Surg Today (2004) 34:968–972
DOI 10.1007/s00595-004-2820-7

SURGERY TODAY

Mucoepidermoid Carcinoma of the Liver Diagnosed as a Liver Abscess: Report of a Case

DONGHO CHOI[1], HANJOON KIM[2], KWANG SOO LEE[3], KYEONG GEUN LEE[3], and CHAN KUM PARK[4]

[1]Department of Surgery, College of Medicine, Soonchunhyang University, Seoul, South Korea
[2]Department of Surgery, College of Medicine, Hallym University, Chunchon, South Korea
[3]Department of Surgery and [4]Department of Pathology, College of Medicine, Hanyang University, Seoul, South Korea

Abstract
Mucoepidermoid carcinoma of the liver is a rare variant of cholangiocarcinoma, containing both mucus-secreting glandular cells and squamous cells mixed in nests. We report a case of mucoepidermoid carcinoma of the liver in a 69-year-old woman who presented with a 1-week history of fever, chills, and right flank pain. On admission, she was not jaundiced, and under a provisional diagnosis of liver abscess, a pigtail catheter was inserted into the abscess cavity. We performed right hepatectomy and partial excision of the diaphragm 1 month later. Microscopically, the tumor was composed of solid and invasive nests of epidermoid and mucin-producing cells with desmoplastic stroma. The epidermoid component of the tumor contained intercellular bridges and individual cell keratinization. Alcian blue and Periodic acid-Schiff (PAS) staining confirmed that there was mucin in the cytoplasm of mucus-secreting cells. The tumor cells, intrahepatic bile ducts, and ductules were consistently reactive with cytokeratin (CK) 7 and negative for CK20. The adjacent non-neoplastic liver cells were CK 7−/CK20−, and P63 immunostaining was positive in the epidermoid cells. The tumor was diagnosed as mucoepidermoid carcinoma arising from the intrahepatic bile duct. Despite aggressive surgical treatment, the patient died of multiple liver metastases 4 months after the right hepatectomy.

Key words Mucoepidermoid carcinoma · Liver · Abscess

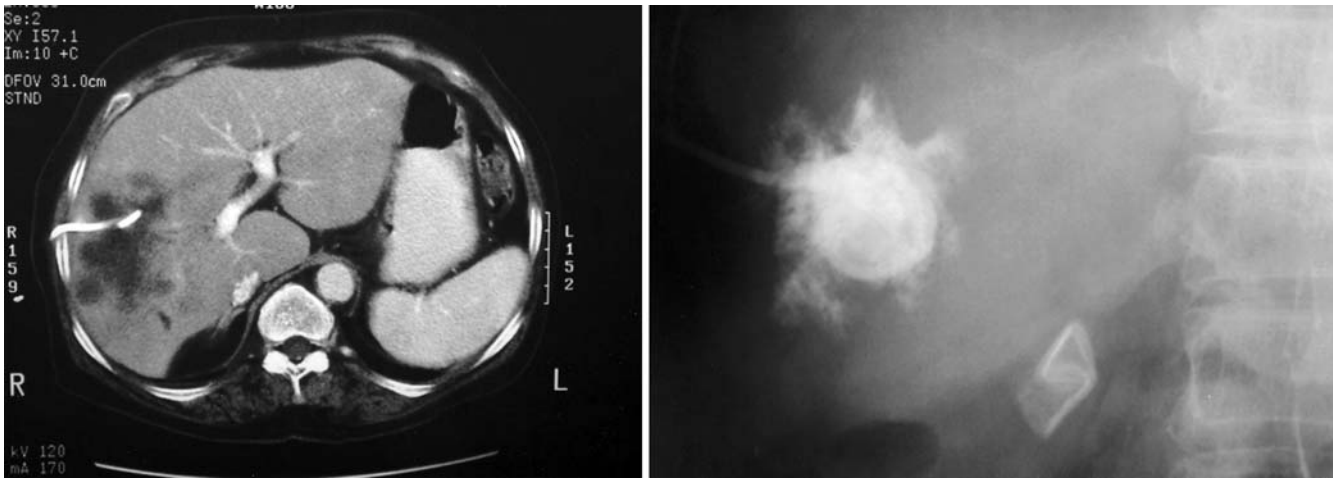
Reprint requests to: K.S. Lee, Haengdangdong 17, Sungdonggu, Seoul 133-792, South Korea
Received: September 2, 2002 / Accepted: March 9, 2004

