Focal Nodular Hyperplasia: A Case Report of Rare Multiple Ruptures of a Common Liver Tumour in a Single Patient

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ABSTRACT

Focal nodular hyperplasia (FNH) is one of the three most common benign solid liver tumours along with hemangiomas and adenomas.[1] FNH is considered a vascular abnormality that usually follows an uneventful course after accidental discovery on CT or MRI for an unrelated medical problem and rarely requires any treatment.[1] These lesions are stable in nature with minimal risk of rupture and essentially no risk for malignant degeneration.[1] The general recommendations for an asymptomatic FNH are observation only, regardless of size of the mass.[1] However, the consequences of a ruptured liver mass can be very serious as abdominal bleeding may be catastrophic, so accurate diagnosis is essential.[1] Here we present the only known case of a patient with multiple FNH nodules and subsequent rupture of two of the lesions; the first treated with a left hepatectomy and the second with embolization. A discussion of the management of the ruptured tumours follows and highlights how little evidence is available for the treatment of multiple ruptures of FNH or for properly risk stratifying patients.

KEYWORDS: *focal nodular hyperplasia, ruptured tumor, liver resection and radiofrequency ablation*

INTRODUCTION

Benign liver tumours are predominantly found in women with the most common usually being categorized as one of the following: hemangioma, adenoma, or focal nodular hyperplasia (FNH).[1] Out of these three, adenomas are most notable for their risk of rupturing and malignant degeneration.[1] FNH is characterized by its benign course, and generally no treatment is recommended.[1] Hemangiomas follow a similar benign course, and again, observation only is recommended.[1] FNH is the second most common benign solid liver tumour, makes up 8 % of all primary hepatic tumours, and is present in up to 3 % of the general population.[1] However, spontaneous rupture and subsequent bleeding is very rare.[1]

The pathophysiology of FNH is not well understood although it is thought to be caused by polyclonal hyperplasia of liver cells as a result of locally enhanced blood flow due to vessel malformations.[2] Lesions that typically present are well-circumscribed with a central scar and are noted most often during X-ray computed tomography (CT) on the arterial phase contrast rather than venous, distinguishing FNH from adenoma.[2] It is important to use imaging to diagnose FNH so as not to miss a more serious diagnosis of a potential malignancy. Using magnetic resonance imaging (MRI) after gadolinium administration, the lesions are hyperintense but then become isointense on later images.[3] The MRI will also show the characteristic central scar of FNH more readily than CT and will often also demonstrate sulfur colloid imaging uptake by Kupffer cells, which does not have the sensitivity and specificity to confirm or refute FNH but is usually not seen in malignancy.[3,4] Unlike adenomas, FNH does not seem to increase in oral contraceptive users but can occur more often in older women.[5] Classically, these lesions remain stable in size, do not rupture, and do not have malignant potential.[5]

> “Prophylactic ablation, embolization, or surgical excision could be considered in high-risk patients.

CASE REPORT

Here we present a case report of a 37-year-old First Nations woman with multiple FNH lesions who first presented to the Emergency Department (ED) with right upper-quadrant abdominal pain and a vague history of back, flank, and abdominal pain of two months duration. Upon ultrasound, a 4 cm solid lesion was detected in

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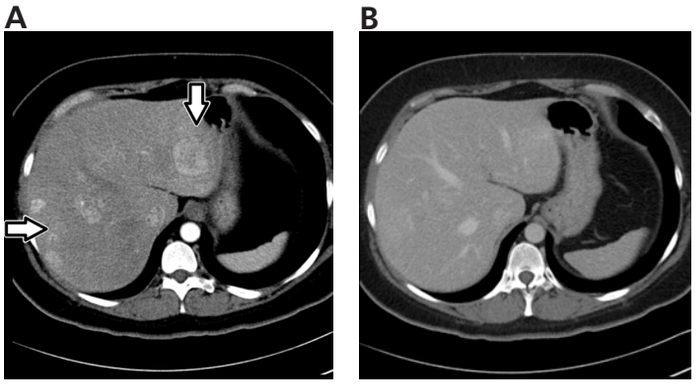

Figure 1. Biphasic CT scan showing typical dynamic phase imaging of an FNH. Arterial phase image (1A) demonstrates early arterial enhancement with portal phase image (1B) demonstrating portal venous washout.

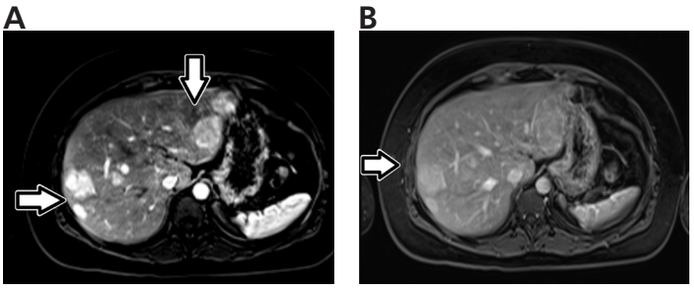

Figure 2. Contrast enhanced MRI also demonstrating similar features as CT scan with arterial enhancement (2A) and portal venous washout (2B).

the left lobe of the liver along with a smaller lesion in the same region. A triphasic CT was performed which showed multiple lesions in her liver seen only in the arterial phase with the largest lesion being 5 cm. The lesions were thought to be consistent with FNH, adenoma, or hepatocellular carcinoma.

