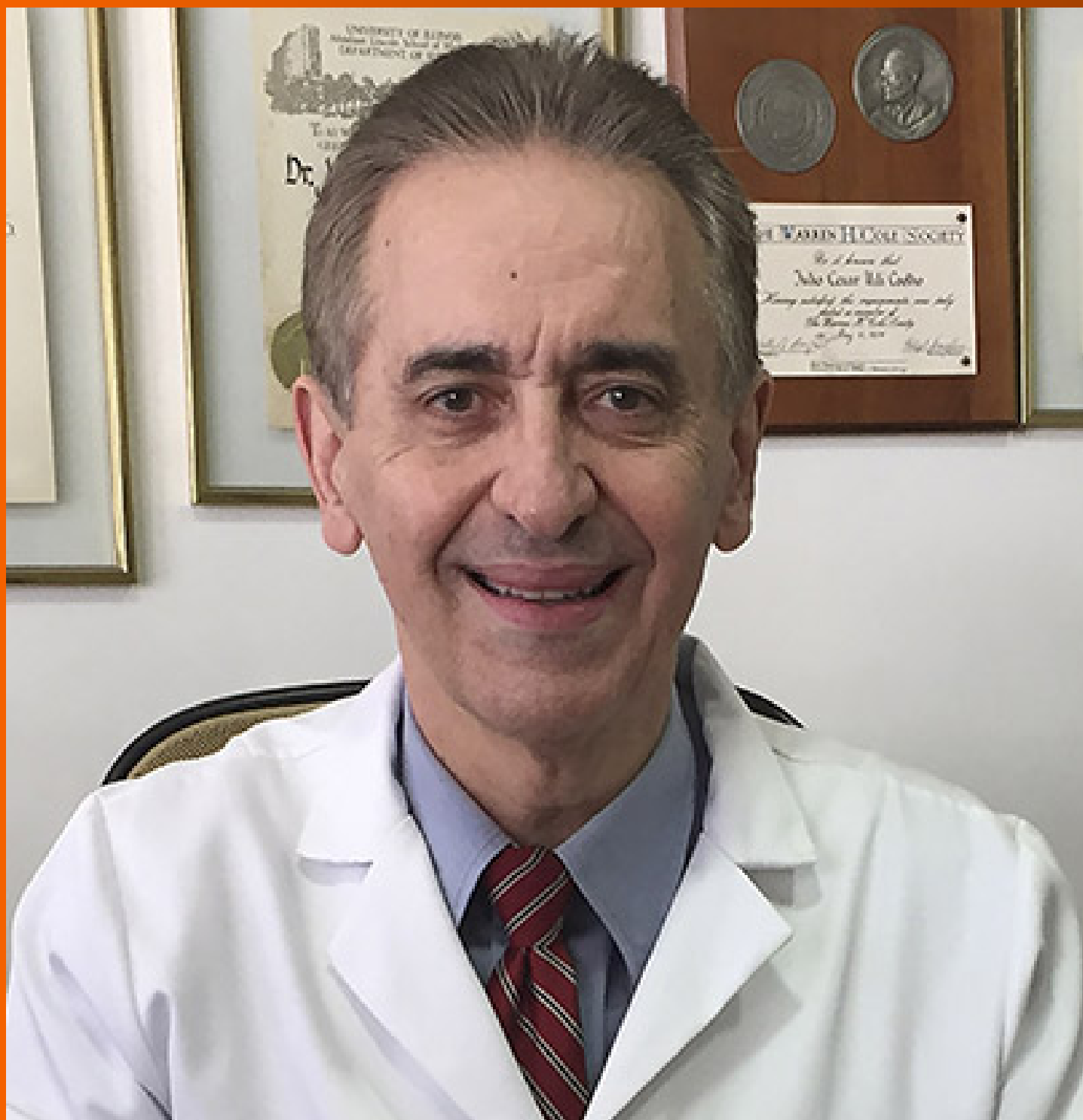


# World Journal of *Hepatology*

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## Focal nodular hyperplasia associated with a giant hepatocellular adenoma: A case report and review of literature

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**Author contributions:** Gaspar-Figueiredo S and Kefleyesus A performed the literature review, collected all the data related to the case report, and recorded/edited the video-vignette related to the case report; Sempoux C did the anatomopathological examination/appraisal; Halkic N and Uldry E did the surgical appraisal; all authors have read and approved the final manuscript.

