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Case Report

# Laparoscopic isolated caudate lobectomy of two symptomatic familiar giant liver hemangiomas, case reports and literature review

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**Abstract**

**Background and objective**: Liver hemangioma (LH) is the most common benign tumour of the liver, but its origin is still not clear and not much is known about a possible familiarity. Caudate lobectomy is the most effective surgical treatment for benign tumors arisen in segment I. The occurrence of giant LH within the same liver segments in different members of the same family has never been described in literature. Herein we report the first two consecutive laparoscopic caudate lobectomy for familiar giant LH in a father and his daughter.

**Methods**: The father showed a lesion in the caudate lobe (CL) suggestive of LH steadily grown, asymptomatic for 24 years until it has caused abdominal discomfort and pain (Dmax 89 mm). The daughter showed multiple hepatic hemangiomas with the biggest one located in the CL compressing the inferior vena cava (Dmax 88 mm).

**Results**: Despite the size of the masses, we opted for a pure laparoscopic approach and a caudate lobectomy was performed in both cases. Operation time was 140 and 180 min. Patients had an uneventful recovery and a good outcome after the scheduled follow up exams 6 months after the procedure.

**Conclusions**: A chance of familiarity transmission for hemangiomas exists and therefore should be further investigated. Laparoscopic isolated caudate lobectomy for symptomatic GLH is feasible and safely performed on selected patients by experienced hepatobiliary surgeons. Prospective randomized studies on larger populations are needed to assess if this minimally invasive approach can be proposed as a standard of care for S-I LH.

**Keywords**

Familial liver hemangioma; Laparoscopic liver surgery; Caudate lobe

## 1. Introduction

Liver hemangioma (LH) is the most common benign tumor of the liver and it's estimated that about 3% to 20% of the general population presents LH. The prevalence in necroscopy and cohort studies ranges between 0.4% and 7.4% [1].

The origin of hemangiomas is still not clear and not much is known about a possible familiarity, although these tumours

are considered benign, congenital and vascular neoplasm [2–5].

Liver hemangiomas are usually small and asymptomatic lesions which are incidentally diagnosed and, in the majority of cases, they do not require any treatment and they can be safely managed by clinical observation [6, 7].

They may result in abdominal discomfort, swelling, abdominal pain, jaundice and thrombocytopenia [8]. Spontaneous rupture of >4 cm LH may occur, and in these situations the mortality rate critically goes up to 78% [9].

The size of LH is a crucial factor for the choice of the right medical intervention modalities.

According to a recent study, asymptomatic LH <4 cm should just be monitored, while when their diameter exceeds >5 cm (in this case defined as giant liver hemangiomas (GLH)) or when associated with occurrence of symptoms, they should undergo surgical treatment in experienced high-volume centers [10, 11].

The optimal management for GLH is still controversial although surgical resection remains a milestone of therapy. Caudate lobectomy is the most appropriate surgical treatment for benign tumors in the caudate lobe (CL) [7].

Herein we describe two cases of laparoscopic caudate lobectomy in a father and his daughter with symptomatic GLH within the same liver segment (S-I).

## 2. Case reports

### 2.1 Case 1

The father, a 61-year-old man, underwent a routine abdominal ultrasound (US) in 1993 that showed an asymptomatic lesion in the CL, suggestive of LH (Dmax 5 cm). A steady growth of the lesion was described until April 2017, when due to the onset of abdominal discomfort and pain, the patient underwent an abdominal magnetic resonance (MRI) revealing a GLH in the CL (89 mm × 59 mm × 52 mm) in contact with the inferior vena cava (IVC) and the portal vein, both compressed and stenosed by the mass (Fig. 1a).

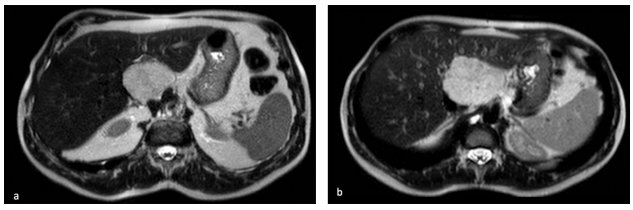

**FIG. 1. Preoperative CT-scan.** (a) Case 1 MRI showing a GLH of CL (89 mm × 59 mm × 52 mm) in contact with IVC and the portal vein. (b) Case 2 MRI displaying a GLH of S-I WITH A diameter of 88 mm and signs of IVC compression.

