Med. J. Kagoshima Univ., Vol. 47, Suppl. 2. 107~110, November, 1995

Case Report

A Case of Adult T-Cell Leukemia/Lymphoma in Stomach

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Summary

A 56 year old Japanese man was HTLV-1 carrier suffering from peripheral T-cell lymphoma pleomorphic small cell type manifesting multiple gastric lymphomatoid polyposis. The first symptom was epigastralgia and within one year clinical course, leukemia, hypercalcemia and lymph nodes swelling were not noted. A diagnosis of adult T-cell leukemia/lymphoma (ATLL) was based on immunohistochemistry and DNA-RNA in situ hybridization of HTLV-1 pX Tax and Env. A small number of lymphoma cells reacted with monoclonal antibody 6C2 against HTLV-1 gp46 Env and its precursor and the most lymphoma cells were labeled by monoclonal antibody HML-1 against a homing receptor. Unusual gastric involvement of this ATLL might be explained by the nature of the lymphoma cells expressing homing receptor.

Key words: ATL, Stomach, Immunohistochemistry, In-situ-hybridization, HTLV-1, HML-1

Introduction

Gastrointestinal involvement of Adult T-cell leukemia/lymphoma (ATLL) has been reported[1,2,3]. We also experienced unusual gastric lymphomatoid polyposis in a HTLV-1 carrier. Histopathological diagnosis of ATLL was based on the results of DNA-RNA in-situ-hybridization (ISH) of HTLV-1 proviral DNA env and pX Tax regions and of paraffin-immunohistochemistry for HTLV-1 gp46 Env[4].

Here, we report a case with the trial of histopathological diagnosis of ATLL.

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Case

Patient was a 56 year old Japanese man. The first symptome was epigastralgia. The first gastroendoscopic findings were those of hemorrhagic gastritis. After one month, he had epigastralgia again. The second gastroendoscopic and radiographic examinations showed a slightly elevated (IIa-like in Japanese classification of endoscopy) lesion on the anterior wall of the pyloric antrum. The endoscopic biopsy specimen was diagnosed as malignant lymphoma (ML). Because of gradual growth of the ML, gastorectomy was performed. In the pre-operative examinations a small number of atypical lymphocytes (Fig. 1) and anti-HTLV-1 antibodies were noted in his peripheral blood. The other laboratory data were within the normal range, including serum level of calcium and LDH. In

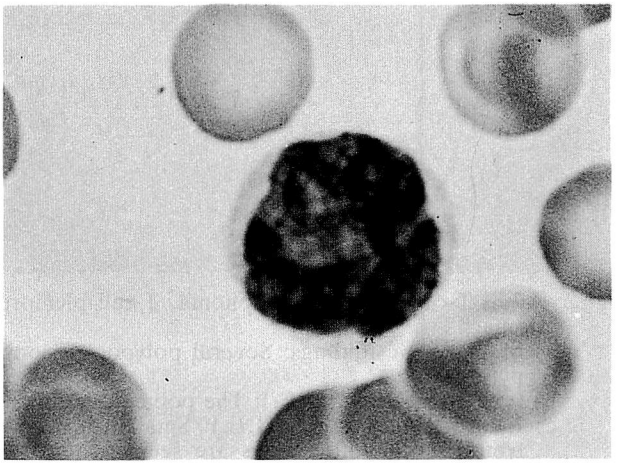

Fig. 1. Atypical lymphocyte in the peripheral blood. This atypical lymphocyte has lobulated nuclei but is small in comparison with the typical flower cells in adult T-cell leukemia/lymphoma.