Introduction

Mucoepidermoid carcinoma is a relatively common neoplasm of the salivary glands, which rarely arises in other sites.[1,2] Mucoepidermoid carcinoma of the bile duct is an extremely rare tumor. A review of the medical literature in the English language disclosed only 14 cases of primary mucoepidermoid carcinoma of the intrahepatic bile duct.[3,4] We report a case of primary hepatic mucoepidermoid carcinoma, which was initially diagnosed as a simple liver abscess.

Case Report

A 69-year-old woman was admitted to the Hanyang University Hospital with a 1-week history of fever, chills, and right flank pain. She had no remarkable medical or family history and had not had viral hepatitis. On clinical examination, she was not jaundiced and there were no perceptible abnormalities. Laboratory findings were as follows: white blood cell count, 15000/mm^3; hemoglobin, 11.7 g/dl; platelet count, 28.9 × 10^4/mm^3; total protein, 6.7 g/dl; albumin, 3.5 g/dl; total bilirubin, 0.7 mg/dl; alkaline phosphatase, 232 U; GOT, 29 U; and GPT, 15 U. α-Fetoprotein and carcinoembryonic antigen were within the normal range and carbohydrate antigen 19-9 was slightly increased to 240 ng/ml. Abdominal ultrasound and abdominal computed tomography (Fig. 1a) both showed a huge liver abscess involving the right lobe of the liver with intrahepatic bile duct stone. Therefore, a preliminary diagnosis of a liver abscess was made and a pigtail catheter was inserted under ultrasonic guidance into the abscess cavity. A tubogram showed an abscess cavity with a large amount of internal debris (Fig. 1b). Aspiration cytology showed no malignant cells. We performed a right hepatectomy with partial excision of the diaphragm 1 month after her admission. A hepatic specimen measuring 16



a b

Fig. 1. a Computed tomography showed multiple septated lesions in the right lobe of the liver. **b** A tubogram showed an abscess cavity filled with internal debris

× 11 × 10 cm and a specimen of the partial diaphragmectomy were submitted for permanent section. The serial sections revealed an ill-defined, huge necrotic mass, 10 × 7 cm in cross diameter, with diffuse central necrosis and ill-defined fibrosepta (Fig. 2a). We also found an impacted stone in the intrahepatic bile duct. The tumor was located 0.3 cm away from the surgical margin. Microscopic examination of the diaphragm revealed direct invasion of mucoepidermoid carcinoma. The main tumor mass was composed of solid and invasive nests of epidermoid and mucin-producing cells with desmoplastic stroma (Fig. 2b). These tumor cells were intermingled or intimately mixed, unlike adenosquamous carcinoma. Most of the tumor cells were epidermoid with intercellular bridges and occasional individual cell keratinization. Glandular structures and intraluminal and intracytoplasmic mucin were frequently noted (Fig. 2b). Mucin-secreting cells were cuboidal, columnar, or goblet-like. There was extensive necrosis with a neutrophilic abscess accompanied by neural invasion, lymphatic and blood vessel invasion, and cellular pleomorphism. Mitotic figures were frequent and there was remarkable neoplastic transformation of the normal duct lining epithelium (Fig. 2c). Some of the neoplastic ducts contained intrahepatic stones (Fig. 2d), which suggested a possible etiological relationship. Electron micrographs revealed tonofilaments and confirmed the squamous nature of the tumor cells (Fig. 3a). Some of the tumor cells contained mucin granules in addition to tonofilaments with microvilli on their apical surface. Immunohistochemical analysis provided evidence of the ductal epithelial origin of this neoplasm. The tumor cells, intrahepatic bile ducts, and ductules were consistently reactive with monoclonal antibody CK7 and negative for CK20. The adjacent non-neoplastic liver cells were CK7−/CK20− (Fig. 3b). Alcian blue and Periodic acid-Schiff (PAS) staining revealed mucin in the cytoplasm of the mucus-producing cells and in some glands (Fig. 3c,d). Immunohistochemical staining using monoclonal antibody p63 (Oncogene Research Products, Boston, MA, USA) revealed positivity in the epidermoid component and negativity in the columnar cells (Fig. 3e). Based on these findings, the tumor was diagnosed as mucuepidermoid carcinoma, arising from the intrahepatic bile duct. The patient had an uneventful postoperative recovery, but died of multiple metastases to the remnant liver 4 months after surgery.

