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SURGICAL MANAGEMENT OF SPONTANEOUS RUPTURED HEPATOCELLULAR ADENOMA

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AIMS: Spontaneous ruptured hepatocellular adenoma (SRHA) is a rare life-threatening condition that may require surgical treatment to control hemorrhaging and also stabilize the patient. We report a series of emergency surgeries performed at our institution for this condition.

METHODS: We reviewed medical records and radiology files of 28 patients (from 1989 to 2006) with a proven diagnosis of hepatocellular adenoma (HA). Three (10.7%) of 28 patients had spontaneous ruptured hepatocellular adenoma, two of which were associated with intrahepatic hemorrhage while one had intraperitoneal bleeding. Two patients were female and one was male. Both female patients had a background history of oral contraceptive use. Sudden abdominal pain associated with hemodynamic instability occurred in all patients who suffered from spontaneous ruptured hepatocellular adenoma. The mean age was 41.6 years old. The preoperative assessment included liver function tests, ultrasonography and computed tomography.

RESULTS: The surgical approaches were as follows: right hemihepatectomy for controlling intraperitoneal bleeding, and right extended hepatectomy and non-anatomic resection of the liver for intrahepatic hemorrhage. There were no deaths, and the postoperative complications were bile leakage and wound infection (re-operation), as well as intraperitoneal abscess (re-operation) and pleural effusion.

CONCLUSION: Spontaneous ruptured hepatocellular adenoma may be treated by surgery for controlling hemorrhages and stabilizing the patient, and the decision to operate depends upon both the patient's condition and the expertise of the surgical team.

KEYWORDS: Adenoma; Surgery; Complications; Liver hemorrhage; Mortality.

INTRODUCTION

Spontaneous ruptured hepatocellular adenoma (SRHA) is an unusual life-threatening condition. Although emergency surgery for ruptured hepatocellular adenoma (HA) of the liver is associated with high mortality and morbidity rates, it remains the treatment of choice.[1,2] Emergency resection of ruptured HA has a mortality rate of between five and ten percent, whereas elective surgery has a mortality rate of less than one percent.[3-5] A recent study showed that conservative management of ruptured HA may be a good alternative treatment, as none of the 12 patients in the study died.[6] However, three of these patients required urgent laparotomy and gauze packing for life-threatening hemorrhage. Liver resection has been recommended for symptomatic or enlarging HA because of the associated risk of intraperitoneal or intrahepatic hemorrhage or even the development of hepatocellular carcinoma. Surgery eventually should be performed in any case of HA, provided it can be done without significant morbidity or mortality.[3,7-10]

Selective arterial embolization for ruptured HA may be a valuable alternative, although reports of this technique being employed are rare.[11-16] The aim of this study was to describe the role of emergency surgery for SRHA.

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METHODS

We reviewed the medical records and radiology files of 28 patients with a proven diagnosis of HA at our institution from 1989 through 2006. Three (10.7%) of 28 patients had a SRHA, two of which were associated with intrahepatic hemorrhage and one with intraperitoneal bleeding. Two patients were female and one was male. The mean age was 41.6 years old (38 to 46 years old). Sudden abdominal pain associated with hemodynamic instability occurred in all patients. The female patients had a background history of oral contraceptive use. Tumor markers including serum CA19-9, alpha-fetoprotein and carcino-embryonic antigen were normal in all patients. No chronic liver diseases were recorded in this series. Liver function tests, ultrasonography and computed tomography (CT) scans were performed in all three cases, and in one patient an MRI was also performed as shown in figures 1 and 2. The criteria for diagnosing hepatic adenoma was the presence of a hypervascular heterogeneous mass on CT scan with intratumoral necrosis or hemorrhage and the presence of a capsule or pseudo-capsule (hypovascular area on CT) as described previously.[17] (Table 1). Selective hepatic artery embolization was not available at the time of rupture, and due to hemodynamic instability all three patients underwent emergency surgery: on two occasions by the emergency room surgeons. and on one occasion by the hepatobiliary team. The liver surgical team advice was always available at the institution and all cases were discussed with the consultant physician. The anesthetic technique used was based on the principles of the acute hypovolemic patient, and the volume of blood loss as well as blood infusion was based on physiological parameters in the operative room; all solutions were warmed prior to infusion and administered via the rapid infusion system, commercially known as Level 1 system. A right subcostal incision was used extending to the left side (the classical "mercedes" incision), permitting full mobilization

