Undifferentiated Spindle and Giant Cell Carcinoma of the Common Bile Duct

Shoichi DOWAKI, Hiroshi KIJIMA^{*}, Hiroyuki KASHIWAGI, Kosuke TOBITA, Yasuo OHTANI, Yoshinori SUGIO, Takafumi SEKKA, R. Yoshiyuki OSAMURA^{*}, Toshihide IMAIZUMI, and Hiroyasu MAKUUCHI

Departments of Surgery, and *Pathology Tokai University School of Medicine

(Received September 30, 2003; Accepted October 31, 2003)

Undifferentiated spindle and giant cell carcinoma of the common bile duct has not been reported previously. We present here a case of 71-year-old man with the undifferentiated spindle and giant cell carcinoma of the common bile duct, including immunohistochemical findings. A nodular infiltrating tumor was located at the lower portion of the extrahepatic bile duct, and measured 1.2×0.6 cm in size. Histologically, the tumor was composed of proliferated sarcomatoid spindle tumor cells. Numerous multinucleated giant cells were intermingled with the sarcomatoid spindle tumor cells. Immunohistochemically, the tumor cells were positive for both cytokeratin and vimentin. We speculated that the tumor originated from epithelial cells, and showed sarcomatoid neplastic changes.

Key words: common bile duct, undifferentiated carcinoma, giant cells, immunohistochemistry

CASE REPORT

A 71-year-old was admitted to our hospital with jaundice, right hypochondralgia and high fever. He noticed white stool and brown urine one week prior to admission. Laboratory data were as follows: leukocyte count $8,000/\mu l$ (normal, 4,000 to $7,900/\mu$ l); erythrocyte $276 \times 10^4 / \mu l$ (normal, 400×10^4 to 540 $\times 10^4/\mu$ l); serum total bilirubin, 6.7 mg/dl (normal, 0.1 to 1.0 mg/dl); direct bilirubin, 4.2 mg/dl (normal, 0 to 0.2 mg/dl); glutamic oxalacetic transaminase (AST), 480 IU/l (normal, 11 to 29 IU/l); glutamic pyruvic transaminase (ALT), 298 IU/l (normal, 9 to 37 IU/l); carcinoembryonic antigen (CEA) 3.2 ng/ml (normal, <5.0 ng/ml). Ultrasonography showed dilation of the intrahepatic bile ducts, but no apparent tumor was observed in the biliary tract. Computed tomography (CT) revealed a non-enhancing obstructed segment at the extrahepatic bile duct. A percutaneous transhepatic cholangeal drainage (PTCD) tube was inserted to decrease the hyperbilirubinemia and for treatment of presumptive cholangitis. Angiography showed only minimal encasement at the posterior superior pancreaticoduodenal artery. These diagnostic imaging examinations could not reach a definite diagnosis of malignancy resulting in the obstructive jaundice. Biopsy specimens were taken from the PTCD catheter route, and showed proliferation of atypical polygonal cells with hyperchromaic nuclei. The biopsy findings highly suggested common bile duct cancer. Under the preoperative diagnosis of common bile duct cancer, pancreaticoduodenectomy (PD) was performed on 18th hospital day. The resected tumor, nodular infiltrating type, was located to the lower extrahepatic bile duct, and measured 1.2×0.6 cm in size (Fig. 1). No distant metastasis was observed at the operation. Histologically, the tumor was composed

Hiroshi KIJIMA, Department of Pathology, Tokai University School of Medicine, Bohseidai, Isehara, Kanagawa 259-1193, Japan Tel: +81-463-93-1121 Fax: +81-463-91-1370 e-mail: hkijima@is.icc.u-tokai.ac.jp



Fig. 1 Gross findings. A nodular infiltrating tumor (arrows) was seen in the lower portion of extrahepatic bile duct, and showed bile duct stenosis.