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### Abstract

#### BACKGROUND

Focal nodular hyperplasia (FNH) and hepatocellular adenoma (HCA) are well-known benign liver lesions. Surgical treatment is usually chosen for symptomatic patients, lesions more than 5 cm, and uncertainty of diagnosis.

#### CASE SUMMARY

We described the case of a large liver composite tumor in an asymptomatic 34-year-old female under oral contraceptive for 17-years. The imaging work-out described two components in this liver tumor; measuring 6 cm × 6 cm and 14 cm × 12 cm × 6 cm. The multidisciplinary team suggested surgery for this young woman with an unclear HCA diagnosis. She underwent a laparoscopic left liver lobectomy, with an uneventful postoperative course. Final pathological examination confirmed FNH associated with a large HCA. This manuscript aimed to make a literature review of the current management in this particular situation of large simultaneous benign liver tumors.

#### CONCLUSION

The simultaneous presence of benign composite liver tumors is rare. This case highlights the management in a multidisciplinary team setting.

**Key Words:** Liver; Focal nodular hyperplasia; Hepatocellular adenoma; Composite tumor; Video vignette; Case report

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**Core Tip:** Focal nodular hyperplasia and hepatocellular adenoma (HCA) are frequent but non-malignant tumors. There is rarely indication for surgery. Combination of these two masses is a very unusual situation. Their diagnosis is mainly based on radiology. Oral contraception is a risk factor for HCA. Malignant transformation of HCA is the predominant argument for surgery. All these cases, especially composite tumors, must be discussed in a multidisciplinary team.

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## INTRODUCTION

Focal nodular hyperplasia (FNH) has become a pretty well-known disease in the past two decades. It is defined by a benign hyperplastic nodule with a central scar, appearing in the normal liver parenchyma, and is composed of normal hepatocytes in a multinodular structure[1]. Its incidence is between 0.6%-3%, predominantly affecting females patients (80%-90%) in their third or fourth decade. The pathophysiology is thought to be due to an increased arterial flow that leads to secondary hepatocellular hyperplasia[2,3]. The correlation with oral contraceptives (OCs) is unproven but very likely, given that OCs are taken almost exclusively by women (sex ratio 9:1) and the proven correlation between OCs and change in lesion size[4,5].

Hepatocellular adenoma (HCA) is a benign lesion with a malignant potential between 4% and 8%, according to recent works of Farges *et al*[6] and Sempoux *et al*[7]. It classically arises in a noncirrhotic liver, in young females with an OC background. However, the understanding of HCA has evolved dramatically and we now know that it can also develop in patients with non-alcoholic steatohepatitis, certain vascular malformations, or alcoholic cirrhosis. Moreover, there are a wide variety of subtypes of this complex disease, making it very difficult to establish treatment guidelines[8-10].

In this present article, we aimed to describe the detailed management of a rare simultaneous case of FNH and HCA and a brief review of the literature.

## CASE PRESENTATION

### Chief complaints

A 34-year-old woman in general good health, with a medical history of oral contraceptives (desogestrel, ethinylestradiol) for 17 years consulted her general practitioner (GP) for a check-up.

### History of present illness

She was completely asymptomatic.

### History of past illness

She had no past illness.

### Personal and family history

The patient had no past medical history except a knee orthopedic surgery 1 year before, had a stable weight with normal body mass index (21.1 kg/m<sup>2</sup>) and no familial medical history.

### Physical examination

During the examination, her GP found a mobile and palpable abdominal mass of more than 10 cm in diameter, with no skin bulging at the Valsalva's maneuver (Figure 1).





Figure 1 Pre-operative patient's supine and stand-up picture – no external signs of tumor.

### Laboratory examinations

The blood exams were normal, except for an elevation in alkaline phosphate level of 519 U/L (normal range = 36-108). Tumoral markers were normal.

### Imaging examinations

Abdominal ultrasound revealed an aspecific giant mass next to the left hepatic lobe. A computed tomography (CT scan) revealed a double mass attached to the left lobe of the liver. The first one had the typical characteristics of FNH and the second one of uncertain dignity. Further magnetic resonance imaging (MRI) confirmed a 6 cm x 6 cm mass suggestive of FNH in the inferior part of segment III. This 6 cm lesion was right next to a second one measuring 14 cm x 12 cm x 6 cm which dignity was unclear. The differential diagnosis was between an HCA, a hepatocellular carcinoma (fibrolamellar variant), or an atypical FNH (Figures 2-5).

