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Preliminary Communication

IDENTIFICATION OF A T CELL LYMPHOMA CATEGORY DERIVED FROM INTESTINAL-MUCOSA-ASSOCIATED T CELLS

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Summary 2 cases of precursor T cell lymphoma and 37 cases of peripheral T cell lymphoma were investigated for their reactivity with the monoclonal antibody (mAb) HML-1, which recognises human intestinal T lymphocytes but not lymph-node T cells. In all but one of the lymphomas studied, the tumour cells were unreactive with the mAb HML-1. The HML-1$^+$ lymphoma was the only tumour that was primarily localised in the epithelium and lamina propria of the small intestine, and was associated with ulcerative jejunitis and coeliac disease. This result suggests that the HML-1$^+$ lymphoma was derived from intestinal mucosa T lymphocytes and differs from precursor T cell lymphoblastic lymphomas and nodal and cutaneous peripheral T cell lymphomas.

INTRODUCTION

SEVERAL groups have suggested[1-5] that the intestinal mucosa contains T cells that differ from those present in lymph nodes. This suggestion has been confirmed by generation of a monoclonal antibody (mAb), designated HML-1, that reacts with nearly all intraepithelial T cells and 40% of the lamina propria T cells of the intestine but with only occasional cells in lymph nodes, tonsils, blood, or skin.[6] If the mucosa-associated T cells give rise to lymphomas, these should be identifiable with the mAb HML-1. To test this hypothesis, we investigated T cell lymphomas occurring at various primary sites including small intestine.

REACTIVITY OF TWO PRECURSOR T CELL AND 37 PERIPHERAL T CELL LYMPHOMAS* WITH THE MONOCLONAL ANTIBODY HML-1

Type of lymphoma	No	Primary location	HML-1$^-$ tumour cells
Precursor T cell (lymphoblastic)	2	Mediastinum	0
Peripheral T cell			
Cutaneous T cell	23	Skin	0
Pleomorphic T cell	5	Lymph node	0
Pleomorphic T cell	1	Jejunum	1
Lennert's	1	Lymph node	0
Angioimmunoblastic	1	Lymph node	0
T anaplastic large cell	5	Lymph node	0
T anaplastic large cell	1	Stomach	0

*Diagnosis established by demonstration of one or more of the T cell antigens CD2, CD3, CD7, CD8, or TCRβ in the absence of the B cell antigens CD19 and CD22, and the macrophage antigens CD11c, Ber-MAC3, and lysozyme.

MATERIALS AND METHODS

39 non-Hodgkin lymphomas of T cell type were studied with the monoclonal antibodies NA1/34 (CD1), T9-10 (CD2), T3-4B5 (CD3), T3-10 (CD4), DK25 (CD8), DK24 (CD7), HD37 (CD19 obtained from DAKOPATTS, βF1 (TCR β chain) purchased from T cell Sciences, S-HCL1 (CD22) and S-HCL3 (CD11c) obtained from Becton-Dickinson, HML-1 (6) kindly donated by Dr N. Cerf-Bensussan and Immunotech, and Ber-MAC3 (macrophage-specific) produced in our own laboratory. These antibodies were applied to acetone-fixed frozen sections. Their binding was displayed by the APAAP method,[7] slightly modified.[8] In addition, each case was histologically classified according to the updated Kiel classification.[9]

Case-report of Pleomorphic T Cell Lymphoma of the Jejunum

A 67-year-old man presented with a 2-year history of weight loss (20 kg) and diarrhoea. A biopsy revealed total villous atrophy. His severe malabsorption syndrome did not improve on a strict gluten-free diet, and laparotomy revealed a 7 cm segment of thickened jejunum with enlarged mesenteric lymph nodes. When opened, the 50 cm of resected jejunum showed some ulcers and multiple tumour nodules. Postoperative healing was uncomplicated

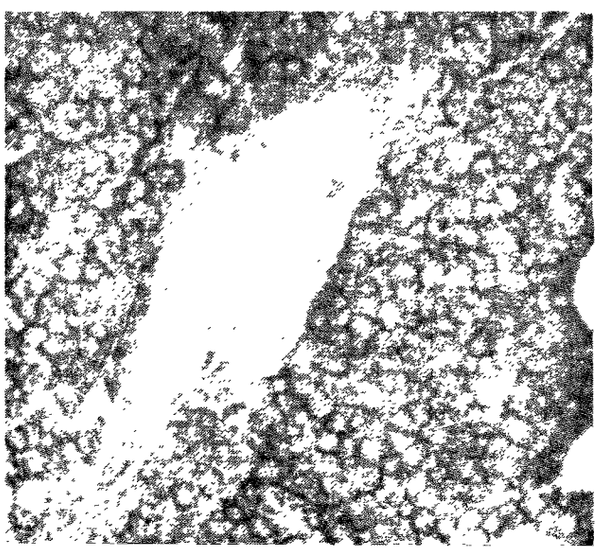

Fig 1—Intestinal lymphoma immunostained with monoclonal antibody HML-1.

Frozen section, APAAP; haemalum counterstain; × 200.

