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Colon Invasive Micropapillary Carcinoma Arising in Tubulovillous Adenoma

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Invasive micropapillary carcinoma (IMPC) is defined as a carcinoma composed of small clusters of tumor cells lying within clear spaces which simulate lymphovascular channels. This histologic pattern has been described in various organs, including the breast, lung, urinary bladder, ovary, stomach, pancreas, and major salivary glands. Although rarely observed as a pure histologic component, IMPC is usually mixed with conventional carcinoma, and is therefore often referred to as carcinoma with a micropapillary component. IMPCs are invariably associated with a high degree of aggressiveness, extensive lymphovascular invasion, extensive lymph node metastases, and poor prognosis. I herein describe a case of primary IMPC originating in colon polyp as a minor histologic component.

Introduction

Invasive micropapillary carcinoma (IMPC) is defined as a carcinoma composed of small clusters of tumor cells lying within clear spaces simulating vascular channels [12]. It is a histological variant of invasive breast carcinoma with poor clinical prognosis [10, 14]. This distinct histologic pattern has been described in various organs, including the urinary bladder, lung, ovary, stomach, pancreas, and major salivary glands [1, 2, 3, 4, 6, 7, 9, 13]. Although rarely observed as a pure histologic component, IMPC is usually mixed with otherwise conventional carcinoma [10], and is therefore often referred to as carcinoma with a micropapillary component. In cases of adenocarcinoma with a micropapillary component, an abrupt transition is usually seen between the invasive micropapillary component and conventional adenocarcinoma [10]. IMPCs are all invariably associated with a high degree of aggressiveness, extensive lymphovascular invasion, extensive lymph node metastases, and poor prognosis [10, 12, 14].

I herein describe a case of primary IMPC originating in colon polyp (tubulovillous adenoma) as a minor histologic component.

A Case Description

An 70-year-old Japanese man was referred to our hospital. The patient had undergone polypectomy for his colon polyp, measuring 11 mm. Microscopically, it was composed mostly of tubulovillous adenoma, and a small focus (3 mm in size) of micropapillary carcinoma was found adjacent to adenomatous component (Fig. 1A). The proportion of the micropapillary component in the tumor was less than 5%. Carcinoma cells invaded the submucosal layer (Fig. 1B), with foci of marked lymphatic invasion (Fig. 2B), although this lesion was small. To examine the immunophenotypes of the tumor, formalin-fixed paraffin-embedded tissue samples were subjected to immunohistochemistry with the use of anti-D2-40 (Nichirei, Tokyo, Japan) and anti-epithelial membrane antigen (EMA, Dako) antibodies. Severe lymphatic invasion and inside-out polarity of the tumor cells were highlighted (Fig. 2 A and B). Based on the above findings, the tumor was diagnosed as colonic invasive micropapillary carcinoma arising in tubulovillous adenoma. According to the above diagnosis, partial sigmoidectomy was carried out. Resected regional lymph nodes revealed no metastases. The patient is alive and free of the disease at the latest follow up.

Discussion

IMPC has distinctive histologic features characterized by tufts of tumor cells arranged in pseudopapillary patterns

devoid of fibrovascular cores and surrounded by empty and clear spaces [12]. This "inside-out growth" structure has been attributed to the rotation of cell polarization, whereby the stroma-facing (basal) surface of the cells acquires "apical" properties [10]. This inversion of cell polarity has been disclosed electron microscopically by the presence of microvilli on the external surface of cells facing the surrounding stroma [13] or immunohistochemically, by the outer membranous staining pattern of EMA only toward the stroma [10, 11]. Immunohistochemically with the anti-EMA antibody, I uncovered the inside-out polarity in the area with a micropapillary histologic feature (Fig. 2A). Compared with conventional carcinomas of similar size, hypothetically this reverse polarization in IMPC facilitates the secretion by tumor cells of molecules, such as metalloproteinases, known to be responsible for stromal and vascular invasion, permitting easier dissemination and a higher tendency for lymph node metastases [10]. Although no lymph node metastases were found in this case, close followup of the patient is requisite.

Recently, IMPC of the colon has been reported to be as high as 10 % of all cases of colorectal carcinoma [5]. No particular etiological background of colonic IMPC is known, but occurrence of the micropapillary component in the colorectal region may be attributable to the continuous exposure of the colonic mucosa to bile acids [7].