## FINAL DIAGNOSIS

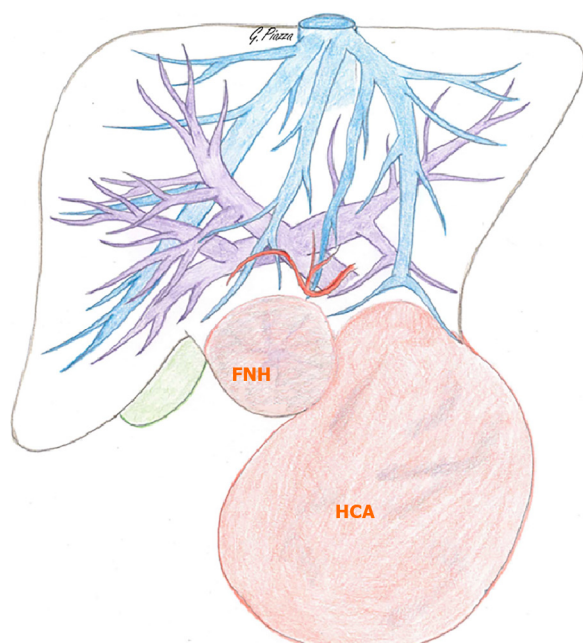
The pathologist's report confirmed the diagnosis of 6 cm FNH resected with good margin and showed a non-beta-catenin-mutated HCA (inflammatory subtype with more risk of malignant transformation) (Figure 6).

## TREATMENT

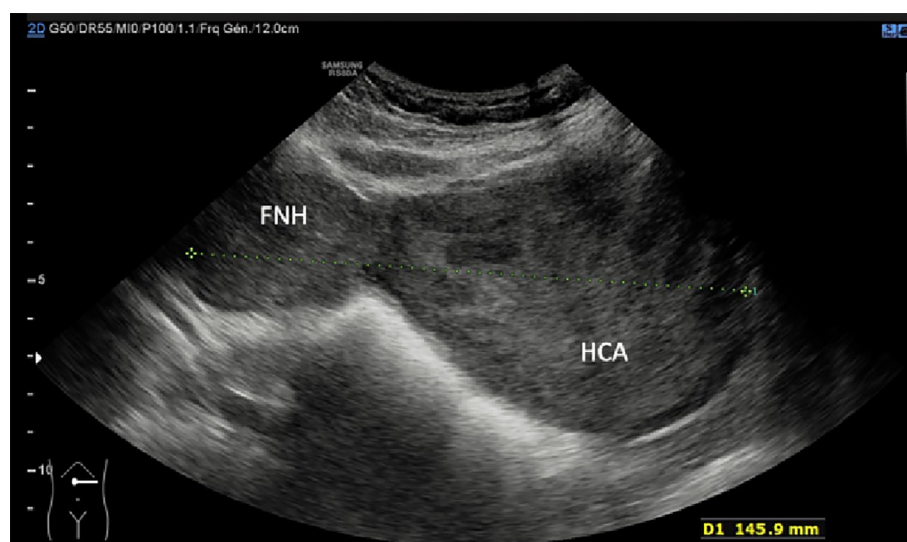
Indication for surgery was retained during a multidisciplinary team (MDT) meeting as the first option for definitive diagnosis and treatment.

The surgery was completed without complication. We summarize hereafter the key points of the minimally invasive procedure. After inserting 4 trocars for the laparoscopy (para-umbilical, right and left flank, subxiphoid) and staying away from the large dual mass which limited the range movements, we performed an ultrasound confirming a pedunculated mass (FNH) highly vascularized attached to segment III and a second component pedunculated between segment II and III. The mass showed no adhesion with the segment IV and the gallbladder allowing a left lobectomy. Dissection was performed with ultrasonic shears (Ultracision Harmonic, Ethicon Inc., NJ, United States) and transection was completed with a 60mm stapler (tri-staple vascular cartridge, Endo-GIA, Medtronic, Minneapolis, MN, United States). We extracted the specimen with both lesions through a suprapubic (Pfannenstiel) incision. The operative time was 122 min. Blood loss was minimal (50 mL) (Video 1).

The postoperative course was uneventful and the patient was discharged on postoperative day 3.



**Figure 2** Preoperative drawing – tumor and liver major vessels' relationship (credits: Dr. Giulia Piazza). FNH: Focal nodular hyperplasia; HCA: Hepatocellular adenoma.