This patient had no history of Hepatitis B or C infection or significant alcohol intake. Her past medical history was unremarkable except for a hospitalization for a Caesarean section and a previous laparoscopy for ovarian pain.

At one-month follow-up, CT scanning, MRI, and nuclear medicine imaging were done. The imaging was highly consistent with FNH including arterial phase hypervascularity, the presence of a central scar, and concordance with sulfur colloid uptake indicating the presence of Kupffer cells within the lesions. These features together are considered pathognomonic of FNH.[3] The largest nodule was in liver segment 7/8 and measured 4.9 cm X 3.5 cm. In segment two, another large nodule measuring 3.8 cm X 3.2 cm was present as well as several other smaller scattered lesions. See Figure 1 for a biphasic CT scan showing typical dynamic phase imaging of FNH. The arterial phase image (1A) demonstrates early arterial enhancement and the portal phase image (1B) demonstrates portal venous washout. See Figure 2 for a contrast-enhanced MRI that also demonstrates similar features as the CT scan with arterial enhancement (2A) and portal venous washout (2B).

Further laboratory work was unremarkable and negative for Hepatitis A Virus, Hepatitis B Surface Antigen, and antibodies to Hepatitis C Virus (anti-HCV). Alpha feto protein levels were also normal. Her pain was attributed to irritable bowel syndrome.

The patient continued to have right upper-quadrant pain for several more months when she presented with sudden increased abdominal pain. Imaging demonstrated evidence of hemoperitoneum and rupture of one of her liver masses. She was taken to the operating room on urgent basis where a left hepatectomy was performed. Pathology confirmed the diagnosis of FNH with a ruptured 7.5 cm nodule. Her postoperative course was uneventful. Specimens were sent to pathology with the results shown in Figure 3 and Figure 4, both demonstrating the classic pathology for FNH: a central scar and surrounding non-dysplastic hepatocytes. A subsequent abdominal sonogram was done that showed three new lesions in the right lobe of the liver with the rest of the exam unchanged.

At her follow-up appointment six months later, she was still complaining of intermittent aches and pains. Discussions ensued regarding the utility of prophylactic embolization or ablation of her remaining lesions. This was not recommended due to lack of evidence and follow-up imaging in six months was the recommended course of action.

The patient remained stable for another six months when she again presented to the ED for recurrence of right upper-quadrant

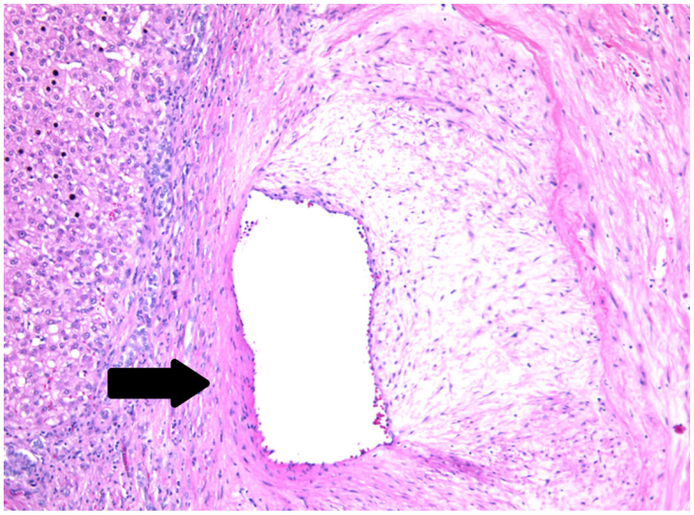

Figure 3. Central scar in the middle of the lesion. Note the vessel partly occluded by organized thrombus. Medium Power (X100) H&E stain.

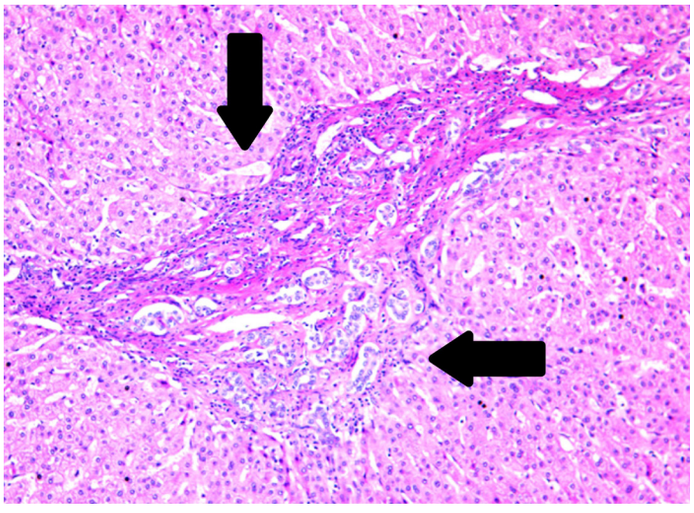

Figure 4. Scarred focus demonstrating bile ductular proliferation with surrounding non-dysplastic hepatocytes. Medium Power (X100) H&E stain.

pain and was investigated on suspicion of a second rupture of one of her smaller FNH lesions. After confirmation by imaging and core biopsy, the recurrent bleed was treated with embolization. Currently the patient is still experiencing ongoing stable non-specific abdominal pain. The plan is for her to undergo sequential ablations of her remaining lesions with repeat imaging.