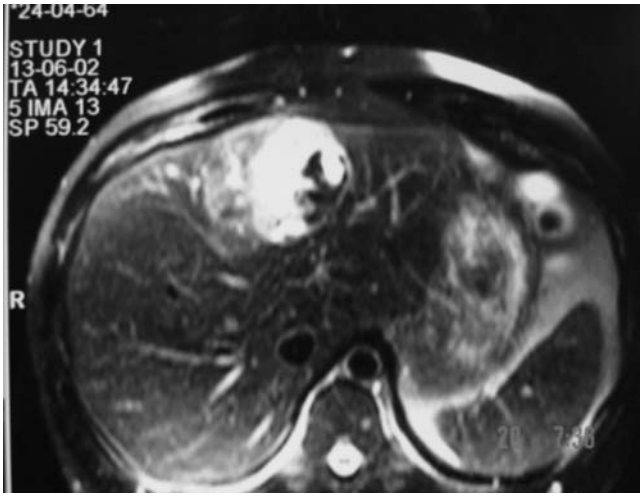

Figure 1 - T2-weighted liver MR image shows a hyper-intense mass located in segment IV

Figure 2 - T1-weighted fat-saturated gradient echo image of the liver shows the heterogeneous mass with high signal intensity (arrow), revealing a recent bleeding

Table 1 - Surgical management of spontaneous ruptured hepatocellular adenoma (SRHA)

n	Sex/Gender	Duration of contraceptive use	Clinical findings	Computed Tomography	Treatment	Tumor Size (cm)	Complications	Length of hospital stay
1	M/46	-	Intraperitoneal bleeding + HI	Heterogeneous image (hypoattenuating)	Right hemihepatectomy (S-V,VI,VII,VIII)	10	Bile leak	25 days
2	F/38	3 years	Intrahepatic bleeding + HI	Heterogeneous image (hyperattenuating) + necrosis/ hemorrhage	Non-anatomic hepatic resection (S-IVb,V,VI,VII,VIII)	12	Subphrenic abscess	43 days
3	F/ 41	5 years	Intrahepatic bleeding + HI	Heterogeneous image (hyperattenuating) + necrosis/hemorrhage	Extended right hepatectomy (S-IVa,IVb,V,VI,VII,VIII)	13	Pleural effusion	28 days

M- male; F- female; HI- hemodynamic instability; S-segments.

of the liver considering that in all cases the teams had a preoperative diagnosis of liver injury. Once laparotomy was performed, hemostasis or damage control was accomplished using absorptive gauzes and two opposing pressure vectors to compress the ruptured tissue between them. Surgical procedures included intraoperative ultrasonography to assess the size and location of the tumor as well as the relationship between the lesion and vascular system. The cases were handled using hepatic surgical techniques including vascular control of the portal pedicle and, in one case, control of the inferior vena cava close to the confluence of the hepatic vein. None of the cases required temporary hepatic inflow occlusion (Pringle maneuver) or clamping of the IVC. Dissection throughout the liver parenchyma was performed using the Kelly clamp crushing technique, an argon beam generator, CUSA®, and ligation of identified vessels with Prolene sutures.

