Icteric Type Hepatocellular Carcinoma: Clinical Features, Diagnosis and Treatment

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Icteric type hepatocellular carcinoma (HCC), a clinical entity of HCC presenting as obstructive jaundice caused by floating tumor debris in common bile duct, is rare. Taiwan has a high incidence of HCC and liver cirrhosis. The clinical features, diagnosis and treatment of this disease entity were reviewed. Not all patients with this disease were terminally ill. With proper management and good palliation, occasional cure are possible. *(Chang Gung Med J 2002;25:496-501)*

Key words: obstructive jaundice, hepatocellular carcinoma, hepatic resection, choledochotomy, biliary tract decompression.

Hepatocellular carcinoma (HCC) is a relatively common malignant tumor throughout the world, and is frequently encountered in Taiwan.[1-3] Jaundice is present in 19-40% of patients with HCC at the time of diagnosis.[4-6] The common causes of jaundice are the underlying liver cirrhosis and/or extensive hepatic parenchymal destruction of tumor.[7] Death from HCC is often heralded by the appearance of jaundice in these patients.[5-8] Obstructive jaundice as the main presenting clinical feature is uncommon.[5,6] The bile ducts can be obstructed by tumor thrombi, hemobilia, tumor compression, or tumor infiltration.[9-16] Lin[17] clinically classified such cases of HCC with obstructive jaundice due to the migration of tumor thrombi as "icteric hepatoma" and stated that they presented difficult problems in differential diagnosis. Specific treatment for HCC in such circumstance is difficult and the prognosis is poor.[8-20] Since the availability of modern diagnostic modalities and surgical techniques, this paper attempts to review the clinical presentation, diagnosis and management of this specific type of HCC.

Clinical features

Most of the patients experienced repeated episodes of jaundice.[15,18,21,22] Upper abdominal pain was presented in some of them. Fever and chills were also noted. Body weight loss, pruritis, nausea, anorexia, vomiting and liver enlargement were the most common signs at admission. Tumor invasion into a branch of the intrahepatic duct system can also cause mechanical obstruction of the main ducts by one of three means: 1) the tumor may grow continuously in a distal fashion, filling the entire extrahepatic biliary system with a solid cast of tumor; 2) a fragment of necrotic tumor may separate from the proximal intraductal growth, migrating to the distal common bile duct and causing obstruction; or 3) hemorrhage from the tumor may partially or completely fill the biliary tree with blood clots. Tumor debris may arise from a neoplasm that directly invades the bile duct or from necrosis of a tumor mass that is adjacent to a major bile duct. The ultimate site of duct obstruction may be close to or quite distant from the main tumor mass, depending on the size of the duct

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Received: Jun. 28, 2002; Accepted: Jul. 22, 2002
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and of the fragment. Obstructive jaundice caused by biliary stones or cholangiocarcinoma usually improves by simply biliary drainage such as nasobiliary drainage or percutaneous transhepatic biliary drainage (PTBD).[23,24] However, in the case of icteric hepatomas, if the HCC itself is not treated in combination with biliary drainage, the tumor in the bile duct may grow and bleed, resulting in inadequate reduction in jaundice. In icteric hepatomas, the tumor thrombus in the bile duct may compress the portal branch since both the portal vein and bile duct are surrounded by the same Glissonian sheath. A decrease in portal blood supply may cause degenerative change in non-cancerous liver parenchyma. Since non-cancerous liver parenchyma in the affected liver segments does not contribute significantly to the total liver function, this should be borne in mind when deciding on the degree of surgical resection.[23,25]

Diagnosis: laboratory and imaging studies

Patients with HCC and obstructive jaundice secondary to ruptured HCC into the biliary tree present difficult and challenging problems in differential diagnosis. This rare complication must be differentiated from jaundice because of hilar invasion, diffuse tumor infiltration, or progressive terminal hepatic failure for which there is no chance of palliation or possible cure. The presence of an elevated alpha-fetoprotein (AFP) level and positive hepatitis B surface antigen (HBsAg) helps to establish the diagnosis. In the absence of this finding, especially with no primary hepatic tumor being detected, a variety of other diagnoses were entertained. Despite remarkable recent improvements in the imaging tools for diagnosis of HCC, such cases were often still incorrectly diagnosed as cholangiocarcinoma or choledocholithiasis.[8-21] Ultrasonography (US) and computed tomography (CT) are helpful in showing hepatic tumors and dilated intrahepatic and /or extrahepatic ducts containing dense material corresponding to tumor debris.[26] Sometimes, the location and cause of biliary obstruction cannot be made clear by US and CT.