### 2.2 Case 2

The daughter, a 38-year-old woman with a two-year history of estrogen exposure, complained of epigastric pain and gastroesophageal reflux since 2010 for which she underwent an abdominal US where multiple hepatic hemangiomas were discovered (S-I, S-III, S-VII and S-VIII). She started a strict follow-up until April 2017 when an abdominal MRI showed an increase of the caudate lobe lesion with a max diameter of 88 mm and signs of IVC compression (Fig. 1b).

Surgery was indicated in both patients because of the size of the hemangiomas and the symptomatic condition. Despite the size of the lesions, we opted for a pure laparoscopic approach and a caudate lobe resection was performed in both cases.

Both patients were placed in a 30 degrees anti-Trendelenburg position with the operator standing between legs. After an umbilical open access with a 10 mm Hasson trocar, pneumoperitoneum was established at 14 mmHg and another four trocars (two 10 mm, two 5 mm) were inserted under direct vision: one in right hypochondrium, three in left hypochondrium and flank respectively (Fig. 2).

An external Pringle maneuver was set using a chest tube introduced from the right hypochondrium trocars, to be used for both right hepato-duodenal ligament retraction and hilum intermittent clamping. An intraoperative US confirmed lesions location.

The hepatogastric ligament was opened and, after a gentle left and cranial retraction of the caudate lobe, a selective clipping and transection of the veins draining into IVC was performed (Fig. 2b). In the same way all the caudate branches coming from the left portal vein and the artery were clipped and cut. For the hepatic tissue transection LigaSure™ Maryland jaw (Covidien, Dublin, Ireland) and laparoscopic Integra® CUSA® Excel (Integra Life Sciences, Plainsboro, NJ, USA) were used. In case 2 we managed another lesion with the same characteristics located in S-III with a wedge resection.

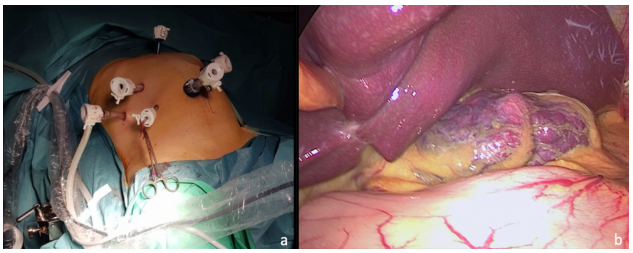

**FIG. 2. Surgical technique.** (a) Trocar placement. (b) Intraoperative finding of caudate giant liver hemangioma.

After being placed in a laparoscopic bag, specimens extraction was performed via an enlargement of the 10 mm trocar in the left hypochondrium, in both cases (Fig. 3).

Both surgical procedures were completed laparoscopically without intraoperative complications, or need of blood transfusions. The operative time was 140 (case 1) and 180 minutes (case 2) and the patient's estimated blood loss was 180 mL and 150 mL respectively.

Postoperative course was uneventful in both patients. The patients were discharged on POD 2 and 3 respectively with normal liver function tests.

Pathology confirmed the preoperative diagnosis of cavernous hemangioma. The patients are in good conditions and

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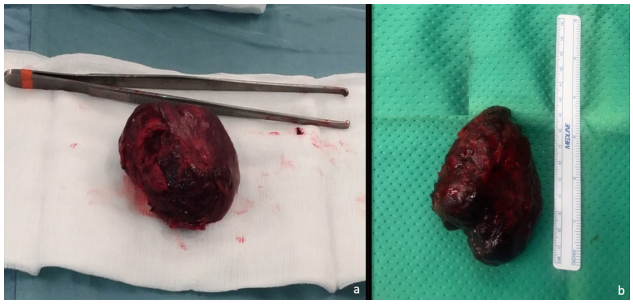

**FIG. 3. Specimen.** (a) Case 1 caudate liver hemangioma of Case 1. (b) Case 2 caudate liver hemangioma.

no sign of recurrence two years after surgery.

A genetic test was performed on both patients without finding any evidence of mutation in the loci of hemangioma-related syndromes.

## 3. Discussion

In the vast majority of cases LH are sporadic tumors but some studies describe a familial autosomal dominant inheritance with difference in expression or penetration but without specific genetic defects. Some familial cases are found in the context of vascular syndromes like Sturge-Weber, Von Hippel-Lindau (VHL) and Rendu-Osler-Weber. In these vascular syndromes some gene mutations have been described.

