Laparoscopic liver resection for hepatocellular adenoma

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AIM: To investigate the role of laparoscopy in the surgical management of hepatocellular adenoma (HA).

METHODS: We reviewed a prospectively collected database of consecutive patients undergoing laparoscopic liver resection for HA.

RESULTS: Thirteen patients underwent fifteen pure laparoscopic liver resections for HA (male/female: 3/10; median age 42 years, range 22-72 years). Two patients with liver adenomatosis required two different laparoscopic operations for ruptured adenomas. Indications for surgery were: symptoms in 12 cases, need to rule out malignancy in 2 cases and preoperative diagnosis of large HA in one case. Symptoms were related to bleeding in 10 cases, sepsis due to liver abscess following embolization of HA in one case and mass effect in one case (shoulder tip pain). Five cases with ruptured bleeding adenoma required emergency admission and treatment with selective arterial embolization. Laparoscopic liver resection was then semi-electively performed. Eight patients (62%) required major hepatectomy [right hepatectomy (n = 5), left hepatectomy (n = 3)]. No conversion to open surgery occurred. The median operative time for pure laparoscopic procedures was 270 min (range 135-360 min). The median size of the excised lesions was 85 mm (range 25-180 mm). One patient with adenomatosis developed postoperative bleeding requiring embolization. Mortality was nil. The median hospital stay was 4 d (range 1-18 d) with a median high dependency unit stay of 1 d (range 0-7 d).

CONCLUSION: The laparoscopic approach represents a safe option for the management of HA in a semi-elective setting and when major hepatectomy is required.

INTRODUCTION

Hepatocellular adenoma (HA) is a rare benign neoplasm of the liver. Its clinical relevance dramatically increased due to the widespread use of oral contraceptive pills in young women[1]. The main causal relationship with estrogen-based oral contraceptives is well recognized and seems to be proportional to the hormonal dose and duration of use.
ration of treatment. The incidence of HA is approximately 3 per 100,000 per year. The estimated incidence rises to 3–4 per 100,000 when considering women with long-term contraceptive use. Uncommon etiologies are: androgens, glycogenosis, Klifefelter’s syndrome, tyrosinaemia and familial adenomatous polyposis.

Liver cell adenomatosis is defined as the presence of more than 10 liver cell adenomas. No clear relationship between hepatic adenomatosis and contraceptive use has been demonstrated.

The natural history of HA is not completely understood. Some studies report regression of the tumor after cessation of the oral contraceptive pill. However, progression of HA to hepatocellular carcinoma (HCC) has also been observed many years after stopping oral contraceptives. A recent review of cases in the literature estimates the risk of malignant transformation at 5% (0–13). The incidence of hemorrhage has been reported to be as high as 30% (9). Pregnancy is a particularly high-risk period as the growth of HA induced by the elevated hormone levels may evolve into potentially fatal rupture and bleeding.

The diagnosis of asymptomatic HA is usually incidental in the course of abdominal imaging for other reasons. HA rupture may manifest as right upper quadrant pain mimicking a cholecystitis. The suspicious lesion at ultrasound scan is usually further investigated with multiphase spiral computed tomography (CT) and multiphase contrast-enhanced magnetic resonance imaging (MRI). Biopsy of HA is not uniformly recommended as this can induce bleeding and tumor dissemination. Furthermore, needle samples from of hepatic adenoma may be interpreted as normal tissue and may be difficult to differentiate from well-differentiated HCC or focal nodular hyperplasia.

There is no uniform consensus regarding the management of HA. Some authors suggest conservative management of non-ruptured asymptomatic HA < 5 cm with few exceptions. More aggressive management is advocated by those who recommend that HA should be removed based on the relatively high incidence of hemorrhage and malignancy. Newer, less invasive ways to treat non-ruptured liver adenoma include radiofrequency ablation and selective transarterial embolization but are still awaiting strong data to support these treatments.

The minimally-invasive approach to liver surgery has been shown to have clear advantages compared to the open approach in terms of better cosmetic results, shorter hospital stay and early return to normal social life. These are particularly appealing for individuals with HA who are candidates for surgery.

Laparoscopic liver surgery has been shown to be feasible and safe. However, single-center series focusing on the laparoscopic management of HA are still lacking and specific data can only be extrapolated from multi-center series or other single-center series on laparoscopic liver surgery. In this paper we present a single-center experience of minor and major pure laparoscopic liver resections for HA with a critical analysis of the indications for surgery and postoperative outcome.

MATERIALS AND METHODS

We reviewed a prospectively collected database of all patients undergoing pure laparoscopic liver resection for HA at Southampton University Hospitals NHS Trust between January 2005 and December 2009.

The data were analysed with regard to patient demographics, type of resection, conversion rate, intraoperative blood loss (calculated by measuring the volume of blood in the suction bottles, after subtracting wash fluid, at the end of surgery with the addition of weighed swabs), patients requiring transfusion, operation time, tumor size (maximum diameter at histological evaluation), length of hospital stay, postoperative complications and mortality (within 30 days from surgery).