Cholangiography

Percutaneous transhepatic cholangiography (PTC) and endoscopic retrograde cholangiopancreatagraphy (ERCP) are of some value in the diagnosis of this disease entity.[27-33] According to Wu et al.,[31] the cholangiographic features of these patients can be divided into the following three categories: 1) Intraductal filling defects resulting in complete or partial obstruction and ductal dilation. 2) Abrupt complete obstruction of the common hepatic duct with an irregular cut surface, and 3) Tumor encasement or stricture of the major hepatic duct without filling defects. Other miscellaneous findings included displacement of the ductal system by the extrabiliary mass effect, a "rat tail" stricture and a bulky tumor growing or polypoid lesions with filling defects on cholangiography. The intraluminal filling defects and irregular cutting surfaces were found to be blood clots and/or necrotic tumor debris. The other differential diagnoses of this type cholangiography include cholangiocarcinoma, intraductal polyps, or mucin-hypersecreting intrahepatic biliary neoplasms.

Magnetic resonance cholangiopancreatography (MRCP)

It is an absolutely noninvasive imaging modality, allowing demonstration of the biliopancreatic system by means of data acquisition and images post-processing reconstruction presenting at the coronal plane similar to conventional cholangiography. It requires neither contrast medium injection nor biliary endoscopic intervention; therefore, it completely avoids the formidable complications inherent to conventional cholangiographic examinations.[34,35] Recent studies of MRCP have claimed high accuracy in depicting various biliary and pancreatic disease entities, with reported sensitivities approaching 90-95% for biliary and pancreatic ductal dilatation and stricture.[36-38] According to Yeh et al.,[34] MRCP and direct cholangiography provided the equivalent diagnostic information on the visualization of the intrahepatic ducts and opacification of the common hepatic duct. The presence of an encapsulated mass with a central scar or internal fat , by means of T2-weighted axial and coronal plane of MR images, are very useful to diagnose icteric HCC.

Angiography

Angiography is indicated when vascular extension is suspected.[23,29] Not always, hypervascular tumors can be found in angiography. Transcatheter

hepatic arterial embolization (TAE) is effective to control hemobilia.[23]

Treatment

General principles

The excellent palliation that has been achieved by our group and others suggest that aggressive examination and treatment are warranted in patients with HCC who have extrahepatic biliary obstruction.[11-16] Identification of specific cause of jaundice in patients with HCC is of great importance. The goals of operative intervention in these patients are biliary decompression, removal of tumor debris, and, if possible, a direct attack on the underlying neoplasm. Operative cholangioscopy is an important adjunct to formal common bile duct exploration in the initial assessment and planning of operative strategy. Direct endoscopic visualization of the bile ducts will facilitate differentiation of neoplastic strictures from filling defects seen at cholangiography.[39,40] Removal of gross tumor debris as much as possible through manual extraction and irrigation is crucial and should be verified at the conclusion of the procedure either by repeated endoscopy or cholangiography. Numerous techniques can be used for biliary decompression and drainage.[41,42] The decision to perform a hepatic resection, internal biliary stenting, or biliary diversion should be based on the nature and location of the main tumor mass, severity of the symptoms, associated neoplastic strictures, and the patient's overall status.[43,44] Most patients will have satisfactory palliation if the appropriate procedures are selected and performed safely.

Operative treatments

It has generally been accepted that pre-operative jaundice reduction is unnecessary for abdominal major surgeries.[45,46] Hatfield et al.[47] reported that there was a negligible difference between pre-operatively treated and control groups. To the contrary, pre-operative reduction of jaundice is essential for the successful hepatectomy for icteric HCC. Icteric HCC-bearing liver is usually related to hepatitis or liver cirrhosis. Accurate pre-operative evaluation of liver function is essential for patient selection to prevent post-operative liver failure.[23]

At the time of duct exploration, one should look carefully for free-floating debris as well as tumor that may have become adherent to the duct wall. These lesions may be vascular, and the debris may consist of tumor mixed with clot. If tumor fragments in the bile duct are not adherent to the wall, they can be extracted easily. However, if the intraductal mass is continuous with the mass intrahepatic tumor, torrential hemorrhage may occur on attempted removal. Hemostasis can usually be achieved by suturing, electrocauterization, compression, Pringle's maneuver, and hepatic arterial ligation. Histologic evaluation of all bile duct debris should be routine and will usually confirm the diagnosis of a primary or metastatic carcinoma.[29]