RESULTS

Clinical and biochemical findings of SRHA are shown in Table 2. All three patients with SRHA had sudden acute right upper quadrant (RUQ) pain. Biochemical examination showed slightly elevated levels of y-glutamyl transpeptidase, bilirubin and alkaline phosphatase. Other liver function tests were within normal limits. Oral contraceptives were taken by two patients. A CT scan was performed on all three patients. Intrahepatic heterogeneous (hyperattenuating) images were seem in all three patients, corresponding with intrahepatic bleeding. In one of those patients hemorrhagic ascites was also detected in the CT scan. Intrahepatic and intraabdominal bleeding occurred in two patients and one patient, respectively. The mean tumor diameter was 11.6 (ranging from 10 to13) centimeters. The standard surgical procedure was anatomic-based hepatic resection (Figure 3) in two patients and a non-anatomical segmental hepatic resection in a third. Complications of the surgical procedure were observed in patients with SRHA. The patient submitted to right hemihepatectomy for intraperitoneal hemorrhage had a bile leak and underwent re-operation on the 18th postoperative day. The bile leak closed six weeks later. The patient submitted to a non-anatomic resection of the liver due to intrahepatic bleeding developed a right subphrenic abscess on the 13th postoperative day requiring a surgical intervention. The patient submitted to an extended right hepatectomy (also due to intrahepatic bleeding) developed a right pleural effusion immediately after the surgery associated with moderate restrictive respiratory insufficiency requiring therapeutic thoracentesis. Lengths of hospital stay were 25, 43 and 28 days, respectively.

Table 2 - Clinical and biochemical findings in patients (n=3) with spontaneous rupture hepatocellular adenoma (SRHA)

Feature	SRHA (3)
Mean age (years)	41.6 (38-46)
Acute RUQ* abdominal pain	03
Oral contraceptive use	02
Palpable mass	03
Elevated alkaline phosphatase	03
Elevated GGT**	03
Elevated bilirubin	03
Intrahepatic bleeding	02
Intraabdominal bleeding	01

*RUQ: right upper quadrant
**GGT: gama-glutamyl transpeptidase

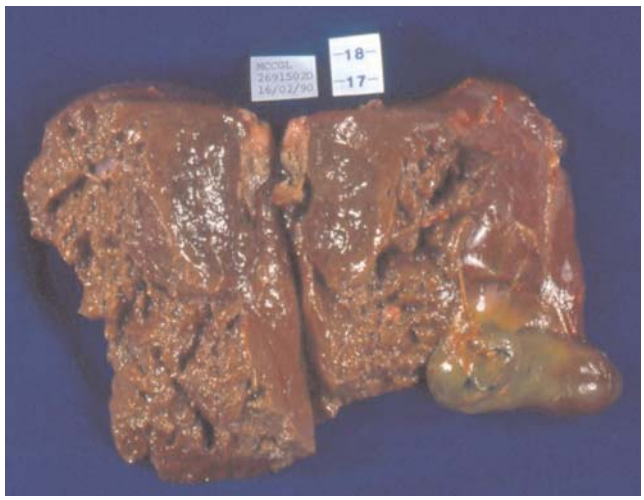

Figure 3 - Spontaneous rupture hepatocellular adenoma showing areas of hemorrhage and liver parenchyma damage

There were no deaths in this series. The mean follow-up was 22 months (ranging from 8 to 62 months). All patients are alive with no evidence of tumor recurrence to date.

DISCUSSION

HA is a rare benign hepatic neoplasm that is of interest for at least three reasons: (1) it may be difficult to distinguish from other benign or malignant hepatic tumors; (2) it may undergo malignant transformation and (3) it has a marked tendency to hemorrhage.[18-21] HA is notoriously difficult to diagnose pre-operatively by clinical, radiographic, or histological means. The diagnostic challenge involves differentiating HA from focal nodular hyperplasia or hepatocellular carcinoma. Clinically, abdominal pain is a frequent presenting symptom[3] but it is not specific for HA versus focal nodular hyperplasia or hepatocellular