HA rupture was defined by clinical symptoms (sudden acute abdominal pain) and radiological findings (intrahepatic or intraperitoneal hemorrhage).

Routine blood tests, ultrasound of the abdomen, CT of the abdomen with tri-phasic liver contrast enhancement and liver specific double contrast MRI scanning were performed in all patients. Liver biopsy was not routinely performed. Prior to surgery, each case was individually evaluated at an open multidisciplinary team meeting with surgeons, pathologists, oncologists, gastroenterologists and radiologists in our center. Patients were assessed for indication, feasibility and the type of resection required, prior to a decision regarding the surgical approach.

Two laparoscopic hepatobiliary-pancreatic surgeons (MAH and NWP) were involved in this series and standard nomenclature was used to describe the resection performed. Pure laparoscopic procedure was attempted in all patients. No hand-assisted or “hybrid” techniques were used.

Our group have previously described the technique for left lateral sectionectomy, segmentectomies and major hemi-hepatectomy.

Median values and range were considered for describing continuous variables.

RESULTS

Thirteen patients underwent fifteen pure laparoscopic liver procedures for HA in the study period (male/female: 3/10; median age 42 years, range 22-72 years). Two patients required two different laparoscopic procedures. Both patients had liver adenomatosis (Table 1).

Indications for surgery were: symptoms in 12 cases, need to rule out malignancy in 2 cases and preoperative diagnosis of large adenoma (> 5 cm) in one case. Symptoms were related to HA rupture in 10 cases, sepsis due to liver abscess following embolization of HA in one case and mass effect in one case (shoulder tip pain). In the two patients with indeterminate diagnosis, the lesions
Table 1 Patients’ demographics, indication for surgery and peri-operative details

| Patient | Sex | Age (yr) | Surgical indication | Emergency presentation | Preoperative embolization | Operation | N of lesions | Complications |
|---------|-----|----------|---------------------|------------------------|---------------------------|-----------|-------------|---------------|
| 1       | F   | 54       | Rupture             | N                      | N                          | Left lateral sectionectomy | 1          | N             |               |
| 2       | F   | 62       | Shoulder tip pain   | N                      | N                          | Right hepatectomy          | 1          | N             |               |
| 3       | F   | 34       | Ipvolemic shock due to intraperitoneal bleeding (adenomatosis) | Y                      | Y                          | Seg 3 resection            | > 10       | Postoperative bleeding |
| 4       | F   | 42       | Rupture (adenomatosis) | Y                      | Y                          | Seg 3, 4, 5, 7 wedge resections | > 10       | N             |               |
| 5       | F   | 22       | Rupture (adenomatosis) | Y                      | Y                          | Seg 4, 7 wedge resections | > 10       | N             |               |
| 6       | F   | 47       | Rupture             | N                      | N                          | Right hepatectomy          | 1          | N             |               |
| 7       | M   | 31       | Rupture (adenomatosis) | N                      | N                          | Left hepatectomy           | > 10       | N             |               |
| 8       | M   | 62       | HCC, cirrhosis      | N                      | N                          | Seg 2, 3 wedge resections | 2          | N             |               |
| 9       | F   | 24       | Rupture             | Y                      | Y                          | Left hepatectomy           | 2          | N             |               |
| 10      | F   | 26       | Rupture             | N                      | N                          | Right hepatectomy          | 3          | N             |               |
| 11      | F   | 44       | Rupture (adenomatosis) | N                      | N                          | Left hepatectomy           | > 10       | N             |               |
| 12      | M   | 35       | Large adenoma       | N                      | N                          | Right hepatectomy          | 1          | N             |               |
| 13      | F   | 72       | HCC                 | N                      | N                          | Right hepatectomy          | 1          | N             |               |

*Patients 3 and 5 required two different pure laparoscopic liver resections. HCC: Hepatocellular carcinoma.*

were suspicious for HCC. In one of these patients the tumor was in the context of cirrhotic liver related to hemochromatosis (Table 1).

Five cases with ruptured bleeding HA required emergency admission and treatment with selective arterial embolization (Table 1). Laparoscopic liver resection was then electively performed.

During three laparoscopic procedures, multiple liver resections were necessary. The types of resections performed were: right hepatectomy (n = 5), left hepatectomy (n = 3), left lateral sectionectomy (n = 2), single sectionectomy (n = 2), wedge resection (n = 3). No procedure was converted to open surgery (Table 1).

The median operative time for pure laparoscopic procedures was 270 min (range 135-360 min). In all patients requiring major hepatectomy, preparation was made for a laparoscopic Pringle manoeuvre by positioning a Nylon tape around the portal triad, passing it through a 10-cm long 14 French rubber tube and leaving it loose within the abdominal cavity. Median blood loss was 500 mL (range 100-2000 mL). In one case, blood transfusion was necessary intra-operatively (ruptured bleeding adenoma). The median size of the excised lesions was 85 mm (range 25-180 mm).