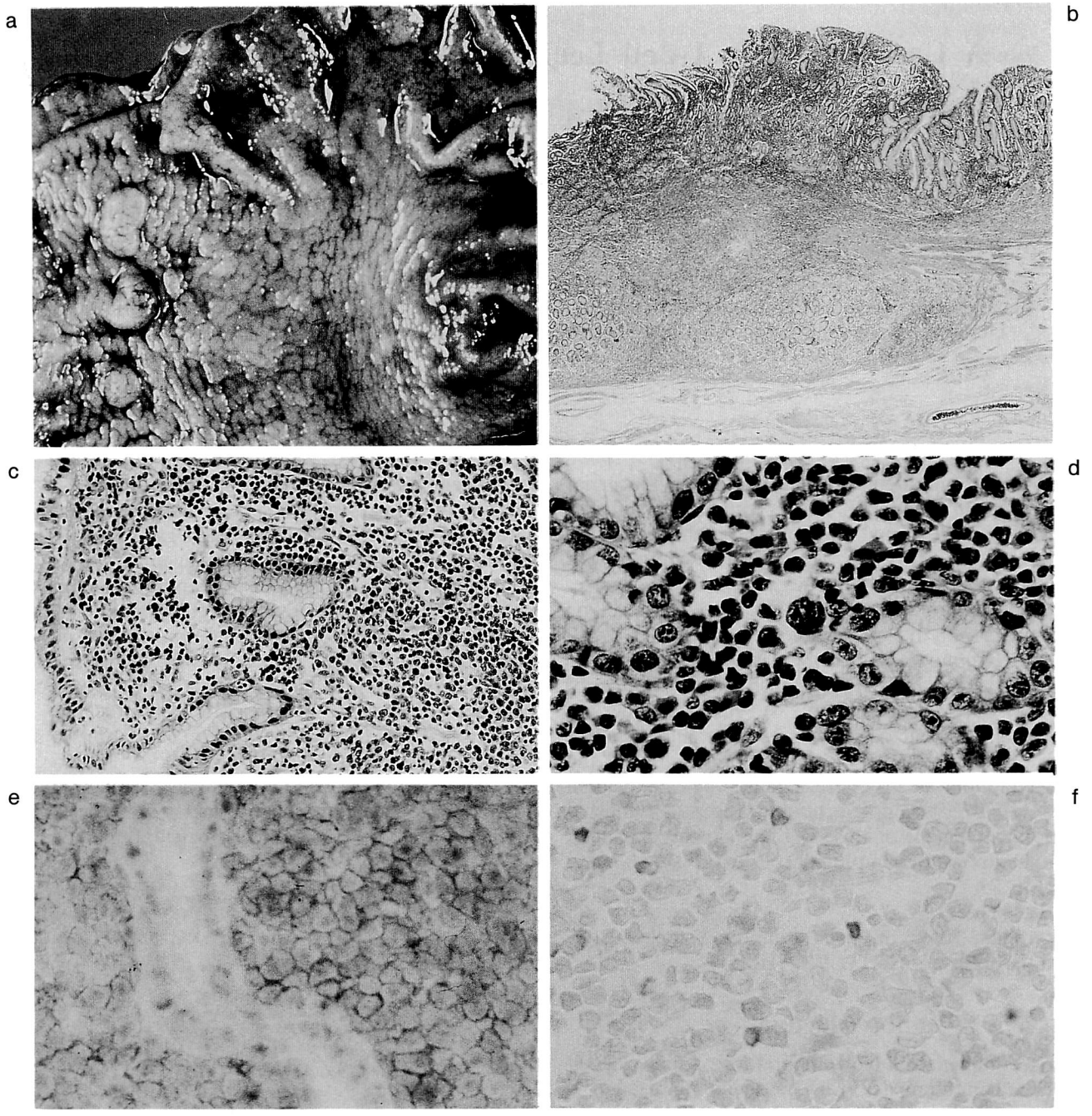

Fig. 2. Adult T-cell leukemia/lymphoma, T-cell plemorphic lymphoma, small cell type, manifesting polypoid lesions in stomach

a) Macroscopic findings: Several polypoid lesions (7mm in the longest axis, in max.) in the anterior wall of the pylorus.
b) Low power view (H.E.): The polypoid lesion shows lymphocytic stroma. The glands present intact appearances.
c) Lymphocytic stroma (H.E.): Small lymphocytes locate in the interstitium and in lymph vessels. No obvious lymphoepithelioid lesions are seen.
d) High power view (H.E.): The small lymphocytes have convoluted and hyperchromatic nuclei. Among them there are a few large or giant lymphoid cells as a hallmark for T-cell pleomorphic lymphoma.
e) HML-1 (frozen-immunohistochemistry): Most of the small lymphocytes show strong positive stains along cell surface.
f) 6C2 (HTLV-1 gp46 Env) (paraffin-immunohistochemistry): There are some lymphocytes revealing cytoplasmic stain.

the clinical course intestinal multiple lymphomatoid polyposis was diagnosed by means of endoscopy. Two months before his death, serum LDH had been increasing up to 1848 W-U. No obvious leukemia was noted. In one year form the first symptome he died suddenly of hemorrhage in a rapidly grown recurrent gastric lymphoma. Autopsy was not performed.