carcinoma.[22] This report describes three patients with SRHA who had sudden right upper quadrant abdominal pain corresponding to the liver area associated with hemodynamic instability. Laboratory assessment of a SRHA may show liver enzyme changes (elevated alkaline phosphatase, GGT and bilirubin) in association with acute expansion of the neoplasm from hemorrhagic necrosis or even intrahepatic hemorrhage. CT permits an accurate diagnosis in typical cases of HA showing hyperdense mass with heterogeneous enhancement,[23,24] however typical features on CT were found in only 75% of the cases.[23] We found SRHA to be a heterogeneous mass in all three patients, however the patient with an intraperitoneal hemorrhage had a hypoattenuating image while the two patients with intrahepatic bleeding had hyperattenuating images, corresponding to liver necrosis on the CT examination. Hussain et al.[25] presented findings of HA on ultrasonography, CT and MRI, and correlating these findings with the pathological analysis. It was noted that in the case of monophasic CT or when arterial phase is performed incorrectly, HA can easily be misdiagnosed, exposing patients to unnecessary delays in diagnosis and proper treatment. It was noted that today, MRI is a state-of-the-art imaging modality due to its ability to provide a more comprehensive and accurate work-up of focal and diffuse liver disease. This is based on the unique properties of MR imaging; it possess a combination of high intrinsic soft tissue contrast of the liver and liver lesions, various distinctly different tissue characteristics for imaging and a high sensitivity for the presence or absence of contrast-uptake and enhancement patterns when using either non-specific or liver-specific contrast media. Some patients with HA are discovered accidentally on routine physical examination or even during exploratory laparotomy for another indication. These patients usually have totally asymptomatic liver masses and no laboratory evidence to suggest liver disease. On the other hand, fifty to sixty percent of patients with HA have intratumoral or intraperitoneal hemorrhages.[25,26] These patients are first seen with a sudden life-threatening intraabdominal hemorrhage. Substantial mortality has been associated with delays in diagnosis of this condition; mortality arises from hemorrhagic shock, rapidly developing coagulopathies, and postoperative complications. Successfully treated patients had liver segmentectomies performed as an emergency procedure. It is apparent that early diagnosis and operation are critical in this group. Three patients in our series had ruptures; two of them intrahepatically and one intraabdominally. The former were treated with non-anatomic hepatic resection associated with right hepatectomy (Figure 3) and the latter with right extended hepatectomy. The risk of HA bleeding increases with increased duration of oral contraceptive use and is related to the hormonal potency of the oral contraceptives used regardless of the duration of use.[27] The two female patients with intrahepatic bleeding were using hormonal contraceptives for at least three years. Whether this use was the cause of their SRHA or not is a matter of speculation because we believe that many factors appear to be interrelated including: (1) the woman's age, (2) the size of the tumor and (3) the potency of the oral contraceptive used. Size of the hepatocellular adenoma is an established independent risk factor for malignancy.[11,13,28] Surgical resection has been recommended for adenomas with an initial diameter of 5 cm or more in symptomatic patients, even during pregnancy.[6,29] The resection of large adenomas has also been recommended because the risk of hemorrhaging is relatively high. For smaller and asymptomatic adenomas, an expectant approach is advocated.[30,31] The main surgical procedure for HA should be local or hepatic segmental resection in order to preserve the normal hepatic parenchyma since the tumor is benign. In the emergency setting, if the surgeon on call at the emergency room have the appropriate surgical skills to handle liver lesions, the full procedure can be safely performed by them; otherwise, the lesion must be handled as in hepatic trauma, with packing and damage control, and after the initial approach the HPB team must be consulted for a definite surgical approach. In the unlikely event of SRHA we recommend an anatomical-based resection of the liver or even non-anatomical resection depending upon the complexity of the intrahepatic or extrahepatic hemorrhage. SRHA is a rare life-threatening condition. In this series there were HAs larger than 10 cm. Today, it is well known that hepatocellular adenomas are only vascularized arterially. This makes embolization safe and successful for stopping hemorrhages in acute settings. In our cases, the interventional radiology group was not yet available to perform the procedure and instead surgery was indicated. Hurmann et al.[16] demonstrated that the ability of selective arterial embolization to induce necrosis of the tumor may indicate a role for this procedure in the management of either bleeding or non-bleeding adenomas with good results and lower complication rates when compared to surgery.

In conclusion, SRHA may necessitate emergency surgery for controlling hemorrhage and stabilizing the patient, and the decision to operate depends both upon the patient's condition and the expertise of the surgical team.

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