In my case files, I have a case of pancreatic cancer with a small foci (2 mm in size) of micropapillary component (manuscript in preparation). No reports describe the prognosis of cancer with such a small portion of mi-

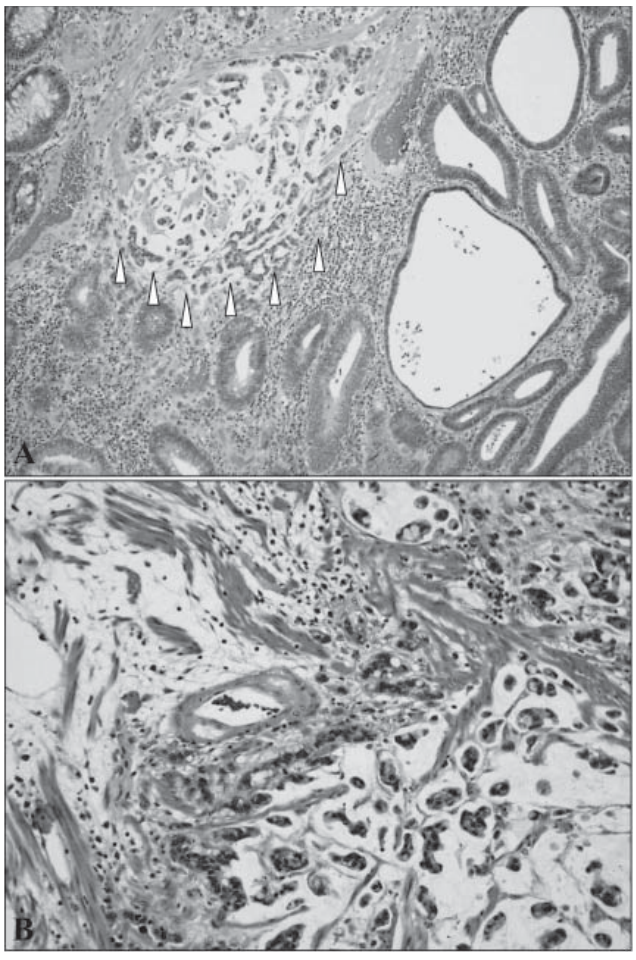

Fig. 1. Histology of the tumor (HE staining). A: tubulovillous adenoma with a small foci of micropapillary component (white arrowheads) (HE staining, x100); B: micropapillary component invading the muscularis mucosae (HE staining, x200).

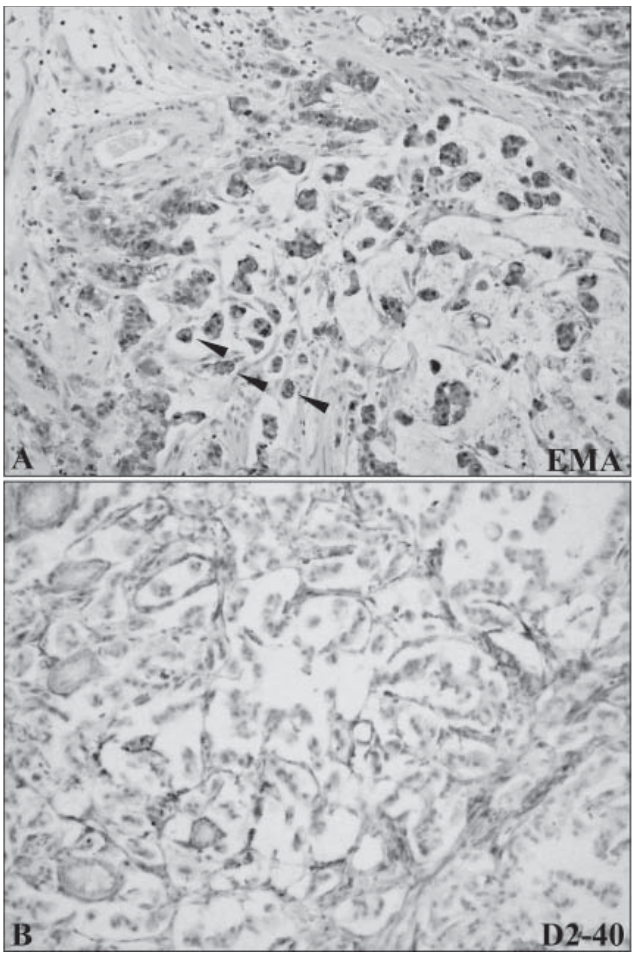

Fig. 2. Histology of the tumor (immunohistochemistry). A: immunohistochemistry of the micropapillary component (EMA, x200); by outer membranous staining, inside-out polarity is evident (black arrowheads); B: immunohistochemistry of the micropapillary component (D2-40, x200); severe lymphatic invasion of the tumor.

cropapillary carcinoma. Because the presence of the minor micropapillary component of the colon cancer may be ignored, carcinomas with a micropapillary component need to be carefully analyzed to understand their pathologic feature.

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