One patient with liver adenomatosis treated with segment 3 resection of a ruptured HA developed postoperative bleeding from another HA. This was treated with repeated selective arterial embolization. The same patient underwent successful segments 3, 4, 5 and 7 wedge resections for recurrent bleeding HA 3 mo later.

In our series postoperative mortality was nil. The median hospital stay was 4 d (range 1-18 d) with a median HDU stay of 1 d (range 0-7 d).

DISCUSSION

The optimal management of HA is still an unresolved question. Difficult preoperative diagnosis, abdominal symptoms, risk of rupture and risk of malignant transformation are the main issues driving operative judgement. Several experts support the surgical management of HA. The arguments in favor of the surgical approach address the difficulty of preoperative imaging in differentiating HA from HCC; the risk of malignant transformation (estimated around 5%); the risk of rupture in approximately 30% with potential fatal consequences; and finally, the fact that surgical excision guarantees a definitive diagnosis and long-term cure. Alternatively, some experts support the wait-and-see policy mainly for asymptomatic HA < 5 cm. The arguments in favor of the conservative approach are that discontinuation of oral contraceptives pills may induce HA regression; it is not always certain that abdominal symptoms are related to the HA; if bleeding occurs this can be managed conservatively and regression of hematoma may reduce symptoms; there is morbidity and mortality associated with surgical resection, which for benign liver tumors range from 10% to 27% and from 0% to 3%, respectively.

Some of the dramatic consequences of invasive liver surgery may be alleviated by the minimally-invasive approach. A better cosmetic result and shorter hospital stay with early return to normal life are the main advantages of the laparoscopic approach compared to open surgery. These are particularly appealing for young women who are highly represented in the HA population. However, laparoscopic liver surgery may be a safe and efficient alternative to the open approach only if performed in specialized centers with extensive experience in hepatic and laparoscopic surgery. As our data show, this surgery can be performed with no mortality and limited morbidity.

Only limited data are available on the laparoscopic role in the management of HA. Specific data may only be...
extrapolated from multicenter series or single-center series on laparoscopic liver surgery. In a recent large review of almost 3000 laparoscopic liver resections, HA represented 13% of all the resected benign liver lesions. In a recent large single-center series reported 23 laparoscopic liver resections for HA out 166 minimally-invasive hepatectomies for malignant and benign diseases. However, in these major series, no specific information regarding surgical indication, laparoscopic technique and outcome after HA resection may be deduced. Deneve et al. in a multicenter pooled analysis of 119 patients with HA undergoing surgical treatment during a 10-year period, showed that the laparoscopic approach was adopted in 3% of ruptured adenomas and in 11% of not ruptured hematomas. Cho et al. reviewed a large single-center series of 41 patients who underwent surgical resection for HA. The laparoscopic approach was limited to 9 patients (22%) who were admitted in an elective setting with non-ruptured HA.

We presented a consecutive single-center series of pure laparoscopic liver resections for HA without conversions to open surgery. Rupture was the main surgical indication (67% of the admissions), including one bleeding HA measuring 25mm. Our data shows that pure laparoscopic hepatectomy for HA may be successfully performed even when major hepatectomies are required and in a semi-elective setting. Right or left hepatectomy was performed in 62% of our patients and in one case after preoperative transarterial embolization of a HA. In five cases, patients were admitted in an emergency setting with acute abdominal pain or hemodynamic instability due to ruptured HA. After prompt resuscitation they underwent transarterial embolization of the bleeding HA and laparoscopic liver resection was then planned. Two patients had liver adenomatosis with bleeding HA requiring two admissions and multiple treatments (Table 1). Multiple resections are the preferable option in patients with liver adenomatosis, unless technically impossible or unsafe. Liver transplantation should be considered only as the last resort.

Molecular biology research could offer important advances for selecting HA with high malignant potential. HA with beta-catenin mutations seem to have a significant risk for malignant transformation. Liver biopsy could therefore have a more relevant role in selecting HA with a genotype correlated to pathological abnormalities. However, there is no supportive evidence of its application in clinical practice at the moment.

Until more evidence from ongoing research is available, our data show that the pure laparoscopic approach represent a safe and effective way for the surgical management of HA. Surgical resection ensures definitive diagnosis and treatment of HA with minimal risk of complications. This is particularly appealing for young individuals and for women who may worry about the risks of HA growth or rupture in future pregnancies. However, each case must be individually evaluated and the risk of surgery weighed against the potential for morbidity and mortality. Optimal individual treatment must always be discussed in a multidisciplinary team meeting and patients’ preferences should be included in the decision-making process. Laparoscopic liver surgery must be only performed in high-volume liver centers with extensive experience in laparoscopic surgery.

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