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Case Report

A Case Reprot of Gastric Tumor Possibly of Histiocytic Origin; True Histiocytic Lymphoma of Stomach?

Ryu-ichi NAGASHIMA, Kunihiko MAEDA,
Mikio MATSUDA, Shigemi FUYAMA and Yutaka IMAI

Department of Pathology, Yamagata University School of Medicine, Yamagata, Japan

Abstract

We encountered an unique case suggesting the diversity of malignant lymphomas or the related neoplasms arising in stomach and their difficult differential diaqnosis from other tumors. The patient was a 63 years old, Japanese male. A palm-sized, transmural tumor with extensive necrodegenerative change was found in the posterior wall of his stomach and surgically resected. Microscopic appearance of this lesion, which consisted of diffusely proliferating large-sized, round or polygonal mononuclear cells, was regarded as diffuse type of malignant lymphoma at initial diagnosis. Our immunohistochemical examinations, however, could not confirm their expression of B- and T-lymphocyte associated antigens including CD3, CD20, CD43, CD45 and CD45RO. Only lysozyme, α 1-antitrypsin and α 1-antichymotripsin were found in the tumor cells constantly and CD15 was expressed on a part of them. The antibodies specific for chromogranin A, NSE (neuron specific enolase) or gastrin labeled faintly the cytoplasm of the tumor cells whereas it was difficult to definite their specificity because of their intense background stainings. These observations suggested the following possibilities as pathological diagnosis for the tumor: 1) monocytic /histiocytic tumor (true histiocytic lymphoma), 2) neuroendocrine neoplasm (atypical carcinoid tumor) and 3) an unique variant of malignant lymphomas.

Key words: immunohistochemistry, histiocytic lymphoma, lysozyme, CD15, α 1-antitrypsin, α 1-antichymotrypsin, neuroendocrine tumor and stomach.

Address for Correspondence: Kunihiko MAEDA, Department of Pathology, Yamagata University School of Medicine, Iida-Nishi 2-2-2, Yamagata 990-23, Japan

Introduction

The stomach is the major extranodal site arising malignant lymphomas or the related tumors. In this report, we are describing our morphological and immunohistochemical observations on the unique case which bore a giant gastric tumor morphologically simulating malignant lymphoma but displaying no cytochemical or immunohistochemical findings to define its cellular lineages except for some indefinite histiocytic markers. This case seems to be suggestive to realize the diversity of this kind of tumor and the differential diangnosis which should be considered for getting appropriate diagnosis.

Case report

The patient is a 63 years old Japanese male. He consulted a private clinic with a complaint of epigastraligia for a month. A giant tumor mass with central ulceration was found in the posterior wall of gastric body by radiological and endoscopical examinations Then he admitted to the First Department of Surgery, the Yamagata University Hospital for surgical treatment. His blood examinations at admission indicated no significant abnormality except for mild anemia and lymphocytopenia. Subtotal gastrectomy was performed and followed by a short course of chemotherapy. He discharged the hospital after the treatment and has kept healthy condition without any signs of relapse or metastasis so far.

Pathological findings

Macroscopic appearance of the lesion.

The lesion, which was a palm-sized (13.5 cm × 8 cm) in size, located in the posterior wall of the gastric body and had a crater-like wide ulceration as shown in Fig.1. The resected stomach adhered tightly to the adjacent transverse colon.

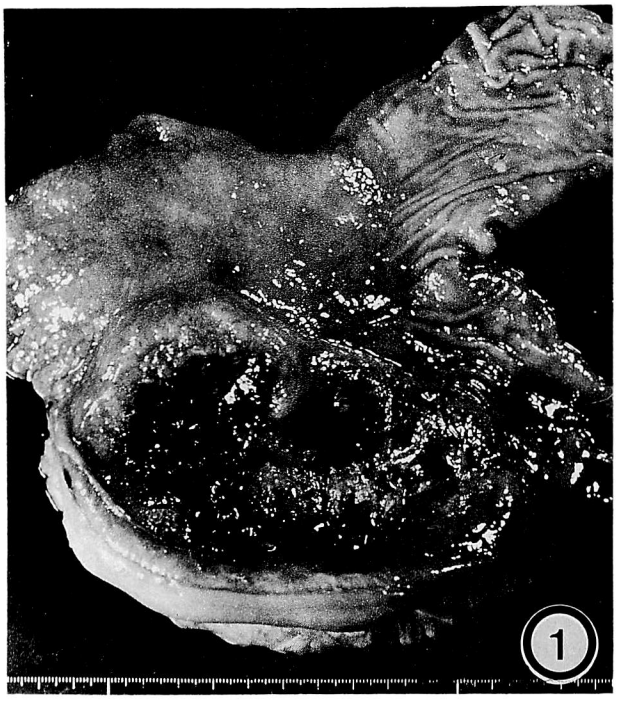

Fig. 1. A macroscopic view of the surdically resected stomach.