The ideal treatment of these patients is hepatic resection.[15,18,20,48-50] Unfortunately, most tumors are unsuitable for resection, because the tumor is often close to the hepatic hilum. In patients with more advanced disease, satisfactory palliation can be achieved with duct exploration and removal of debris followed by tube decompression or a biliary-enteric bypass. Although a simple T-tube may be easier to place than a transhepatic tube, the latter has several advantages. Transhepatic tubes can be more easily irrigated over a long period and provide better drainage than T-tubes.[51] In addition, properly placed transhepatic tubes can be changed periodically using fluoroscopic guidance when the tubes become occluded. For operable tumors, a staged approach with initial biliary decompression followed by hepatic resection as a second procedure may have been done because of the poor general condition of some of these patients at the initial examination.[19,20]

Recurrent episodic jaundice or cholangitis suggests extrahepatic biliary obstruction in most patients with tumors. The clinical manifestation is uncommon in patients with extensive parenchymal hepatic metastases. In the absence of definite tumor progression or evidence of generalized clinical deterioration, the presence of episodic jaundice or cholangitis should promote the search for extrahepatic obstruction as a cause of jaundice.[18-20] The prognosis of patients with obstructive jaundice due to HCC is dismal; however, with proper management, good palliation and occasional cure are still possible in some patients.[52]