Patients with VHL syndrome are heterozygous for VHL mutations and they are prone to develop angiogenic tumors when the function of the remaining wild-type VHL allele is lost in the VHL gene (located on chromosome 3p25.5) [3–6].

Gunel *et al.* [12] proposed that a mutation in CCM1 gene at 7q21–q22 could be responsible for abnormal endothelial tube formation, explaining the pathogenesis of familial cerebral cavernous malformations.

Regarding families with cutaneous venous malformations, a mutation of the TIE2 receptor (a gene located on chromosome 9p21) or a deficiency of the ligand may disturb a normal development of the vessels [13, 14].

The role of these mutations in familial GLH has still not been investigated.

We studied both patients for identification of the vascular syndromes mentioned above, and no evidence of other vascular lesions was found using brain-MRI, Fundus Oculi, Thyroid-US.

These benign tumors can occur in people of all ages, but they are more commonly found in young adult females (Female : Male ratio = 5 : 1) [15]. Some authors describe a correlation with chronic estrogen exposure and the pathogenesis of LH as in our female patient [16].

An interesting flow chart published by Buell *et al.* [17] indicates that when asymptomatic benign liver masses arising in non-cirrhotic livers are diagnosed, these should be managed with a 6-months follow-up, in order to detect possible changes in dimension or features.

Yamagata *et al.* [18] suggested that a GLH should be surgically treated if the tumor itself becomes symptomatic or shows a rapid growth. Spontaneous or traumatic ruptures are rare indications for emergency surgery. In our hospital these are the indications for surgery for hemangiomas [18–20].

Generally, LH can be removed by hepatic resection or enucleation. Enucleation is a safe, fast, and radical method that is easy in the case of anterior and superficial lesions, but becomes more difficult, with a higher bleeding risk, when the tumor is deeply located within the hepatic parenchyma [21].

In cases where large and deep hemangiomas are in proximity to vascular structures, some surgeons prefer to perform typical liver resections [22].

Use of laparoscopy for benign liver neoplasm has been increasingly adopted since its first description was made in 1992 by Gagner [23]. The caudate lobe, has generally been considered a "difficult" lobe to manage via laparoscopy because of its anatomic position that technically interferes with the application of the usual laparoscopic approach. However, the indications for minimally invasive surgery for segment I seem to be slowly gaining acceptance during the last few years.

In fact, according to The First International Consensus Conference on Laparoscopic Liver Surgery held in Louisville in 2008, "difficult" resections with lesions located in posterior-superior segments (sI-VII-VIII) were included in major resections and were not universally accepted as standard of care [24]. However, in some very experienced liver units, even these lesions in selected patients can be addressed laparoscopically [25, 26].

At the Second International Consensus Conference on Laparoscopic Liver Surgery held in Morioka in 2014, the major laparoscopic liver resections (including isolated segment I resections) were classified according to the Balliol IDEAL recommendations as IDEAL stage 2b: "procedures in which considerable preliminary data supporting the safety of the procedure are present, but there is still a risk associated with novelty" [27]. These kinds of liver surgery should be performed by experienced surgeons.

Recently, a "difficulty" scoring systems for LLR have been developed, taking into consideration such different characteristics as: tumor size, tumor location, major vessels proximity, extent of resection, liver function obesity and platelet count [28]. Due to the paucity of isolated caudate lobectomies present in these studies, the impact of tumors located in segment I could not be evaluated; hence the corresponding scores could not be assigned.

Despite this limitation, in our opinion, the deep dorsal location of the CL and its proximity to multiple major vessels place this kind of procedure among the most complex LLR, and should only be approached by experienced surgeons.

Therefore, a laparoscopic approach for lesions located in the postero-superior liver segments seems to be associated with significantly longer operative times and a greater need of intraoperative transfusions. Nevertheless, this strategy has been proven to be equally feasible and safe, with comparable morbidity rates as reported in a recently published monocentric series [29, 30].