Discussion

Mucoepidermoid carcinoma of the liver is very rare and regarded as a variant of cholangiocarcinoma, comprised of both mucus-secreting glandular type and squamous type cells.[5] The diagnosis of mucoepidermoid carcinoma of the bile duct is based on the presence of both mucin-secreting and epidermoid malignant cells, intimately mixed in nests.[5] Pianzola and Drut reported the first case in 1971 and suggested that this type of carcinoma arose from the terminal ramifications of bile canaliculi in association with squamous metaplasia.[6] However, the etiology of mucoepidermoid carcinoma of the bile duct is still unclear. Several authors proposed that mucoepidermoid carcinoma of the liver might originate from a congenital cyst because the main tumors were located in the vicinity of multiple seromucinous cysts lined with columnar, cuboidal glandular epithelium with no connection to the biliary system and no bile content.[7,8] It is speculated that the

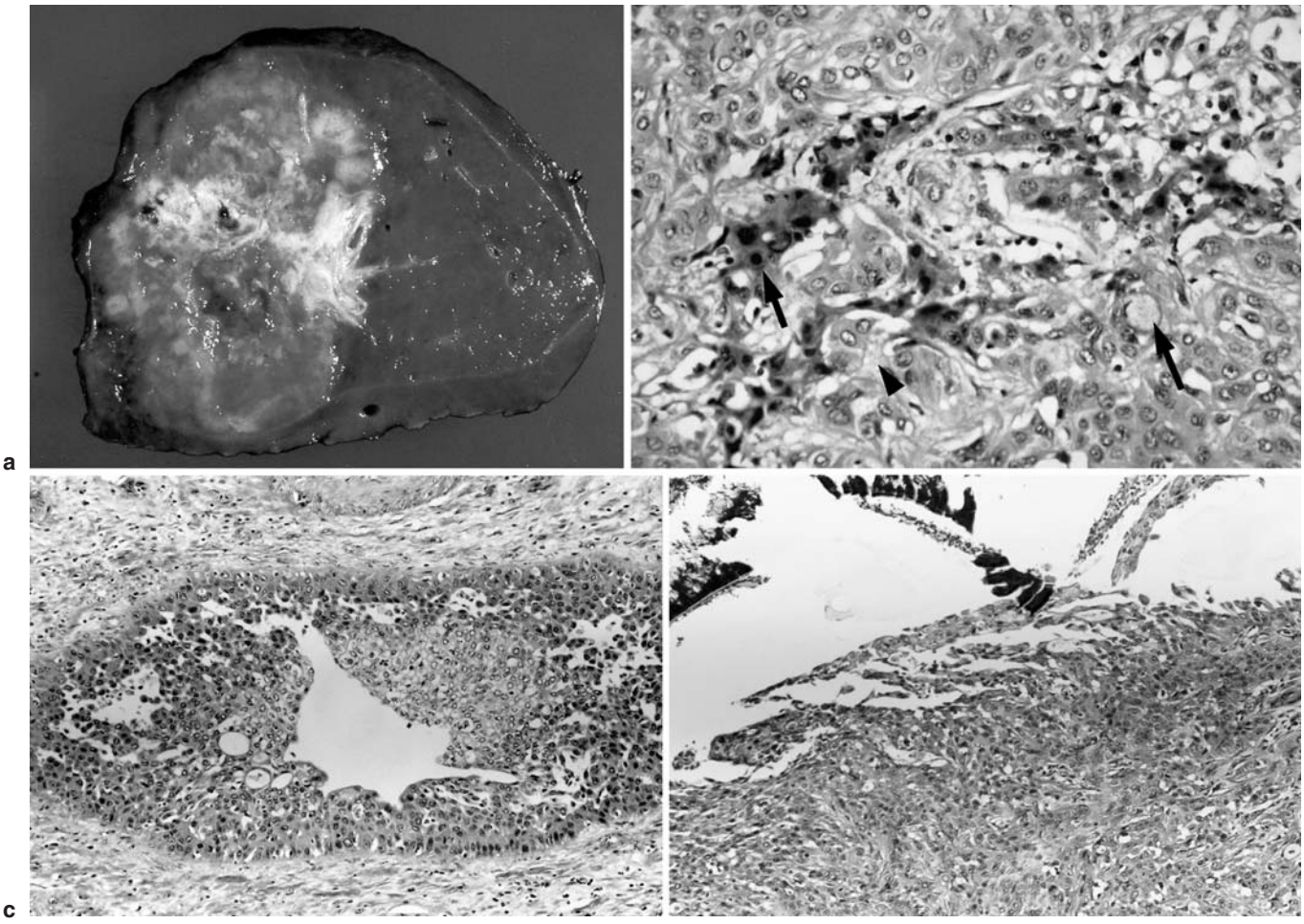


Fig. 2. **a** Cut surface of the right hepatectomy specimen showing an ill-defined necrotic tumor mass. 10 × 7 cm in size, which was pale pinkish-yellow, with fibrous septae. An impacted stone was found in the intrahepatic bile duct. **b** Photomicrograph showing the intimate association of mucin-secreting cells (*long arrow*) and squamous cells. Intercellular bridges (*arrowhead*) and individual keratinization (*short arrow*) indicated epidermoid cells (H&E, ×200). **c** Neoplastic transformation of the normal duct epithelium was seen in the bile duct (H&E, ×100). **d** An intrahepatic duct stone was seen in the neoplastic duct (H&E, ×100)

