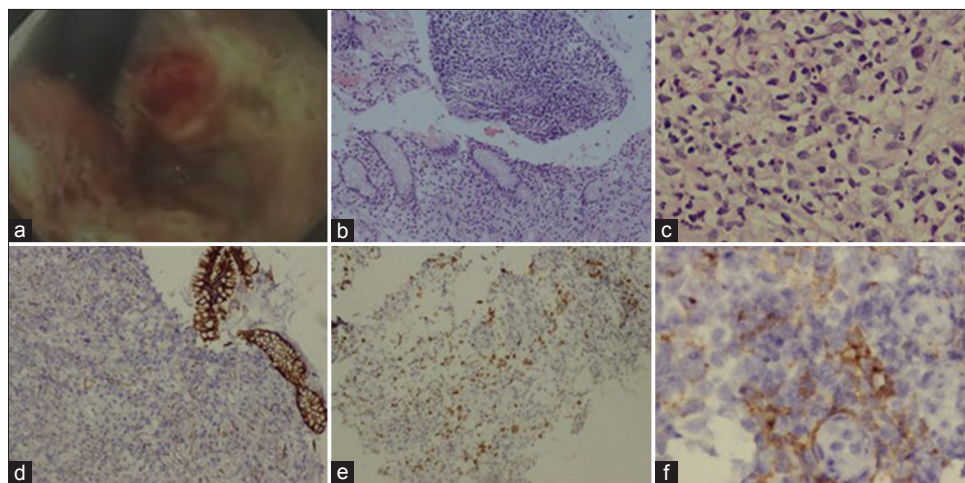
A whole-body FDG positron emission tomography-computed tomography (PET-CT) was done, which showed increased uptake and thickening of the stomach wall with perigastric and aortocaval lymph nodes and another 4 cm × 3 cm lesion in the left adrenal with increased uptake and diffuse uptake in the bone marrow. Bone marrow biopsy did not show any lymphomatous involvement.

The patient was diagnosed and staged as Hodgkin's lymphoma Stage IV (Ann Arbor Staging); IPSS score 2/7.

### Question 3

How common is Hodgkin's lymphoma of the stomach?

Answer: Hodgkin's lymphoma of the stomach is a rare entity. Colucci et al. reviewed 721 cases of primary gastric lymphoma diagnosed between 1973 and 1990 and identified only 17 as Hodgkin's lymphoma. If IHC would have been



**Figure 1: Endoscopy and histology.** (a) Ulcer in the fundus of the stomach. (b) Low-power view showing ulcerated gastric mucosa and aggregation of atypical lymphoid cells in an inflammatory background. (c) High-power view of large atypical neoplastic cells. (d) The neoplastic cells are cyokeratin negative whereas the gastric epithelial cells are positive. (e) The neoplastic cells and the B cells are PAX5 positive. (f) The neoplastic cells are CD30 positive