Microscopic findings of the tumor.

The tumor exhibited extensive necro-degenerative change, especially in the central area, and invaded transmurally into the serosa of the adjacent transverse colon. The whole part of the resected stomach was fixed in 3-5% formalin solution routinely. Materials, which were snap frozen without fixation or fixed in the particular fixatives for more sensitive immunohistochemistry, molecular biological analysis or electron microscopy, were not available. The relatively not degenerative portions of the tumor were selected and processed for conventional paraffin sections. The lesion consisted of diffusely proliferating large, round or polygonal-shaped mononuclear cells (Fig.2A). Their nuclei were oval-shaped and showed heterochromatic aggregation of chromatin with one or two prominent nucleoli. Their cytoplasms were relatively abundant and slightly eopinophilic (Fig.2B).

Cytochemical features of the tumor cells.

The tumor cells exhibited no significant reactivity for PAS (periodic acid-Schiff reaction), mucous staining by Alucian-blue and naphtol-ASD chloroacetate esterase reaction.

Immunohistochemical features of the tumor cells.

The immunostaining on conventional paraffin sections were performed using indirect immunoperoxidase method or SAB (streptavidin-biotin) staining kit. Table 1 summarized the results. Tumor cells did not displayed significant reactivity with B- and T-lymphocyte associated antigens such as CD3, CD20cy (L-26), CD43 (MT-1), CD45 (LCA), CD45RO (UCHL-1), CDw75 (LN-1), HLA-DR (LN-3), MB-1, MB-2 and each class of immunoglobulins nor epithelial cell associated antigens such as EMA (epithelial membrane antigen), CEA (carcino-embryonic antigen), cytokeratin, Ber-Ep4 and CA19-9. Only antibodies against lysozyme, α 1-antichymotrypin (ACT) and α 1-antitrypsin (AT) demonstrated weak but constant reactivity in their cytoplasm and LeuM1 (CD15) reacted with scattered tumor cells (Fig.3) whereas KP1 (CD68) and LN-5 did not display any reactivity. The tumor cells were labeled faintly by antibodies specific for NSE (neuron specific enolase), chormogranin A and gastrin whereas it was difficult to evaluate their specificities because intense back ground staining were simultaneously observed.

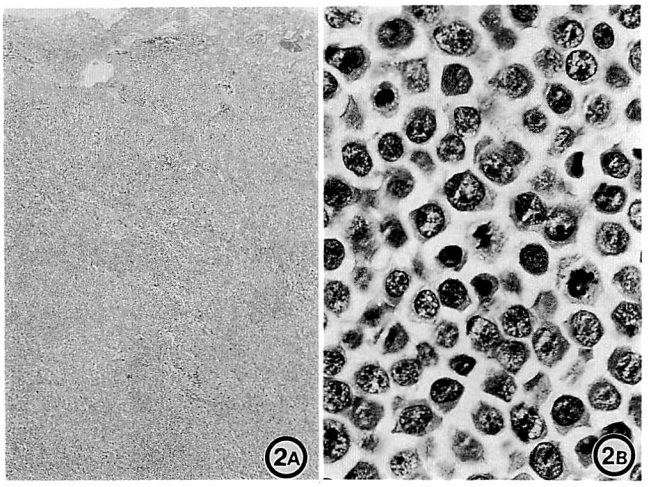

Fig. 2. Photomicrographs showing histological features of the tumor. Fig2A demonstrates a low power view of the lesion and Fig.2B demonstrates the higher magnification. (Fig.2A ×35, Fig.2B ×350; Hematoxyline & Eosin)

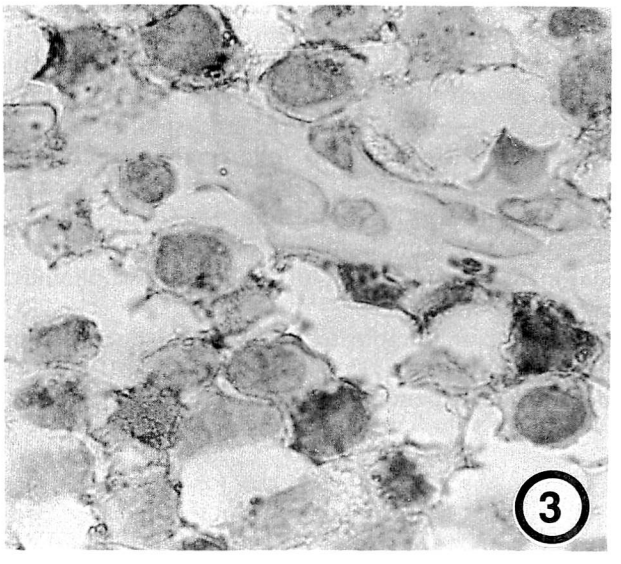

Fig. 3. A Photomicrographs showing immunoreactivity of the tumor cells for Leu M1 (CD15). (X780, Indirect immunoperoxidase labeling.)