intermediate cells in mucoepidermoid carcinoma of the salivary gland may arise from the ductal epithelia and the capable of differentiating into other types of tumor cells.[9,10] Based on the histological similarity of the tumor, it is conceivable that the lining epithelia of the congenital cysts in the liver may be transformed into the pluripotential intermediate cells, which may differentiate into both mucus-secreting and squamous cells. Furthermore, *Clonorchis sinensis* infestation, primary cholangitis, and Thorotrast administration have all been suggested as predisposing factors.[11,12] In Korea, cholangiocarcinoma associated with *C. sinensis* infestation is not uncommon, especially in the Southwestern region around the Nakdong river.[13] However, to our knowledge, only one case of mucoepidermoid carcinoma of the bile duct has been described in the English medical literature.[3] Interestingly, Higuchi et al.[14] suggested the possibility that primary mucoepidermoid carcinoma of the liver is sometimes misdiagnosed as cholangiocarcinoma with squamous metaplasia or as adenosquamous cell carcinoma.

The use of CK7/CK20 immunostaining could help to distinguish hepatocellular carcinoma from other liver tumors, such as cholangiocarcinomas of the peripheral type and colorectal carcinoma metastasis, which are generally CK7−/CK20−, CK7+/CK20−, and CK7−/CK20+, respectively.[15] The CK immunoprofile of cholangiocarcinoma varies according to the location of the tumor in the biliary tract, peripheral cholangiocarcinoma being more often CK7+/CK20− as in our patient, whereas nonperipheral cholangiocarcinoma is more often CK7+/CK20+.[15] Based on the CK immunoprofile, we suggest that mucoepidermoid carcinomas arise from the peripheral biliary tract. The p63