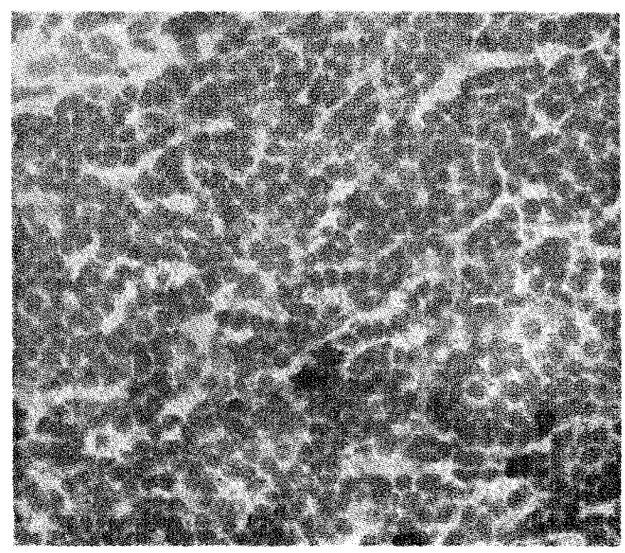

Fig 2—Primary nodal peripheral T cell lymphoma of pleomorphic type immunostained with HML-1.

Tumour cells are negative. The few positive cells represent reactive, possibly recirculating intestinal mucosa T cells. Frozen section; APAAP; haemalum counterstain; × 200.

but the patient deteriorated continuously despite parenteral nutrition. Tentative irradiation of the abdomen with 3 × 1·5 Gray/week had to be abandoned after the fifth session because of a sharp deterioration of the patient's general condition. Thereafter, staphylococcal sepsis developed, and he died of cardiovascular failure six months after first admission.

RESULTS

Tumour cells from all 39 T cell lymphomas were unreactive with antibodies for B cells and macrophages. The tumour cells were positive for one or more T cell antigens. Only one T cell lymphoma, that from the patient with jejunal tumour, reacted with HML-1 (table and figs 1 and 2). This lymphoma of pleomorphic T cell type was confined to the jejunum, growing mainly in the lamina propria and the epithelial layer. It was associated with ulcerative jejunitis and complete villous atrophy.

DISCUSSION

The findings in the case of jejunal lymphoma suggest that this tumour was derived from intestinal mucosa T lymphocytes. This conclusion is in keeping with the primary localisation of this lymphoma in the lamina propria of the jejunum and the spread of the HML-1$^+$ tumour cells within the intestinal epithelium and the expression of CD8 and CD3 in the absence of CD4, since the majority of intraepithelial T cells also carry CD8 and CD3 on their surface.[6] The negative reaction of all other T cell lymphomas, including those with primary involvement of lymph nodes, skin, mediastinum, and stomach, indicates that the specificity of the mAb HML-1 for intestinal mucosa T cells holds true for cells that have undergone malignant transformation.

The HML-1$^+$ T cell lymphoma is of particular interest because it was associated with ulcerative jejunitis and coeliac disease. Malignant lymphomas occurring in association with ulcerative jejunitis and coeliac disease were first recognised in 1937.[10] In 1978, Isaacson and Wright[11,12] reported evidence that this lymphoma is of a single histogenetic type. These workers regarded the lymphoma as a special form of malignant histiocytosis, because it met the criteria for a diagnosis of malignant histiocytosis and immunological analysis seemed to confirm the histiocytic properties of the malignant cells. In a joint immunohistological and genotype study in 1985,[13] when a wide range of mAbs and a T cell receptor-specific DNA probe were available, the T cell nature of this lymphoma was demonstrated.

At the first meeting of the European Society for Haematopathology (April 14, 1988) Isaacson reported another case of intestinal T cell lymphoma associated with coeliac disease that was reactive with the HML-1 antibody. It therefore seems possible that all T cell lymphomas of the small intestine that arise in coeliac disease will react with the mAb HML-1.

Might there be gastrointestinal tract T cell lymphomas that are not associated with coeliac disease, but express the antigen specific for intestinal mucosa T cells? To answer this question, a larger series of primary gastrointestinal lymphomas should be studied with the HML-1 antibody. Whatever the results, it is already clear that HML-1$^+$ primary intestinal T cell lymphomas should be included in classification schemes as a unique entity.

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References at foot of next column

Reviews of Books

Medical Decision Making

Harold C. Sox, Jr, Marshal A. Blatt, Michael C. Higgins, and Keith I. Marton. Boston, London: Butterworths. 1988. Pp 406. £25. ISBN 0-409900915.

THIS was a difficult book to review: on the one hand it offers fascinating analysis of clinical decision making; on the other it strays frequently into unnecessarily complex mathematical analysis. The latter feature is so off-putting that I found it almost impossible to finish a single chapter completely. The really annoying thing is that many of the formulae express quite simple concepts, and to un-numerate clinicians figures like this can be a real deterrent. The authors do say in their preface that they are also aiming at computer-equipped statistically minded doctors.

There are many excellent aspects; it does a clinician good to stop to question how history-taking leads to differential diagnosis, how test results are weighed, how treatments are decided, and how outcome is measured. Two particularly important subjects are presented in considerable depth. The first is Bayes' theorem, by which the effects of a given test result on the probability of disease can be mathematically calculated. This leads not only to critical evaluation of the power of a test (based on its sensitivity and specificity) but also to the decision on whether to use it at all—there is no point if the diagnosis is already highly probable and the test is of low predictive value. The second important subject is decision making; here the authors use algorithms to show how a clinical decision can be reached with optimum results to the patient. Each algorithm includes chance nodes (points in the decision tree where chance decides the next path), and decision nodes (points where there are choices for the clinician). At each node probabilities of outcome are quoted

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