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Adenosquamous Carcinoma of the Ampulla of Vater
- A Report of Two Cases -

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Primary adenosquamous carcinoma of the ampulla of Vater is extremely rare. We report two cases of adenosquamous carcinoma of the ampulla of Vater in a 48-year-old female and an 80-year-old female patient. The gross appearance was a polypoid mass in both cases. Histologically, the majority of the two tumors was composed of squamous cell carcinoma with some intermingled glandular adenocarcinoma components in both cases. Squamous cell carcinomas showed an abrupt transition from the normal glandular epithelium or glandular adenocarcinoma. Although the two cases revealed duodenal wall invasion and lymph node metastasis was found in case 2, both patients are still alive at 19 and 46 months after surgery, respectively.

Key Words : Carcinoma, adenosquamous; Ampulla of Vater

Adenosquamous carcinoma (ASC) is a rare malignant tumor that contains both malignant glandular and squamous elements. Primary ASCs of the bowel can arise in any part of the gastrointestinal tract, but they are rather uncommon. Only two cases of ASC of the ampulla of Vater (AoV) had been reported in English-language literature.[1,2] We have experienced two such rare cases of ASC arising in the AoV. To the best of our knowledge, no such cases have been previously reported in the Korean literature. Here we present two rare cases of ASC of the AoV.

CASE REPORT

Case 1

A 48-year-old woman presented with pruritis that she had experienced for one month. She visited a local hospital, but the symptoms were not relieved. Shortly before her admission to our hospital, she had a fever and a chilling sensation, and the blood chemistry test showed elevated liver enzymes. Radiologic examinations via ultrasonography (US) and abdominal computer tomography (CT) revealed a dilated distal portion of the common bile duct and a dilated main pancreatic duct. She was referred to Samsung Medical Center under the impression of AoV cancer. On admission, the laboratory examination revealed a serum total bilirubin level of 2.0 mg/dL, an aspartate aminotransferase (AST) level of 86 IU/L, an alanine amintransferase (ALT) level of 100 IU/L, and a gamma glutamyl transpeptidase (GGT) level of 185 IU/L. Endoscopic examination demonstrated a friable polypoid ampullary mass. Biopsy was performed, and the histopathological diagnosis was a poorly differentiated carcinoma. We then performed pylorus preserving pancreaticoduodenectomy (PPPD). On the gross examination, the AoV showed a polypoid tumor that measured 1.4 × 1.2 cm. The serial cut section revealed a whitish polypoid mass at the AoV (Fig. 1). Microscopically, the majority of tumor was composed of moderately differentiated squamous cell carcinoma (SCC) (Fig. 2A). A focal glandular adenocarcinoma component was confined to the ampullary surface mucosa (Fig. 2B). Squamous cell carcinoma showed an abrupt transition from the normal glandular epithelium or

from the glandular adenocarcinoma (Fig. 3A). The tumor component that showed invasion to the proper muscle of the duodenum was squamous cell carcinoma. Immunohistochemically, low-molecular-weight-cytokeratin (keratin type 8) was reactive in both the glandular cells and the adenocarcinoma (Fig. 4A). In contrast, high-molecular-weight-cytokeratin (keratin type 1, 5, 10, 14) showed strong immunoreactivity in the squamous cell carcinoma (Fig. 4B). Regional lymph node metastasis was absent and the patient's postoperative course was uneventful. The patient has been alive without any evidence of disease for 19 months after surgery.

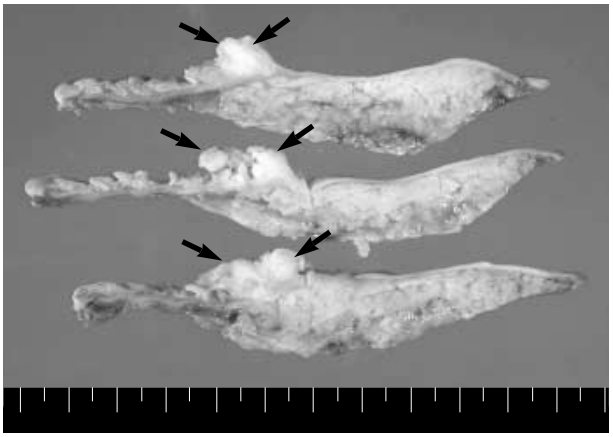

Fig. 1. The serial cut section reveals a small polypoid ampullary tumor (arrows).