**Figure 3** Ultrasonography with a sagittal view of focal nodular hyperplasia and hepatocellular adenoma. D1: Greater axis length. FNH: Focal nodular hyperplasia; HCA: Hepatocellular adenoma.

## OUTCOME AND FOLLOW-UP

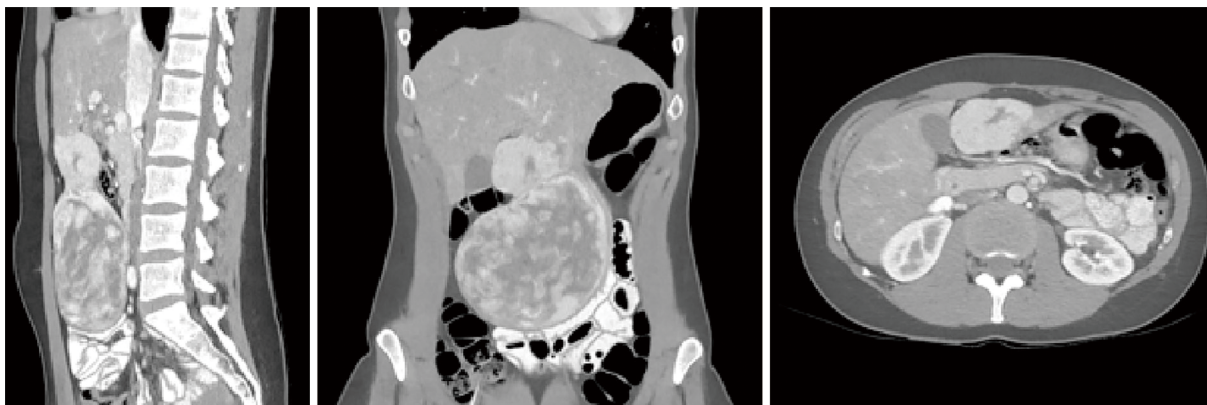
The MDT meeting proposed a 1-year MRI follow-up with oral contraceptive discontinuation.

One month after surgery, the patient was good without any complaint, her scar evolution was satisfactory and there was no sign of an early incisional hernia.

