Micropapillary Carcinoma of the Gallbladder

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Micropapillary carcinoma (MPC) is a rare variant of carcinoma, and it is composed of small papillary neoplastic cell clusters lying within clear lacunar spaces that simulate lymphovascular channels. This tumor has been described in several organs such as the breast, lung, urinary bladder and salivary gland and it is known to be frequently associated with a high incidence of lymphatic invasion and metastasis in lymph nodes, resulting in poor clinical outcome. We present here a case of MPC in the gall bladder, and this type of case has not been previously described. Histologically, the tumor was composed of micropapillary carcinoma with tight clusters of micropapillary aggregates in the background of tubular adenoma. Focal invasive micropapillary components were also noted in the submuscular connective tissue. A metastatic lesion in a regional lymph node also showed an entirely micropapillary pattern.

Key Words: Carcinoma, papillary; Gallbladder; Metastasis

CASE REPORT

A 67-year-old woman with complaints of right upper quadrant abdominal pain and nausea visited the Gangneung Asan Hospital in May 2005. Acute cholecystitis with gallbladder stone was clinically suspected on the physical examination and the patient was admitted for further evaluation. The CT findings revealed a distended gallbladder with a discontinuity of the wall and a mesenteric fat infiltration, which was suspicious of acute cholecystitis with microperforation. An irregular focal wall thickening of the fundus of the gallbladder was also noted. A laparoscopic cholecystectomy was successfully performed. The resected gallbladder revealed an elevated lesion in the fundus, and this lesion measured 2.5 × 2.0 × 0.8 cm. The cut surface of the lesion was whitish yellow and firm to solid. The remaining mucosa was multi-focally eroded.

Histologically, the tumor was composed of a tubular adenoma of the pyloric gland type (2.5 cm in the greatest dimension) with some areas of the MPC composed of tight clusters of micropapillary aggregates in the lamina propria (0.5 cm in the greatest dimension) (Fig. 1, 2A). A few small clusters of micropapillary tumor cells were also present on the surface of the tumor (Fig. 3A). Multi-focal invasive micropapillary components were also noted in the submuscular adipose tissue (Fig. 3B). A regional lymph node was entirely occupied by the metastatic micropapillary carcinoma (Fig. 2B, 3C).

Immunohistochemically, MUC-1 was strongly expressed at the stromal edge of the micropapillary tumor cells (Fig. 3D). The tumor cells were also positive for CK7 and CEA, while they were negative for CK20. The cells lining most of the empty spaces around the micropapillary clusters were negative for CD34,
factor VIII related antigen and D2-40.

The patient is alive and doing well at 29 months after the surgery.

**DISCUSSION**

Since the first report of the micropapillary carcinoma in the breast by Siriaungul and Tavassoli in 1993, this tumor has been described in some other organs such as the lung, urinary bladder, ureter, salivary gland and colon. MPC has high incidence of regional lymph node metastases and a poor clinical outcome. Histologically, MPC is characterized by four histologic features as follows: 1) slender, delicate filiform processes or small tufts of the tumor cells on the surface and tight clusters of micropapillary aggregates in the deep portions and metastatic areas; 2) the absence of psammoma bodies, which are frequently seen in papillary serous carcinoma of the ovary; 3) pseudo-micropapillary aggregates without fibrovascular cores, surrounded by clear and empty spaces that resemble vascular spaces; and 4) focal vascular invasion. The peculiar inversion structure of the pseudopapillary clusters lying within the clear empty spaces has been
attributed to reversion of cell polarization, that is, the so called ‘inside out growing’ pattern. This reversed arrangement of the epithelial cells has been confirmed by detecting the inversion of the apical membranous staining pattern for MUC1.

MUC1 is a glycoprotein that’s normally expressed in the apical membrane of the normal glandular epithelium of the secretory organs such as the salivary glands, breast and lung. MUC1 has been known to play an important role in lumen formation and it generally inhibits interaction between cells and stroma in the detachment of cells from the stroma, and it could play an important role in determining the characteristic morphological features of MPC.

The proportion of the micropapillary carcinoma component for making the diagnosis of IMPC has not yet been decided for these above-mentioned organs. MPC may occupy the entire lesion or it may occur focally within the more typical carcinomas in those organs. However, the recognition of a micropapillary carcinoma component is very important because of the presence of this component is associated with a poor prognosis regardless of the amount of the tumor cells.

In our case, the differential diagnosis could include 1) an ordinary papillary adenocarcinoma with extensive lympho-vascular invasion, which is one of the variants of the adenocarcinoma in the gallbladder, and 2) processing artifacts that were caused by dehydration. The ordinary papillary adenocarcinoma is predominantly composed of papillary structures lined by cuboidal or columnar epithelial cells and the structures often contain variable amounts of mucin. However, these usual histologic features of papillary adenocarcinoma are obviously different from those of MPC, and the tumor tufts revealed the reversed apical membranous staining pattern for MUC1 immunostaining. In addition, the lining cells of most of the empty and clear spaces around the micropapillary tumor cells were negative for factor VIII related antigen, CD34 and D2-40. As another differential diagnosis, a metastatic MUC1 from other organs should be also considered. However, this possibility could be ruled out by detection of the transitional area between the adenomatous epithelium and the micropapillary carcinoma.

For adenocarcinoma of some other organs, such as the urinary bladder, lung, breast and colon, it has been well known that the presence of micropapillary components is associated with a poor clinical prognosis because of the high incidence of lympho-vascular invasion. Although our patient is alive at 29 months after the surgery without the clinical evidence of recurrence, the clinical significance of MPC of the gallbladder is unclear. Further studies for more cases of MPC should be performed to characterize this unique histologic variant of adenocarcinoma in the gallbladder.

REFERENCES