**Table 1: Immunohistochemistry findings of Hodgkin's lymphoma of stomach in various case reports**

| Author                                 | Years | IHC  |
|--|-------|--|
| Ogawa <i>et al.</i> <sup>[5]</sup>     | 1995  | CD30 <sup>+</sup> , CD45 <sup>+</sup> CD15 <sup>-</sup> , EMA <sup>-</sup>   |
| Mori <i>et al.</i> <sup>[6]</sup>      | 1995  | CD30 <sup>+</sup> , CD3 <sup>-</sup> , CD15 not done   |
| Zippel <i>et al.</i> <sup>[7]</sup>    | 1997  | -  |
| Venizelos <i>et al.</i> <sup>[8]</sup> | 2005  | CD30 <sup>+</sup> , CD15 <sup>+</sup> , EMA <sup>-</sup> CD20 <sup>+</sup> (weak), CD79a <sup>-</sup>  |
| Penázová <i>et al.</i> <sup>[9]</sup>  | 2007  | CD15 <sup>+</sup> , CD30 <sup>+</sup>  |
| Saito <i>et al.</i> <sup>[10]</sup>    | 2007  | CD30 <sup>+</sup> , CD20 <sup>+</sup> , CD79a <sup>+</sup> , CD3 <sup>-</sup> , CD15 <sup>-</sup> , EMA <sup>-</sup> , Oct-2 <sup>+</sup> , Bob-1 <sup>+</sup>                 |
| Hossain <i>et al.</i> <sup>[11]</sup>  | 2007  | CD15 <sup>+</sup> , CD30 <sup>+</sup> , EBV-LMP1, CD20 <sup>+</sup> (weak), CD79a <sup>-</sup> , CD3 <sup>-</sup> , bcl-2 <sup>-</sup> , bcl-6 <sup>-</sup>                    |
| Jung <i>et al.</i> <sup>[4]</sup>      | 2012  | CD30 <sup>+</sup> , CD20 <sup>+</sup> , CD79a <sup>+</sup> , CD3 <sup>-</sup> , CD15 <sup>-</sup> , EMA <sup>-</sup> , ALK1 <sup>-</sup> , c-kit <sup>-</sup>                  |
| Current case                           | -     | PAX5 <sup>+</sup> , CD30 <sup>+</sup> , MUM1 <sup>+</sup> , LCA <sup>-</sup> , CD15 <sup>-</sup> , ALK <sup>-</sup> , CD20 <sup>-</sup> , CD3 <sup>-</sup> , LMP1 <sup>-</sup> |

IHC: Immunohistochemistry

done, probably, many cases would be recategorized as non-Hodgkin's lymphoma.

She was started on ABVD chemotherapy regimen. After three cycles, the patient's symptoms showed improvement and PET-CT showed residual disease. She received three more cycles of ABVD. PET- CT done after six cycles showed residual disease in the stomach and left adrenal gland. UGI and stomach biopsy were repeated. Biopsy revealed similar morphology and IHC staining of neoplastic cells. The patient did not consent for biopsy of adrenal lesion or perigastric lymph nodes. Currently, the patient is being planned for second-line salvage therapy with GDP followed by autologous stem cell transplantation if favorable response is noted.

## Discussion

GI involvement by lymphoma may be seen in advanced disseminated cases. In 1961, Dawson *et al.* proposed a set of criteria to distinguish primary GI lymphoma from secondary involvement in the context of disseminated disease. These are (1) absence of peripheral lymphadenopathy at the time of presentation, (2) lack of enlarged mediastinal lymph nodes, (3) normal results for a complete blood count and differential, (4) predominance of the bowel lesion, despite the presence of disease in adjacent lymph nodes, and (5) absence of any lymphomatous involvement of the liver or spleen.<sup>[2]</sup> This case fits into the above criteria except for the fact that adrenal lesion was present.

Moreover, Hodgkin's lymphoma of the stomach is a rare entity. It constitutes <1% of lymphoma of the stomach. Colucci *et al.* reviewed 721 cases of primary gastric lymphoma diagnosed between 1973 and 1990 and identified only 17 as Hodgkin's lymphoma. If IHC would have been done, probably, many cases would be recategorized as non-Hodgkin's lymphoma.<sup>[3]</sup> In addition, literature review identified only eight other cases of Hodgkin's lymphoma of the stomach excluding the current case [Table 1].

Diagnosis is difficult due to the tissue being interspersed with inflammatory cells and paucity of malignant cells. They resemble RS cells morphologically, and on IHC, majority almost all cases are CD30 positive, and majority are CD15 positive with variable expression of CD20 and

other B-cell markers. A close differential is anaplastic large cell lymphoma and is differentiated by the lack of T-cell markers and ALK negativity.<sup>[4]</sup>

Prognosis of Hodgkin's lymphoma is difficult to ascertain due to rarity of cases and incomplete treatment and follow-up details. Our patient had incomplete response to chemotherapy, and we plan to proceed with partial gastrectomy and adrenal lesion biopsy in case of inadequate response with the second-line therapy. This will aid in reconfirming diagnosis in view of the rarity of Hodgkin's lymphoma of the stomach and paucity of tissue specimen with endoscopic biopsy.

## Conclusion

Primary Hodgkin's lymphoma of the stomach is a rare entity. Many cases are misdiagnosed which may lead to inappropriate treatment and poor outcomes.

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## Conflicts of interest

There are no conflicts of interest.

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