Fig. 2 Microscopic findings. The nodular infiltrating tumor extended down into the subserosa (A; left, top; hematoxylin and eosin, original magnification × 10). The tumor was composed of proliferated undifferentiated tumor cells with hyperchromatic nuclei. Numerous multinucleated giant tumor cells were intermingled with the undifferentiated tumor cells (B; right, top; hematoxylin and eosin, original magnification×50). Immunohistochemically, some tumor cells were positive for cytokeratin (WSS) (C; left, bottom; indirect method, original magnification×75), while the tumor cells were diffusely positive for vimentin (D; right, bottom; indirect method, original magnification×75).

of proliferated sarcomatoid tumor cells with hyperchromatic nuclei, i.e., undifferentiated tumor cells (Figs. 2A and 2B). Numerous multinucleated giant tumor cells resembling osteoclasts were intermingled with the sarcomatoid tumor cells. The tumor extended down into the subserosa, but showed neither vascular/perineural invasion nor lymph nodal metastasis. Immunohistochemically, the sarcomatoid tumor cells were diffusely positive for vimentin, while some tumor cells were also positive for cytokeratin (WSS) (Figs. 2C and 2D). Diffuse immunoreactivity of p53 oncoprotein was detected in the tumor cell nuclei. CEA, CA19-9 and epithelial membrane antigen (EMA) were negative. The multinucleated giant cells were positive for CD68. MIB-1 (Ki-67) labeling index of the tumor cells was 13.3 %. These findings were interpreted as undifferentiated spindle and giant cell carcinoma. The patient had no postoperative emplication, and was discharged on 39th day after the operation. He has survived without recurrence for 5 years and 10 months after the surgical treatment.

DISCUSSION

The majority of common bile duct neoplasms are adenocarcinoma, and the other histological types are rather uncommon [1-3]. Cases of undifferentiated spindle and giant cell carcinomas are very rare, and have been reported in the pancreas, gallbladder, lung and thyroid gland [1, 4-13]. There has been only one case report of the undifferentiated spindle and giant cell carcinoma in the hepatic hilum [14]. The tumor we described here is the first case of undifferentiated spindle and giant cell carcinoma of the common bile duct (extrahepatic bile duct).

Several reports have demonstrated that the undifferentiated spindle and giant cell carcinoma have high malignant potentials with frequent metastases [15-18]. In the present case, the tumor was small in size $(1.2 \times 0.6$ cm), while it extended into the subserosa. The tumor showed neither vascular/perineural invasion nor lymph nodal metastasis, and the patient has survived over 5 years. We considered that the case exhibited a relatively good prognosis, although the majority of the reported cases were highly malignant.

Histogenesis of undifferentiated carcinoma, including undifferentiated spindle and giant cell carcinoma, has not yet clarified [19-21]. We demonstrated that some of the tumor cells were immunohistochemically positive for both cytokeratin and vimentin. Based on the findings and review of the literature [22, 23], we speculated that this tumor originated from epithelial cells and showed sarcomatoid neoplastic changes with multinucleated giant cells.

