Subtotal hepatectomy following neoadjuvant chemotherapy for a previously unresectable hepatocellular carcinoma

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Abstract
An awareness of variant hepatic vascular anatomy provides vital information in the preoperative evaluation of patients with hepatocellular carcinoma. The authors present a patient with unresectable hepatocellular carcinoma who responded to combination systemic and regional chemotherapy. Because of the presence of an enlarged inferior right hepatic vein, the patient subsequently underwent successful subtotal hepatectomy with resection of all three main hepatic veins. This case illustrates that the combination of innovative neoadjuvant chemotherapy and well-planned surgical approaches may benefit a small number of patients previously deemed unresectable.

Key words: Subtotal hepatectomy · Hepatocellular carcinoma · Neoadjuvant chemotherapy

Introduction
Surgical resection remains the only potentially curative treatment for patients with hepatocellular carcinoma (HCC). Because most patients have unresectable disease at the time of diagnosis, their prognosis is poor. Although randomized trials have failed to show that chemotherapeutic agents alone improve survival in patients with HCC, chemotherapy in the neoadjuvant setting combined with more aggressive surgical techniques may enable resection with curative intent in selected cases.1 In 1987, Makuuchi and colleagues proposed a resection technique — later termed subtotal hepatectomy — in which only the inferior right hepatic vein (IRHV) was preserved as outflow for the right posterior liver when all three main hepatic veins were resected. In this report, we describe a case in which a patient with unresectable HCC received neoadjuvant chemotherapy and, subsequent to tumor shrinkage, underwent resection with subtotal hepatectomy.

Case report
A 56-year-old woman was initially seen at another institution for a 2-month history of nausea and right upper quadrant pain. An abdominal computed tomographic scan revealed a large hepatic mass involving the left liver and the right anterior sector. The pathologic interpretation of a fine-needle biopsy of the liver tumor was initially adenocarcinoma. Because the patient had undergone a modified radical mastectomy for invasive ductal carcinoma (T1N1) of the left breast 5 years prior to this presentation, she was presumed to have recurrent breast cancer with hepatic metastases. Systemic chemotherapy with docetaxel (75mg/m2 i.v. every 3 weeks × four courses) and capecitabine (500mg p.o. twice daily for approximately 82 days) was administered, with no reduction in the size of the hepatic mass. The patient was then referred to The University of Texas M. D. Anderson Cancer Center for consultation.

On evaluation at M. D. Anderson Cancer Center, repeat computed tomographic imaging revealed a large mass centered in the medial left liver with extension into the anterior sector of the right liver (Fig. 1). All three suprahepatic veins were involved by tumor. Because of the extent of the vascular involvement, surgical resection was not deemed possible. Imaging characteristics suggested the possibility of HCC, rather than breast cancer, and the serum alpha-fetoprotein level supported this suspicion (3900ng/ml). Direct comparison of the liver biopsy to the original breast carcinoma revealed that the cytology and histology were convincingly different and were diagnostic of HCC in the liver tumor. Immunohistochemical stains on the liver biopsy (carbohydrate antigen [CA]225, cytokeratin [CK7,
AE1/AE3, carcinoembryonic antigen [CEA]) were negative (metastasis from breast cancer would be expected to be CK7 and AE1/AE3+).

Transarterial chemoembolization (TACE) with doxorubicin (30mg i.a.) and mitomycin-C (15mg i.a.) led to a fall in alpha fetoprotein and a radiographic response, but the tumors remained unresectable due to extensive persistent involvement of the left and middle hepatic veins, and persistent tumor in contact with the proximal right hepatic vein (Fig. 2). Due to concerns over the tissue diagnosis, the patient’s primary oncologist pursued further chemotherapies directed at a cancer of unknown primary and/or breast cancer. These included single-agent paclitaxel (100mg/m² i.v., three weekly doses over 4 weeks), and then combination chemotherapy (gemcitabine, 800mg/m² i.v.; 5-fluorouracil, 500mg/m² i.v.; and leucovorin, 500mg i.v., for four weekly doses over 5 weeks). A modest reduction in tumor size was noted, and consideration was given to resection if further response could be achieved. After further consultation at M. D. Anderson Cancer Center and with focus on the diagnosis of HCC, treatment with a modified PIAF regimen was initiated (cisplatin, 20mg/m² i.v. days 1–4; mitoxantrone, 12mg/m² i.v. day 1; 5-fluorouracil, 400mg/m² i.v. days 1–4; and alpha-interferon, 5 million units/m² s.c. days 1–4; prior doxorubicin exposure led to substitution with mitoxantrone). The first course was administered with a 15% dose reduction and all subsequent courses were administered at full doses. After four (monthly) cycles of modified PIAF treatment, the serum alpha-fetoprotein level decreased to 6ng/ml, and the tumor mass was markedly smaller. In addition, the IRHV, which had been visible but diminutive on prior imaging, appeared more prominent after tumor shrinkage (Fig. 3). An extended left hepatectomy with resection of all three main hepatic veins, preserving the IRHV, was judged to be possible.

At the time of laparotomy, tumor involvement of Couinaud segments I through V, VIII, and the superior portion of VII was found, with sparing of the right posterior portal structures, segment VI, and the inferior portion of segment VII. Sonography confirmed the CT findings, including an enlarged venous branch anterior to the right posterior portal branch (Fig. 3a); large tribu-