Case 2

An 80-year-old previously healthy female patient presented with low abdominal pain and melena of one week duration. She then visited the local hospital. The laboratory tests showed a total bilirubin level of 3.4 mg/dL, an AST level of 274 IU/L, an ALT level of 493 IU/L and an alkaline phosphatase (ALP) level of 917 IU/L. Endoscopic examination revealed a small polypoid mass at the AoV. The histopathologic diagnosis of the ampullary biopsy was a poorly differentiated carcinoma. The patient was referred to Samsung Medical Center for surgery. Abdominal CT demonstrated nodular ampullary tumor and two cystic lesions in the pancreas head and neck that measured 2.3 cm and 1.6 cm, respectively. PPPD was then performed. Grossly, the AoV showed a polypoid tumor that measured 1.4 × 0.9 cm. Microscopically, the ampullary tumor was mainly composed of moderately differentiated squamous cell carcinoma, but there were intermingled adenocarcinoma components (Fig. 3B). The tumor extended to proper muscle layer of the duodenum. One choledochocal lymph node revealed tumor metastasis of squamous cell carcinoma. The cystic lesions of the head and neck of the pancreas were intraductal papillary mucinous neoplasm of borderline malignancy. The patient's postoperative course was uneventful. The patient has been alive without any evidence of the disease for 46 months after surgery.

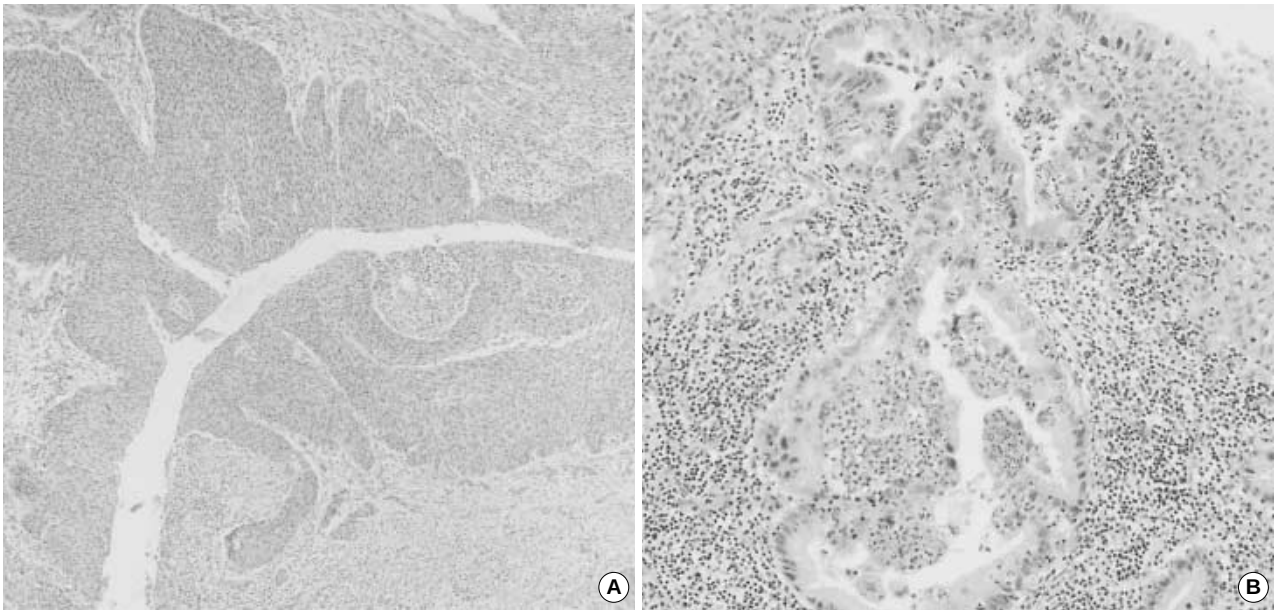

Fig. 2. The majority of tumor was composed of moderately differentiated squamous cell carcinoma (A). Focal adenocarcinoma component was confined to the ampullary surface mucosa (B).