REFERENCES

- Albores-Saavendra J, Henson DE, Kitamura DS: Tumor of the gallbladder, extra hepatic bile ducts, and ampulla of Vater. Atlas of Tumor Pathology, Third Series Fascicle 27. Armed Forces Institute of Pathology, Washington, D. C., 2000.
- Dunbar LL, Adkins RB, Farringer J, Waterhouse G, O'Leary JP: Carcinoma of the gallbladder and bile ducts: A retrospective review. Am Surg 49: 94-104, 1983.
- Sons HU, Borchard F: Carcinoma of the extrahepatic bile ducts: A postmorterm study of 65 cases and review of the literature. J Surg Oncol 34: 6-12 1987.
- Nishihara K, Tsuneyoshi M: Undifferentiated spindle cell carcinoma of the gallbladder: a clinicopathologic, immunohistochemical, and flow cytometric study of 11 cases. Hum Pathol 24: 1298-1305, 1993.
- 5) Guo KJ, Yamaguchi K, Enjoji M: Undifferentiated carcinoma of the gallbladder. A clinicopathologic, histochemical and immunohistochemical study of 21 patients with a poor prognosis. Cancer 61: 1872-1879, 1988.
- Diebold-Berger S, Vaiton JC, Pache JC, d'Amore ES: Undifferentiated carcinoma of the gallbladder. Report of a case with immunohistochemical finding. Arch Pathol Lab Med 119, 1995.
- 7) Kurihara K, Nagai H, Kasahara K, Kawai T, Saito K, Kanazawa K: Pleomorphic carcinoma of the pancreas with massive lymphocytic stromal infiltration and long-term survival after resection. Int J Pancreatol 27: 241-248, 2000.
- Addis BJ, Dewar A, Thurlow NP: Giant cell carcinoma of the lung-immunohistochemical and ultrastructural evidence of dedifferentiation. J Pathol 155: 231-240, 1988.
- Albores-Saaverda J, Molberg K, Henson DE: Unusual malignant epithelial tumors of the gallbladder. Sem Diag Pathol 13: 326-338, 1996.
- Appelman HD, Coopersmith N: Pleomorphic spindle cell carcinoma of the gallbladder: relation to sarcoma of the gallbladder. Cancer 25: 535-541, 1970.
- Bac M, Teglbjaerg PS: Pleomorphic (giant cell) carcinoma of the intestine. An immunohistochemical and electron microscopic study. Cancer 64: 2557-2564, 1989.
- 12) Carcangiu ML, Steeper T, Zampi G, Rosai J: Anaplastic thyroid carcinoma. A study of 70 cases. Am J Clin Pathol 83: 135-158, 1985.
- 13) Caruso RA, Famurari C, Giuffre' G, Mazzeo G: Pleomorphic carcinoma of the gallbladder. Tumori 77: 523-526, 1991.
- 14) Haratake J, Yamada H, Horie A, Inokuma T: Giant

cell tumor-like cholangiocarcinoma associated with systemic cholelithiasis. Cancer 69: 2444-2448, 1992.

- 15) Diebold-Berger S, Vation JC, Pache JC, Emanueles S, d'Amore G: Undifferentiated carcinoma of the gallbladder. Report of a case with immunohistochemical findings. Arch Pathol Lab Med 119: 279-282, 1995.
- 16) Fishback NF, Travis WP, Moran CA, Guinee DG Jr, McCarthy WF, Koss MN: Pleomorphec (spindle giant cell) carcinoma of the lung. A clinicopathologic correlation of 78 cases. Cancer 73: 2936-2945, 1994.
- 17) Tschang T, Garza-Garza R, Kissane JM: Pleomorphic carcinoma of the pancreas: an analysis of the 15 cases. Cancer 39: 2114-2126, 1977.
- 18) Yamaguchi K, Enjoji M: Carcinoma of the gallbladder. A clinicopathology of 103 patients and newly proposed staging. Cancer 62: 1425-1432, 1988.
- Albores-Saavedra J, Molberg K, Henson DE: Unusual types of gallbladder carcinoma. A report of 16 cases.

Arch Pathol Lab Med 105: 287-293, 1981.

- Jarnagin WR: Cholangiocarcinoma of the extrahepatic bile ducts. Semin Surg Oncol 19: 156-176, 2000.
- 21) Mokuno Y. Katoh T, Yoshida K, Abe T, Maeda M, Chigira H: Undifferentiated spindle cell carcinoma of the extrahepatic bile ducts. A case report. Hepatogastroenteroloogy 47: 1234-1237, 2000.
- 22) Kijima H, Takeshita T, Suzuki H, Tanahashi T, Suto A, Izumika H, Miki H, Terasaki Y, Nakamura M, Watanabe H, Tamaoki N, Omiya H: Carcinomsarcoma of the ampulla of Vater-A case report with immunohistochemical and ultrastructural studies. Am J Gastroenterol 94: 3055-3059, 1999.
- 23) Nagai E, Shinohara M, Yonemasu H, Kishikawa H, Tsuneyoshi M: Undifferentiated carcinoma of the common bile duct. Case report and review of the literature. Hepatobiliary Pancreat Surg 9: 627-631, 2002.