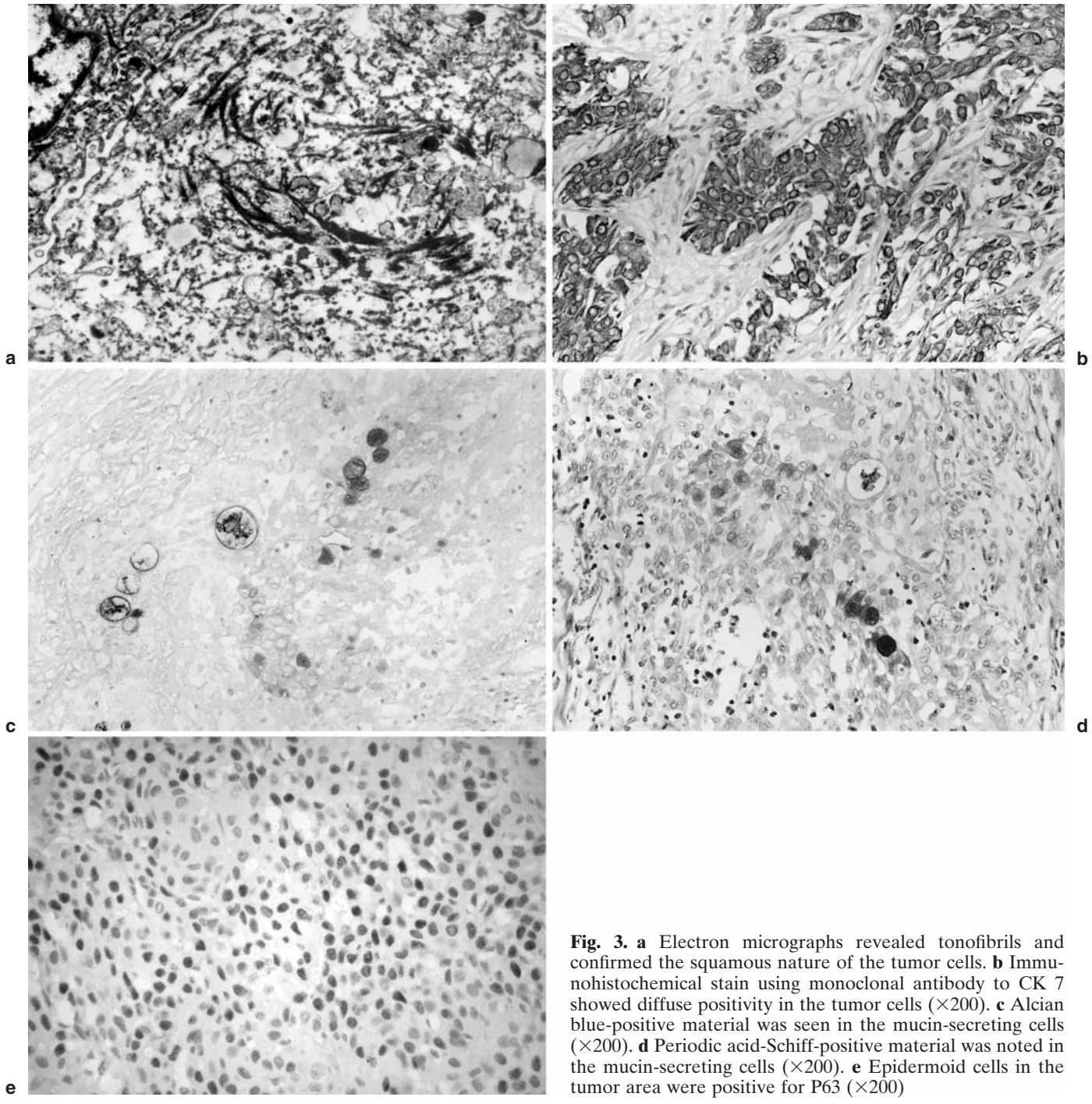


Fig. 3. a Electron micrographs revealed tonofibrils and confirmed the squamous nature of the tumor cells. **b** Immunohistochemical stain using monoclonal antibody to CK 7 showed diffuse positivity in the tumor cells (×200). **c** Alcian blue-positive material was seen in the mucin-secreting cells (×200). **d** Periodic acid-Schiff-positive material was noted in the mucin-secreting cells (×200). **e** Epidermoid cells in the tumor area were positive for P63 (×200)

transcription factor belongs to a family that includes two structurally related proteins, p53 and p73. Whereas p53 plays a well-established role in tumor suppression, p63 and p73 play specialized roles in morphogenesis.[16] It was recently found that p63, a specific marker of human corneal and epidermal stem cells,[16] is useful for detecting squamous cells and for differentiating between squamous cell carcinomas and nonsquamous cell carcinomas. Adenocarcinomas are usually negative for p63. In the present case, p63 was positive in the epidermoid component and negative in the glandular component of the tumor.