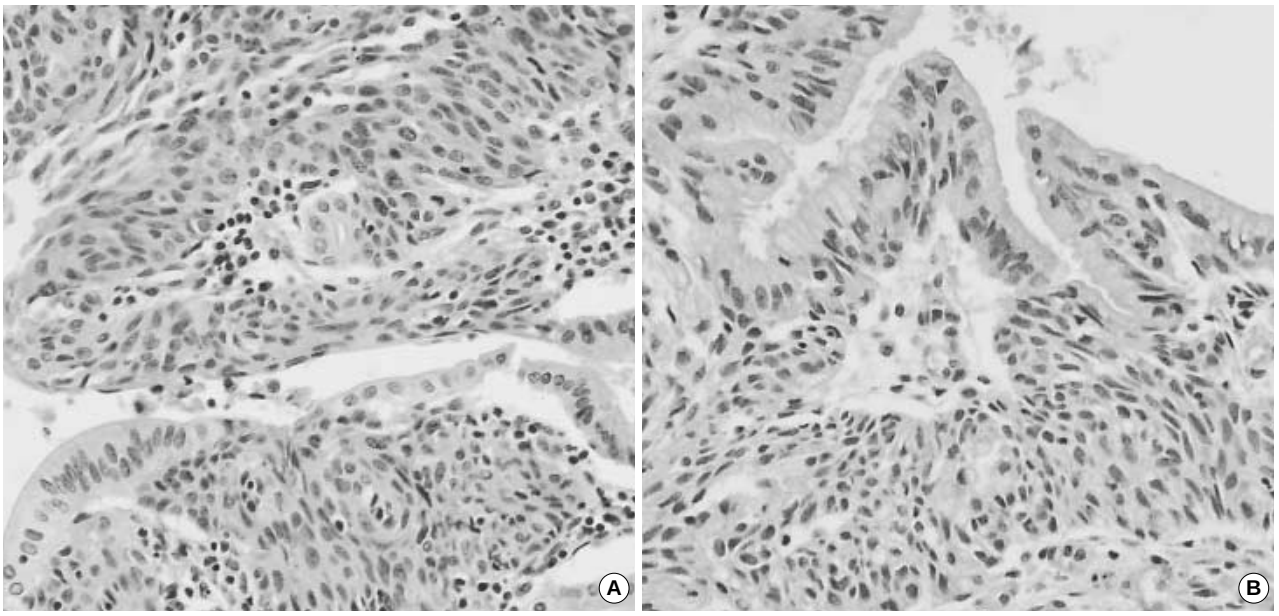

Fig. 3. Squamous cell carcinoma showed an abrupt transition from normal glandular epithelium or glandular adenocarcinoma in case 1 (A) and case 2 (B).