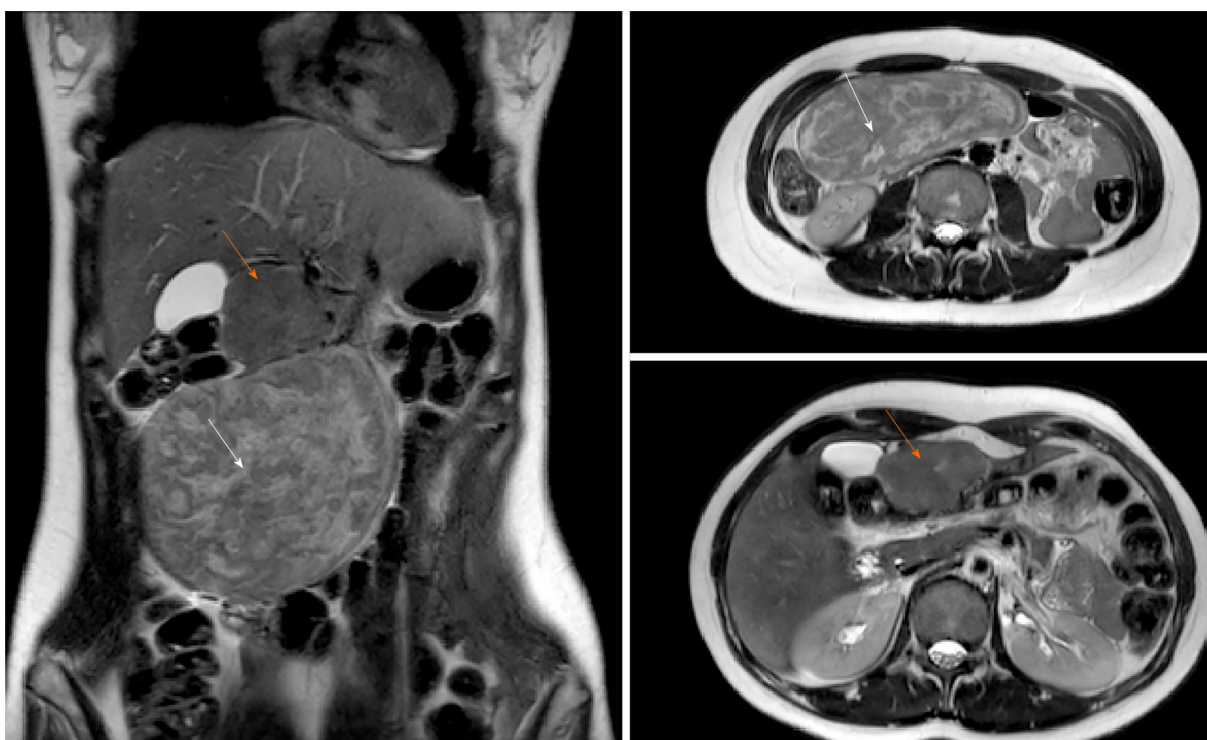
## DISCUSSION

The interest of this case lies in the simultaneous discovery of 2 adjacent but pathologically different benign liver lesions: the first one (FNH) without a strong indication for surgery and the second one requiring surgery because of its uncertain diagnosis.





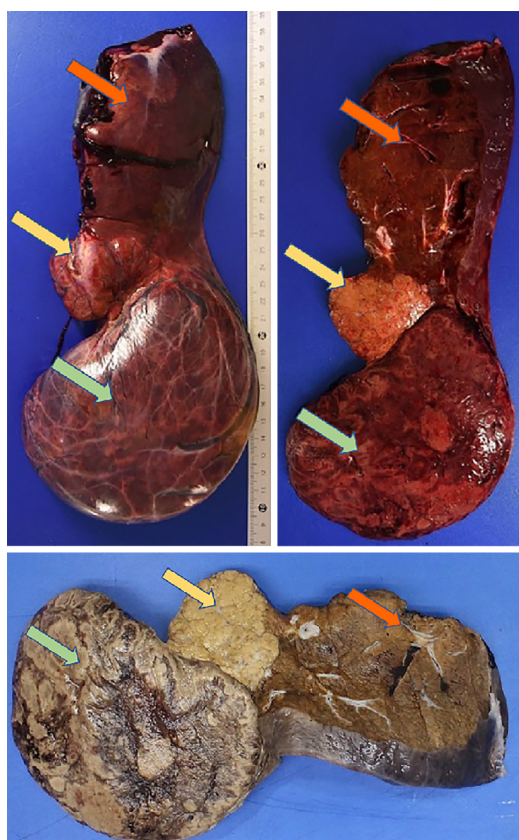
**Figure 4** Computed tomography late portal phase, with a multiplanar reconstruction of focal nodular hyperplasia and hepatocellular adenoma.



**Figure 5** Magnetic resonance imaging – T2 sequence. Orange arrow: Focal nodular hyperplasia; White arrow: Hepatocellular adenoma.

FNH has no recognized risk of malignant transformation or bleeding and usually has an uneventful course. Therapeutic abstention is usually recommended for asymptomatic patients with a definitive diagnosis[11]. Surgical management is reserved for symptomatic patients or with diagnosis uncertainty despite a complete workup[12,13]. Twelve cases of spontaneous rupture of FNH are described and considering these extremely rare events, conservative treatment is the actual well-established standard of care [English-language literature until 2019; NCBI.gov with terms “spontaneous; rupture; FNH]. Close follow-up is however recommended for FNH more than 5 cm. Some authors advocate for upfront surgery with FNH larger than 5 cm[14-16]. However, we do not recommend a surgical resection in our daily practice but advocate for a close follow-up strategy. In the present case report, the diagnosis of FNH of the segment III lesion was radiologically typical and in the absence of the HCA component, a 1-year MRI follow-up would have been recommended.

On the contrary, the risk of malignant transformation of HCA is 4%-5%. As reported by Sempoux *et al*[7], risk factors for complications of HCA (bleeding or malignant transformation) are the size (> 5 cm), male gender, activating mutation in  $\beta$ -catenin,



**Figure 6** Anatomopathological pictures (top: fresh sample; bottom: formalin-fixed sample), sagittal section plane. Yellow arrow: Focal nodular hyperplasia; Green arrow: Hepatocellular adenoma; Orange arrow: Left liver (segment II).

and specific clinical background (glycogen storage disease, androgens, vascular diseases). The resulting recommendations for surgery are based on initial size (> 5 cm), imaging or histological signs of malignancy, size progression after OC discontinuation, and male patients. Selected patients and those who are not fit for surgery can benefit from embolization[17-19]. When the diagnosis cannot be achieved with imaging, a percutaneous biopsy or resection may be required[20].