Establishing a preoperative diagnosis is difficult because of the rarity of these tumors and the fact that there are no specific landmarks in the radiologic examinations. Conventional CT and ultrasonography show

an intrahepatic mass. Liver abscess or peripheral cholangiocarcinoma are often compatible with the diagnosis of these lesions. Our patient's initial symptoms were fever, chills, and right flank pain, suggesting that the intrahepatic mass was a liver abscess, but pigtail catheter drainage was not effective.

Mucoepidermoid carcinoma is generally a slow-growing tumor, and its prognosis is better than that of ordinary carcinoma.[12] The biological behavior and prognosis of mucoepidermoid carcinoma of the liver is still undetermined, although Shuangshoti reported that the survival period of 11 patients with mucoepidermoid carcinoma of the liver ranged from 2 weeks to 11 months.[4] Of these patients, three were not treated, one was treated with chemotherapy alone, and the other seven were treated with various types of hepatectomy. Consequently, mucoepidermoid carcinoma of the liver is regarded as an aggressive tumor with poor prognosis despite surgical treatment. Our patient survived for only 4 months after aggressive surgical intervention including the excision of the diaphragm. Therefore, further multi-institutional studies are needed to clarify the histogenesis and biological behavior of primary mucoepidermoid carcinoma of the liver.

References

1. Sato H, Kuroda M, Maruta M, Maeda K, Koide Y. Mucoepidermoid carcinoma of the ascending colon: report of a case. Surg Today 2002;32:1004–7.
2. Onoda N, Kang SM, Sugano S, Yamashita Y, Chung YS, Sowa M. Mucoepidermoid carcinoma of the pancreas: report of a case. Surg Today 1995;25:843–7.
3. Kang H, Park YN, Kim SE, Sohn KR, Yoo NC, Park JY, et al. Double primary mucoepidermoid carcinoma and hepatocellular carcinoma of the liver — a case report. Hepatogastroenterology 2003;50:238–41.
4. Shuangshoti S Jr, Shuangshoti S. Primary mucoepidermoid carcinoma of the intrahepatic bile duct: a case report with review of literature. J Med Assoc Thai 2000;83:197–203.
5. Gibson JB, Sobin LH. Histological typing of tumors of the liver, biliary tract and pancreas. International histological classification of tumors. No. 20. Geneva: WHO; 1978. p. 23–4.
6. Pianzola LE, Drut R. Mucoepidermoid carcinoma of the liver. Am J Clin Pathol 1971;56:758–61.
7. Kutsuda S, Nakanishi I, Kajikawa K, Takabatake S. Mucoepidermoid carcinoma of the liver. Acta Pathol Jpn 1984;34:153–7.
8. Hayashi I, Tomoda H, Tanimoto M, Furusawa M, Katsuda Y, Shirai S, et al. Mucoepidermoid carcinoma arising from a preexisting cyst of the liver. J Surg Oncol 1987;36:122–5.
9. Foote FW, Frazell EL. Tumors of the major salivary glands. Cancer 1953;6:1065–133.
10. Stewart FW, Foote FW, Becker WF. Mucoepidermoid tumors of salivary glands. Ann Surg 1945;122:820–44.
11. Lambrianidase AL, Askew AR, Lefevre I. Thorotrast associated mucoepidermoid carcinoma of the liver. Br J Radiol 1986;59:791–2.
12. Koo J, Ho J, Wong J, Ong GB. Mucoepidermoid carcinoma of the bile duct. Ann Surg 1982;196:140–8.
13. Rhim HJ. Clonorchiasis in Korea. Korean J Parasitol 1990; 28(suppl):63–78.
14. Higuchi T, Harada T, Okazaki M, Kikuchi M. Primary adenosquamous carcinoma of the liver. Aust N Z J Surg 1993;63:319–23.
15. Rullier A, Le Bail B, Fawaz R, Blanc JF, Saric J, Bioulac-Sage P. Cytokeratin 7 and 20 expression in cholangiocarcinomas varies along the biliary tract but still differs from that in colorectal carcinoma metastasis. Am J Surg Pathol 2000;24:870–6.
16. Pellegrini G, Dellambra E, Golisano O, Martinelli E, Fantozzi I, Bondanza S, et al. p63 identifies keratinocytes stem cells. Proc Natl Acad Sci USA 2001;98:3156–61.