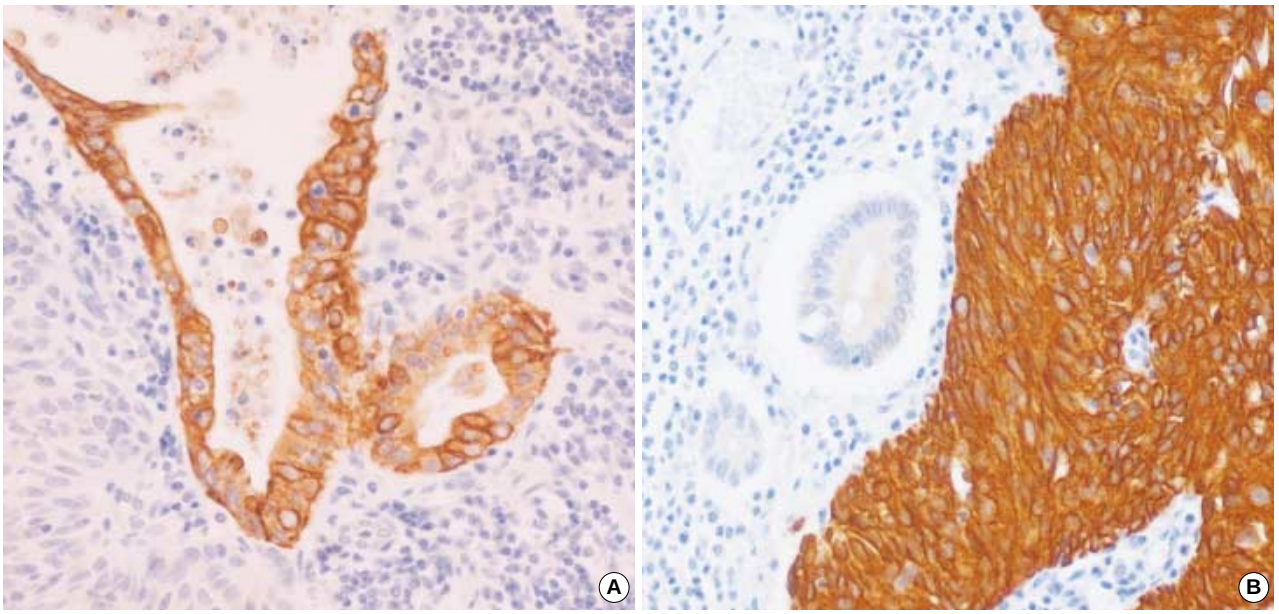

Fig. 4. Immunohistochemically, low-molecular-weight-cytokeratin (keratin type 8) was reactive in the glandular cells and adenocarcinoma (A). In contrast, high-molecular-weight-cytokeratin (keratin type 1, 5, 10, 14) showed strong immunoreactivity in the squamous cell carcinoma (B).

DISCUSSION

ASCs are malignant tumors that contain both malignant glandular and squamous components. ASC of the gastrointestinal tract has been reported in the esophagus, stomach, small intestine and the colorectum.[1-9] However, ASC of the AoV and pancreatobiliary tree is relatively rare,[1,2] and it comprises only 1 to 3% of all ampullary carcinomas.[10] There are only two previous case reports of ampullary ASC in the English literature.[1,2]

By convention, the squamous component should be significant (greater than 25 percent) before the diagnosis of adenosquamous carcinoma is made. Farthermore, a tumor that is composed almost

entirely of squamous elements should be considered adenosquamous when only focal glandular differentiation is found.[10] In the past, the diagnostic term "adenoacanthoma" was used to describe tumors that contained both malignant glandular and squamous components. The World Health Organization tumor classification system makes a clear distinction between an adenosquamous carcinoma, in which both the glandular and squamous elements are histologically malignant, and an adenoacanthoma, which represents adenocarcinoma that contains foci of benign sqamous metaplasia.[11] According to the above criteria, our two cases could be classified as ASCs.

The histogenesis of ASC in the intestinal tract is still uncertain, but several possibilities have been suggested.[7] Crissman suggested that chronic irritation, such as is noted in ulcerative colitis, or other direct stimuli could lead to the "unmasking" or unleashing of a pluripotential epithelial stem cell that is capable of both malignant transformation and differentiating into the squamous and glandular lines.[5] This illustrates the general concept that tumors often originate from the transformation of normal stem cells, which has been well established for the malignancies of the hematopoietic system such as chronic myelocytic leukemia.[12] This concept can also be applied to cancers in different organs. In support of the existence of a totipotent stem cell, an ultrastructural analysis of 2 cases of colonic adenosquamous carcinoma demonstrated concurrent glandular and squamous differentiation in the same cell.[13] It is known that squamous carcinoma may arise from squamous metaplasia in the intestinal mucosa, and this is a well-recognized phenomenon in adenomas of the colorectum.[14] Adenosquamous carcinoma that represents squamous metaplasia of adenocarcinoma has been reported in the pancreas.[15] Yet the histopathological finding of an abrupt transition of the squamous cell carcinoma in our two cases supports the theory of a pluripotent stem cell with dual differentiation rather than a malignant transformation from the squamous metaplasia of adenocarcinoma.

There have been some reports that adenosquamous carcinoma of the colorectal region exhibits a more aggressive biologic behavior and this is associated with a worse prognosis than that for conventional adenocarcinoma.[9,13] Many such cases show metastatic disease at the time of initial diagnosis. However, the clinical course of ASC seems to be different depending on the affected site. For example, there is a report suggesting that ASCs have a better prognosis than conventional SCCs or adenocarcinoma in the esophagus.[8]

Although both our two cases showed duodenal wall invasion and one case had lymph node metastasis, both patients are still alive at 19 and 46 months, respectively, after surgery. There has been a case report suggesting that ampullary ASC showed a poor prognosis, and in that case the patients died of wide spread metastasis 10 months after surgery.[1] Given the small number of known cases of primary ampullary adenosquamous carcinoma, it is difficult to draw any definite conclusions regarding the aggressiveness of this tumor compared with conventional adenocarcinomas of the AoV.

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