Pathology

The resected stomach showed multiple IIa-like mucosal polypoid lesions in the anterior wall (Fig. 2a). The polypoid lesions in the pyloric glandular mucosa (Fig. 2b) showed dense lymphocytic stroma comprising small to medium-sized lymphocytes (Fig. 2c). A few large lymphoid cells having convoluted nuclei were seen among the lymphocytes (Fig. 2d). So-called lymphoepithelial lesions were not found. A few atypical large or giant lymphoid cells were seen in parts and the small to medium-sized lymphocytes had convoluted nuclei (Fig. 2d).

Frozen-immunohistochemistry showed that the lymphocytes were positive for CD2, CD3, CD4, CD25, HLA-DR and HML-1 (Fig. 2e) and negative for CD1, CD7, CD8, CD15 (Leu M1, Leu M3, Leu7), CD20, CD22, CD30 and Ber H2. Seventy to 80% of the lymphocytes were positive for Ki-67. Paraffin-immunohistochemistry showed that the lymphocytes were positive for CD3, UCHL-1, MT-1 and LN-2 and negative for MB-1, L26, LN-1, LN-3, Leu M1, Ber H2 and antibodies for immunoglobulin heavy and light chains. In paraffin-immunohistochemistry with microwave pretreatment[5] the lymphocytes were weakly positive for CD25.

Anti-HTLV-1 gp46 Env antibody (6C2, Cellular Product Inc.) reacted positively with some lymphocytes (Fig. 2f) in its paraffin-immunohistochemistry[4].

DNA-RNA in situ hybridization employing HTLV-1 pX Tax and Env biotinylated probes produced by means of polymerase chain reaction [6,7] showed weak signals only in a few lymphocytes.

The gastric lesion was diagnosed histopathologically as peripheral T-cell malignant lymphoma, pleomorphic small cell type and etiologically as adult T-cell leukemia/lymphoma (ATLL) manifesting multiple lymphomatoid polyposis in the stomach. The all regional lymph nodes of the stomach were free from the malignant lymphoma.

Discussion

The definite diagnosis of ATLL is made by proving monoclonal integration of HTLV-1 proviral genome in neoplastic peripheral T-cells. In frozen-immunohistochemistry the most ATLL cells have interleukin 2 receptor (IL2R, CD25) on their surface. In histochemistry using routine paraffin sections, methods for diagnosis of ATLL have been developing. In paraffin-immunohistochemistry with microwave antigen-retrieval pretreatment[5] IL2R (CD25) could be visualized in ATLL cells. Monoclonal antibody 6C2 was introduced to detect HTLV-1 gp46 Env and its precursor in paraffin-immunohistochemistry[4] and the antibody 6C2 labeled some lymphoma cells in this case (Fig. 2f). We succeeded to detect signals of HTLV-1 proviral DNA[6,7] but in some cases such as this case only a few ATLL cells showed the signals. The histochemical detection of proteins and signals of HTLV-1 proviral DNA means HTLV-1 infection in ATLL cells but can not prove monoclonal integration of HTLV-1 proviral DNA in ATLL cells. Recently inverse polymerase chain reaction (IPCR) method to detect monoclonal integration of proviral DNA of HTLV-1 has been developed by M. Matsuoka and K. Takatsuki (Kumamoto Univ.). We expect application of the IPCR method to a small amount of DNA extracted from paraffin sections.

Unusual gastric involvement of this ATLL might be explained by a horming receptor recognized by HML-1 on the lymphoma cells, although the antigen recognized by HML-1 may be one of the activating antigens in ATLL[8]. Through the stay of ATLL cells having the homing receptor in the mucosa, the ATLL cells proliferate to form a tumor in the mucosa and do not recirculate into the other organs.

Acknowledgement

Authors thank Dr. M. Tokunaga (Director Dr., Department of Pathology, Kagoshima City Hospital) for his examination by means of frozen-immunohistochemistry of this case.

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