REFERENCES

1. Beasley RP, Hwang LY, Lin CC, Chien CS. Hepatocellular carcinoma and hepatitis B virus: a

prospective study of 22707 men in Taiwan. Lancet 1981; ii:129-35.
2. Liaw YF, Lin DY, Chen TL, Chu CM. Natural course after the development of cirrhosis in patients with chronic type B hepatitis: a prospective study. Liver 1989; 9:235-41.
3. Chen DS. From hepatitis to hepatoma: lesions from type B viral hepatitis. Science 1993;262;369-73.
4. Sung JL, Wang TH, Yu JY. Clinical study on primary carcinoma of the liver in Taiwan. Am J Dig Dis 1967;12: 1039-49.
5. Okuda K. Clinical aspects of hepatocellular carcinoma: analysis of 134 cases. In: Okuda K, Peters RL, editors. Hepatocellular carcinoma. New York: John Wiley, 1976;387-436.
6. Lai CL, Lam KC, Wang KP, Wu PC, Toad D. Clinical features of hepatocellular carcinoma: review of 211 patients in Hong Kong. Cancer 1981;47;2746-55.
7. Lee NW, Wang P, Siu KF, Wong J. Cholangiography in hepatocellular carcinoma with obstructive jaundice. Clin Radiol 1984;35:119-23.
8. Pawarode A, Voravud N, Sriuranpong V, Kullavanijaya P, Patt YZ. Natural history of untreated hepatocellular carcinoma: a retrospective study of 157 patients. Am J Clin Oncol 1998;21:386-91.
9. Satoh S, Ikai I, Honda G, Okabe H, Takeyama O, Yamamoto Y. Clinicopathologic evaluation of hepatocellular carcinoma with bile duct thrombi. Surgery 2000;128:779-83.
10. Belghiti J, Hiramatsu K, Benoist S, Massault P, Sauvanet A, Farges O. Seven hundred forty-seven hepatectomies in the 1990s: an update to evaluate the actual risk of liver resection. J Am Coll Surg 2000;191:38-46.
11. Lauffer JM, Mai G, Berchtold D, Curti CG, Triller J, Baer HU. Multidisplininary approach to palliation of obstructive jaundice caused by a central hepatocellular carcinoma. Dig Surg 1993;16:531-6.
12. Wang HJ, Kim JH, Kim WH, Kim MW. Hepatocellular carcinoma with tumor thrombi in the bile duct. Hepatogastroenterol 1999;46:2495-9.
13. Shimoji H, Shiraishi M, Hiroyasu S, Isa T, Kusano T, Muto Y. Common bile duct blood clot: an usual cause of ductal filling defects for calculi. J Gastroenterol 1999; 34:420-3.
14. Hu J, Pi Z, Yu MY, Li Y, Xiong S. Obstructive jaundice caused by tumor emboli from hepatocellular carcinoma. Am Surg 1999;65:406-10.
15. Chen MF, Jan YY, Jeng LB, Hwang TL, Wang CS, Chen SC. Obstructive jaundice secondary to ruptured hepatocellular carcinoma into the common bile duct. Cancer 1994;73:1335-40.
16. Chen MF, Hwang TL, Jeng LB, Jan YY, Wang CS, Chou FF. Hepatic resection in 120 patients with hepatocellular carcinoma. Arch Surg 1989;124:1025-8.
17. Lin TY. Tumor of the liver. In: Bockus UL, editor, Gastroenterology. Philadelphia: WB Saunders, 1976;522-33.
18. Lau WY, Leung WC, Li KC. Management of hepatocellular carcinoma presenting as obstructive jaundice. Am J Surg 1990;160:280-2.
19. Afroudakis A, Bhuta SM, Ranganata KA, Kaplowitz N. Obstructive jaundice caused by hepatocellular carcinoma: report of three cases. Dig Dis Sci 1978;23:609-17.
20. Tsuzaku, T, Ogata Y, Iida S, Kasajima M, Takahashi S. Hepatoma with obstructive jaundice due to migration of a tumor mass in the biliary tract: report of a successful resection. Surgery 1979;85:593-8.
21. Ueda M, Takeuchi T, Takayasu T, Takahashi K, Okamoto S, Tanaka A. Classification and surgical treatment of hepatocellular carcinoma with bile duct thrombi. Hepatogastroentol 1994;41:349-54.
22. Huang GT, Sheu JC, Lee HS, Lai MY, Wang TH, Chen DS. Icteric type hepatocellular carcinoma: revisited 20 years later. J Gastroenterol 1998;33:53-6.
23. Tada K, Kubota K, Sano K, Noie T, Kosuge T, Takayama T, Makuuchi M. Surgery of icteric-type hepatoma after biliary drainage and transcatheter arterial embolization. Hepatogastroenterol 1999;46:843-8.
24. Cherqui D, Benoist S, Malassague B, Huneres R, Rodriguez V, Fagniez PL. Major liver resection for carcinoma in jaundiced patients without preoperative biliary drainage. Arch Surg 2000;135:302-8.
25. Lau WY, Leung K, Leung TW, Liew LT, Chan MS, Yu SC, Li AK. A logical approach to hepatocellular carcinoma presenting with jaundice. Ann Surg 1997;225:281-5.
26. Matzen P, Malchow-Moller A, Bran B, Gronval A, Haubek A, Henriken JH. Ultrasonography, computed tomography and cholescintigraphy in suspected obstructive jaundice: a prospective comparative study. Gastroenterol 1983; 84:1492-7.
27. Muller PR, Harbin WP, Ferruci JT Jr., Wittenberg J, van Sonnenberg E. Fine-needle transhepatic cholangiography: reflection after 450 cases. Am J Radiol 1981; 136:85-90.
28. Silvis SE, Rohrmann CA, Venners JA. Diagnostic accuracy of ERCP in hepatic biliary and pancreatic malignancy. Ann Intern Med 1979;84:438-46.
29. Roslyn JJ, Kuchembecker S, Longmire WP, Tompkins PK. Floating tumor debris: a cause of intermittent biliary obstruction. Arch Surg 1984;119:1312-5.
30. Law WY, LeowCK, Leung KC, Leung TW, Chan M, Yu SC. Cholangiographic features in the diagnosis and management of obstructive icteric type hepatocellular carcinoma. HPB Surg 2000;11:299-306.
31. Wu CS, Wu SS, Chen PC, Chiu CT, Lin SM, Jan YY, Hung CF. Cholangiography of icteric type hepatoma. Am J Gastroenterol 1994;89:774-7.
32. Lee NW, Wong KP, Siu KF. Cholangiography in hepatocellular carcinoma with obstructive jaundice. Clin Radiol 1984;35:119-23.
33. Legge DA, Carlson HC. Cholangiographic appearance of