The first laparoscopic caudate lobectomy for hemangioma

**TABLE 1. Literature review of reported familial LH.**

| Author/Year | Members of the family affected | Size and location of LH | Other locations of Hemangiomas | Associated disorders and syndromes |
|---|---|---|---|---|
| Filling-Katz *et al.*, 1992 [31] | 1 F, 22 years old | ns | Skin, retina, brain | Familial Cavernous Angiomatosis |
| Moser *et al.*, 1994 [5] | 3 F, symptomatic | Giant | Skin, muscle | Thyroid Adenomas |
| | 2 F, asymptomatic | | | |
| Drigo *et al.*, 1994 [32] | 3 F of 4 generations | ns | Brain | - |
| Admiraal *et al.*, 2004 [3] | 3 F, sisters | 14 cm, right lobe | - | G-6PD |
| | | 15 cm, left lobe | | hypertension |
| | | 8.6 cm, ns | | |
| Diez Redondo *et al.*, 2004 [2] | 4 F, 2 M of 3 generations | 9 cm, right lobe | Face | - |
| | | Small multiple bilobar | | |
| | | 1 small ns | | |
| | | 4 cm, 2 cm, right lobe | | |
| | | 1.8 cm, left lobe | | |
| Toldo *et al.*, 2009 [33] | 5 F of 3 generations | ns | Brain, retina, skin, vertebral column | CCM1 gene mutations |
| Li *et al.*, 2013 [34] | 1 M, 49 y | 6 cm, S VI + multiple bilobar | - | Dubin-Johnson |
| | 1 F, sister | ns | | |

ns, not specified.

was published by Descottes *et al.* [31] in 2003 reporting the results of a retrospective multicentric European Study. In this study only one isolate caudate lobectomy was reported and only 5% of resected benign tumors were located in posterior segments. A comprehensive review on 2.804 LLR published in 2009 indicated that LH accounted for 18% of the overall amount of all procedures described in the literature. Moreover, eight cases of laparoscopic caudate lobectomy were also described, and when compared to anterolateral segments resections they resulted in longer operative time, but still are technically feasible and safe, with comparable morbidities [32].

In the literature we have found few cases reporting familial liver hemangiomas not linked with the vascular syndromes above mentioned.

To the best of our knowledge, these are the first two reported cases of familial GLH located in the same liver segments (CL in this case), and successfully treated by laparoscopy.

Filling-Katz *et al.* [33] were the first to report a familial liver hemangioma in a young lady in 1992 with other multiple lesions in others organs. Moser *et al.* [5] described the cases of 5 women in the same family with GLHs and Drigo et al. [34] depicted the cases of 3 women in 4 different generations and Toldo *et al* [35]. Five women in three generations with a mutation in CCM1 loci. Admiraal *et al.* [3] reported 3 sisters with GLH associated with a defect of glucose 6 phosphate dehydrogenase deficiency. In Diez-Redondo *et al.*[2] and Li *et al.* [36] reported cases where men were involved; the former study reported 6 famil members with multiple hemangiomas located even in the face while the latter reported a brother and sister with hemangiomas and Dubin-Johnson syndrome [2–5, 33, 34, 34, 36].

Anyway, the occurrence of GLH in the same liver segment in different members of the same family has never been described; as well as the location of LH in the caudate lobe, which is not described in any of these papers (Table 1, Ref. [2, 3, 5, 31–34]).

## 4. Conclusions

These cases demonstrate familiarity transmission for liver hemangiomas could exists and therefore a possible correlation should be further investigated. Genetic tests are useful in excluding syndromes where hemangiomas are characteristic. Laparoscopic isolated caudate lobectomy for symptomatic GLH is feasible and safe when performed on selected patients by experienced hepatobiliary surgeons. Studies on larger populations, possibly prospective and randomized are needed to assess if minimally invasive approach can be a standard of care for caudate LH.

## Abbreviations

LH, liver hemangioma; CL, caudate lobe; GLH, giant liver hemangiomas; IVC, inferior vena cava; VHL, Von Hippel-Lindau; LLR, Laparoscopic Liver Resections.

## Author contributions

AA and DS and LS have contributed to study conception and design and drafting of manuscript. MP, CG, AGE, LT, AP and GT have contributed to acquisition of data, analysis and interpretation of data and they made substantial intellectual contribution. GT critically revised the manuscript. All authors have read and agreed to the published version of the manuscript.

## Ethics approval and consent to participate

For this study, ethical and ethnical approval are not required. Written informed consent was obtained from the patients for publication of this case report and accompanying images. This work follows the surgical case report guidelines (SCARE).

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## Conflict of interest

The authors declare no conflict of interest.

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