Moreover, Bröker *et al*[21] 2012 advocated the surgery for adenoma greater than 5 cm with patients who had planned a pregnancy. Our patient didn't have a pregnancy plan but size and uncertainty of diagnosis were our principal arguments for surgery.

We made a literature review of the simultaneous cases of FNH and HA. Although there is some case reports in the eighties, the article was not available for consulting [22-25]. Table 1 summarizes the other cases with enough data.

Case 1 was operated on because of the lack of obvious radiological evidence[26]. The authors of case 2 don't clearly explain the indication for the operative procedure but they interestingly explain the possible same pathophysiological etiology for 4 different simultaneous hepatic masses[27].

Shih *et al*[28] made a left hepatectomy for a case with common features between FNH and HA and operate for the uncertainty of diagnosis.

The French group of Laurent *et al*[29] found in their records 5 over 30 patients operated for "benign hepatocytic nodules" with simultaneous HNF and adenoma. All of them went under surgery when the radiology reports an HA or unidentified mass. The diagnosis of FNH was already known at the time of the surgical procedure except for one case where the FNH was too small[29].

Concerning the surgical technique, the laparoscopic approach is relatively recent. Unfortunately, Shih *et al*[28] didn't report this in their paper although they did the same procedure for a similar patient. Despite the lack of high-level evidence data (randomized control trials, meta-analysis), current literature about laparoscopic *vs* open liver surgery for benign tumors suggests an advantage for the minimal-invasive technique[30,31]. On the other hand, evidence for laparoscopic malign liver resection is much more consistent. Furthermore, safety, feasibility, and long-term results confirmed the advantages of laparoscopy for malign liver tumors[32-34].

Table 1 Summary of current literature review

No.	Ref.	Sex, age	OC	Pathology - Size (cm)	Location (segment)	Symptoms	Treatment
#1	Dimitroulis <i>et al</i> [26], 2012	F, 18 yr	No	FNH - 2.5 HA - 6	S3 S5-6	RUQ pain	Wedge resection Lt S5-6
#2	Di Carlo <i>et al</i> [27], 2003	F, 25 yr	No	FNH - < 5 HA - NA HH - > 4 HCy - NA	S4 S4 S2 S5	RUQ pain	<i>En bloc</i> (+ gallbladder) Enucleation Enucleation <i>En bloc</i> (+ gallbladder)
#3	Shih <i>et al</i> [28], 2015	F, 40 yr	Yes	FNH - 6 HA - 9.5 & small ones (max 1.5 cm)	III III for the largest, small ones on both lobes	Abdominal pain	LH
#4	Laurent <i>et al</i> [29], 2003	F, 45 yr	Yes	FNH - 1 HA - NA	S3 S7	Fatigue	Lt S3 segmentectomy + wedge Lt RH
		F, 40 yr	Yes	FNH - 5 FNH - 4 NA - 3 HA - 3	S6 S7 Left lobe Left lobe	None	Biopsy Biopsy Lt LH Lt LH
		F, 38 yr	Yes	HA surrounded by FNH -13	Right lobe	None	Lt RH
		F, 29 yr	Yes	HA - 5 × 1 FNH - 1	S1 (bleeding), S2, 3, 7, 8 S6	Abdominal pain + shock	Lt LH + S1
		F, 41 yr	Yes	HA - 1 FNH - 1	RL RL	Abdominal pain	Lt RH
#5	Our case-report	F, 38 yr	Yes	6 × 614 × 12 × 6	S3	None	Ls LL

FNH: Focal nodular hyperplasia; HA: Hepatic adenoma; HCy: Hepatic hydatid cyst; HH: Hepatic hemangioma; RL: Right lobectomy; LH: Left hepatectomy; LH: Left hepatectomy; LL Left lobectomy; RUQ: Right upper quadrant; Lt: Laparotomy; Ls: Laparoscopic; F: Female; OC: Oral contraception.

## CONCLUSION

We hereby report a laparoscopic resection of a macro-adenoma associated with focal nodular hyperplasia. The review of the literature shows that the simultaneous presence of these two masses is rare and that every case must be discussed in a multidisciplinary board. Factors like age, pregnancy wish, size, and uncertainty of diagnosis must be considered for shared decision in the setting of a multidisciplinary team. The laparoscopic approach should be preferred as much as possible.

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