DISCUSSION

FNH remains a largely asymptomatic disease that patients often only discover after vague abdominal symptoms or from imaging for another medical concern.[1] The current hypothesis is that FNH occurs from a vascular origin, which is supported by the presence of associated bile ducts, veins, and the hyperperfused area of parenchyma. In comparison, a liver cell adenoma has only hepatocytes and no associated structures such as bile ducts are seen.[6] FNH also has an association with hemangiomas, as do hepatic adenomas, but only FNH and hemangioma are associated with vasculature.[6,7]

Accurate diagnosis is important in FNH as it dictates the course of treatment. It is particularly important to distinguish the diagnosis of FNH from liver cell adenomas as larger liver cell adenomas (> 4 cm) are at increased risk for bleeding or malignant degeneration.[1,4] Fortunately, FNH lesions can be identified on imaging as they are well circumscribed with a central scar.[1] Confirmation can be made on contrast-enhanced MRI or a CT scan with MRI having the highest sensitivity and specificity (70 % and 98–100 %, respectively).[2,3,6] On MRI, an important differentiating factor of FNH from malignant hepatic tumors is that FNH often shows strong homogenous activity in the hepatic parenchyma due to the Kupffer cells phagocytosing the dye.[1,3] Malignant tumours will usually have no uptake at the focal defects.[1,3]

The unknown pathology of FNH grouped with its benign nature has resulted in a lack of research into the best treatment for FNH.[6] The accepted recommendations are for observation only. After a literature review, less than 10 cases of FNH ruptures have been reported and no cases of multiple ruptures were found. The rupture of any liver tumour, including FNH nodules, can lead to serious medical consequences, but the factors that increase the risk of rupture in a patient with an FNH are unknown. Routine imaging may be beneficial following discovery of larger or multiple lesions. Prophylactic ablation, embolization, or surgical excision could be considered in high-risk patients. The obvious question is, "What constitutes high-risk?" as no data exists to define this group of patients.

CONCLUSION

The consequences of a ruptured FNH nodule can be very serious for patients, especially those who may not have immediate access to tertiary centres if surgical intervention is needed. Patients that have a high risk of rupture may be considered for prophylactic hepatic resection, ablation, or embolization where appropriate. However, the benefits of these procedures must be weighed against the generally low incidence of ruptured nodules in patients with FNH, and the invasive nature of these treatments as preventative measures. Complications related to FNH resulting in ruptured nodules are rare. As a result, it is unclear as to which patients with FNH require more frequent follow-up versus those whose nodules will never rupture. Surveillance protocols for FNH patients are required so that risk factors for a rupture can be identified. The paucity of literature on this topic makes it difficult to provide specific recommendations that are evidence-based. Patients have to be individualized in their approach to therapy, risk factors, and potential benefits.

SOAP Note

Subjective

- 37-year-old woman presented with increasing vague abdominal pain and enlarging mass in the left lobe of the liver
- History of progressive, vague, chronic upper abdominal and back pain for 1 year, including a visit to the ER and a CT scan showing multiple FNH-like nodules
- Patient denies history of blood transfusions, tattoos, IV drug use, HIV, or significant alcohol intake
- No fevers, chills, or significant weight loss
- Presents again 6 months later for increasing right upper quadrant pain

Objective

- No palpable mass on examination, no palpable hepatomegaly
- AFP ranged from 1.9–2.4 ng/mL over the course of hospital stay (N < 11 ng/mL)
- Hepatitis A and B serology negative
- Carcinogenic Embryonic Antigen 0.8 µg/L (N 0–5 µg/L)
- CBC unremarkable with the exception of MCV 81 fL (N 82–100 fL)
- Liver function tests unremarkable
- Lipase 42 U/L (0–60 U/L)
- Hemoperitoneum
- Pathology results from first rupture indicate central scar in the middle of the lesion and a scarred focus demonstrating bile ductular proliferation with surrounding non-dysplastic hepatocytes
- Follow-up MRI 6 months after second rupture, MRI report showed little change to the numerous hepatic nodules consistent with focal nodular hyperplasia and a central area of necrosis/calcification

Assessment

- History, pathology, lab results, and imaging confirm FNH with multiple ruptures

Plan

- Stabilization of vitals (transfusion if required) and intervention
- Hepatic resection after first rupture, embolization after second rupture
- Continue to follow with imaging and prophylactic ablation of larger lesions to prevent further rupture

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