Table 1 Immunohistochemical features of the tumor cell.

antibody	specificity or CD	reactivity	source
rabbit polyclonal CD3	CD3	−	DAKO
L26	CD20cy	−	DAKO
1F8	CD21	−	DAKO
Ber-H2	CD30	−	DAKO
MT-1	CD43	−	Bio-Science
LCA	CD45	−	DAKO
UCHL-1	CD45RO	−	DAKO
LN-2	CD74	−	Histoclone
LN-1	CDw75	−	Histoclone
LN-3	HLA-DR	−	Histoclone
MB-1	B-cell subset	−	Bio-Science
MB-2	B-cell subset	−	Bio-Science
DBA44	B-cell subset	−	Immunotech
DBB42	pan B-cell	−	Immunotech
IgG (mouse monoclonal)		−	BAKO
IgA (mouse monoclonal)		−	DAKO
IgM (mouse monoclonal)		−	DAKO
IgD (mouse monoclonal)		−	DAKO
IgE (mouse monoclonal)		−	DAKO
κ-light chain (mouse monoclonal)		−	DAKO
λ-light chain (mouse monoclonal)		−	DAKO
α 1-antitrypsin		+	DAKO
α 1-antichymotrypsin		+	DAKO
lysozyme		+	DAKO
LeuM1	CD15	+*	DAKO
Kp-1	CD68	−	DAKO
LN-5	macrophage & B-cell	−	Histoclone
ferritin		−	DAKO
S-100		−	DAKO
NSE (neuron specific enolase)		(+/−)**	DAKO
chromogranin A		(+)**	DAKO
gastrin		(+)**	DAKO
glucagon		−	DAKO
somatostatin		−	DAKO
serotonin		−	DAKO
calcitonin		−	DAKO
synaptophysin		−	DAKO
neurofilament		−	DAKO
hCG (chorionic gonadtropin)		−	DAKO
EMA (epithelial membrane antigen)		−	DAKO
CEA (monoclonal)		−	DAKO
AFP (α-fetoprotein)		−	DAKO
MNF116	cytokeratin	−	DAKO
Ber-Ep4	epithelial cell	−	DAKO
CA19-9		−	CIS Ltd
vimentin		−	DAKO
desmin		−	DAKO
smooth muscle actin		−	DAKO

* scattered cells are positive.
** (+/−) or (+) means equivocal or positive reactivity with intense back ground staining.

Discussion

Our initial diagnosis based on the conventional histological sections of this tumor was an diffuse type of malignant lymphoma of stomach. Indeed, some of the participants of the seminar supported our initial diagnosis. Nevertheless, immunohistochemical results were not consistent with the diagnosis. Considering both of the morphological and immunohistochemical features of the tumor. Lennert suggested the following possible diagnosis; 1) monocytic/histiocytic tumor including true histiocytic lymphoma and 2) granulocytic sarcoma. The latter can be excluded by the negativity of naphtol ASD-chroloacetate esterase reaction. In addition, no progression sign has been noted over a year after treatments while it has been known that most cases of granulocytic sarcomas readily developed to overt leukemia within a couple of months. The former is most rational to explain the immunohistochemical results but it is still indefinite to confirm its histiocytic origin. Because the tumor cells did not react with Kp-1 (CD68) and LN-5, which were accepted generally as the most reliable histiocytic markers in paraffin section immunochemistry[1,2] and each of LeuM1, lysozyme, ACT and AT is not specific for the histiocytic lineage but sometimes reacts with certain lymphocytes and epithelial cells. Actually there have been recently some reports indicating that certain carcinoid tumors expressed some of these antigens[3,4]. Interestingly our immunolabeling using antibodies against chromogranin A, NES and gastrin also demonstrated faint reactivity in the cytoplasm of the tumor cells even if it was difficult to define the reactivity since their high back ground staining. Accordingly, the neuroendocrine neoplasm such as atypical form of carcinoid tumors may not be excluded from candidates for diagnosis.

Close follow-up and further analyses, especially using molecular biological methods available formalin fixed tissues, may provide more suggestive evidences to define the cellular lineage.

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