primary carcinoma of the bile duct. Radiology 1972;102:259-66.
34. Yeh TS, Jan YY, Tseng JH, Chiu CT, Chen TC, Hwang TL, Chen MF. Malignant resonance cholangiopancreatographic findings. Am J Gastroenterol 2000;95:432-40.
35. Wallner BK, Schumacher KA, Weidenmaler W,Friedrich JM. Dilated biliary tract: Evaluation with MR cholangiography with a T2-weighted contrast-enhanced fast sequence. Radiology 1991;181:805-8.
36. Lomanto D, Pavone P, Laghi A, Panebianco V, Mazzocchi P, Fiocca F, Lezoche E, Passariello R, Speranza V. Magnetic resonsnce cholangiopancreatography in the diagnosis of biliopacreatic diseases. Am J Surg 1997; 174:33-8.
37. Fulcher AS, Turner MA, Capps GW, Zfass AM, Baker KM. Half-Fourier RARE MR cholangiopancreatography: experince in 300 subjects. Radiology 1998;207:21-32.
38. Barish MA, Yucel EK, Soto JA, Chuttani R, Ferrucci JT. MR cholangiopancreatography: Efficacy of three-dimensional turbo spinecho technique. Am J Radiol 1995; 165: 295-300.
39. Chen MF, Jan YY, Wang CS, Jeng LB, Hwang TL. Intraoperative fiberoptic choledochoscopy for malignant biliary obatruction. Gastrointest Endosc 1989;35:545-7.
40. Jan YY, Chen MF. Obstructive jaundice secondary to hepatocellular carcinoma rupture into the common bile duct: choledochoscopic findings. Hepatogastroenterology 1999;46:157-61.
41. Nakayama T, Ikeda A, Okuda K. Percutaneous transhepatic drainage of the biliary tract: technique and results in 104 cases. Gastroenterology 1978:74:554-9.
42. Ferrucci JT Jr., Mueller PR, Harbin WP. Percutaneous transhepatic biliary drainage technique, results and application. Radiology 1980;135:1-13.
43. Shimada M, Takenaka K, Hasegawa H, Shirabe K, Gion T, Kano T, Sugimachi K. Hepatic resection for icteric type hepatocellular carcinoma. Hepatogastroenterology 1997;44:1432-7.
44. Buckmaster MJ, Schwartz RW, Carnahan GE, Strodel WE. Hepatocellular carcinoma embolus to the common hepatic duct with no detectable primary hepatic tumor. Am Surg 1994;60:699-702.
45. Lai EC, Mok FP, Fan ST. Preoperative endoscopic drainage for malignant obstructive jaundice. Br J Surg 1994;81:1195-8.
46. Pitt HA, Gomes AS, Lois JF. Does preoperative percutaneous biliary drainage reduce operative risk on increase hospital cost? Ann Surg 1985;201:545-53.
47. Hatfield AR, Tobias R, Terblanche J. Preoperative external biliary drainage in obstructive jaundice. A prospective controlled clinical trial. Lancet 1982;2:896-9.
48. Tanoue K, Kanematsu T, Matsumato T, Shirabe K, Sugimachi K, Yasunaga C. Successful surgical treatment of hepatocellular carcinoma including into biliary tree. H P B Surg 1991;4:237-44.
49. Tantawi B, Cherqui D, Tran van Nhieu J, Kracht M, Faguiez PC. Surgery for biliary obstruction by tumor thrombi in primary liver cancer. Br J Surg 1996; 83:1522-5.
50. Mok KT, Chang HT, Lin ST, Jow NW, Tsai CC, Wamg BW. Surgical treatment of hepatocellular carcinoma with biliary tumor thrombi. Int Surg 1996;81:284-8.
51. Cameron JL, Gayler BW, Znidema GD. The use of silastic transhepatic stents in benign and malignant biliary strictures. Ann Surg 1978;188:552-9.
52. Jan YY, Chen MF, Chen TJ. Long term survival after obstruction of the commonbile duct by ductal hepatocellular carcinoma. Eur J Surg 1995;161:771-4.

黃疸性肝癌：臨床症狀、診斷及治療

陳敏夫

黃疸型肝癌是泛指肝癌侵犯至總膽管進而產生阻塞性黃疸。台灣地區雖好發肝癌及肝硬化，但本病症非常少見。本文將此病症之臨床症狀、診斷及處理原則做一綜合性報告。此病並非絕症，經過適當的處置而緩解，少數病人偶然亦會有長期的存活。(長庚醫誌 2002;25:496-501)

關鍵字：阻塞性黃疸，肝細胞癌，肝切除，總膽管切開引流，膽道解壓。

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