

# "Gipsy" Focal Nodular Hyperplasia: A case report

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## ABSTRACT

Focal nodular hyperplasia (FNH) is a common benign lesion of the liver of uncertain pathogenesis that is more common in women. Lesions are often asymptomatic and diagnosed incidentally. Magnetic resonance imaging with liver-specific contrast allows non-invasive and accurate diagnosis. Most FNHs remain stable over long periods of follow-up. However, some rare cases of partial or complete spontaneous regression have been described in the literature. In this report, we discuss the case of a 38-year-old female patient who experienced not only complete regression of two liver lesions compatible with FNH, but also the appearance of a similar lesion in a different liver segment. To our knowledge, no similar cases have been reported.

## CASE REPORT

### CASE REPORT

A 38-year-old woman with a history of focal nodular hyperplasia (FNH) presented for routine hepatology consultation. She reported no past medical history. She presented with an adequate diet and regular bowel movements, two full-term pregnancies, and an allergy to macrolides. The patient denied intravenous drug use, alcohol consumption, and cigarette smoking, although she reported a history of smoking 10 cigarettes per day for at least 16 years. The patient denied any pharmacological drug therapy at home except oral contraceptive pill (OCP) for 3-4 years in the past. Physical examination revealed a normal abdomen with no palpable masses. The patient denied any abdominal pain or discomfort. Routine blood tests, including liver function, were within normal limits.

### Imaging findings and follow up

In 2011, an upper abdominal ultrasound (US) revealed 2 hepatic lesions in the left liver. Therefore, the patient subsequently underwent magnetic resonance imaging (MRI) with contrast, which confirmed the presence of 2 well-defined lesions located in S1 (15x15x14 mm, Figure 1) and S3 (12x11x12 mm, Figure 2). These lesions showed strong homogeneous enhancement in the arterial phase, which appeared as isointense and homogeneous hyperintense in the delayed/hepatobiliary phase.

In September 2023, the patient underwent a repeat contrast-enhanced MRI. Unexpectedly, the previously described FNH lesions were no longer identifiable, resulting in their complete disappearance (Figure 3). Furthermore, a new lesion of 10x10x10

mm with the same radiological characteristics compatible with FNH was surprisingly seen in S6 (Figure 4).

Given the rarity of these findings, the images were reviewed by expert radiologists who confirmed the above.

### DISCUSSION

#### Etiology and demographics

FNH is a well-defined, non-capsulated hepatic lesion with no risk of malignant transformation. It is more common in women (up to 90% of cases) of 20-50 years of age and is one of the most common benign liver lesions, second only to haemangiomas [1,2]. The pathogenesis is not well understood; by definition, FNH usually occurs in a normal liver due to hepatocellular proliferation in response to abnormal perfusion. The resulting oxidative stress induces stellate cells to form a typical central fibrous scar. In addition, multiple FNHs are commonly seen in vascular liver diseases such as Budd-Chiari syndrome or congenital vascular disorders [3]. Although female hormones have been considered as a possible cause, it is now well established that oral contraceptives or pregnancy do not correlate with the appearance and dimensions of FNH [4,5]. Most cases are asymptomatic and up to 50% of diagnoses are incidental.

#### Clinical and imaging findings

MRI is the gold standard for diagnosis of FNH due to its high sensitivity and specificity, especially in combination with hepatobiliary extracellular contrast, and its suitability in women of childbearing age [6]. Typical FNH shows an isointense signal peripherally with central hypointensity on T1 scan, while the

central scar shows a hyperintense signal on T2 scan. On T1-contrasted images, FNH shows peripheral enhancement in the arterial phase that persists in the delayed/hepatobiliary phase [7]. Biopsy is only necessary in equivocal cases, especially when the size is greater than 3 cm.

### Treatment, prognosis, and follow-up

The natural history of FNH is controversial due to a lack of long-term studies. Most FNH remain stable over time and therefore no follow-up or treatment is usually recommended, although caution is advised in women on OCP treatment [8,9]. A 2013 retrospective study of 44 patients who underwent MRI reported dimensional regression in only 7 FNH lesions [9]. In a 2021 study involving 150 patients, 77% of analysed FNHs remained dimensionally stable during follow-up (6-64 months), while 38 patients showed an average growth or regression rate of 0.6 and 0.5 cm, respectively [10].

Nevertheless, spontaneous and complete regression has been described in the past. For example, two FNH cases of almost complete involution and regression were reported in 2015 [11]. Furthermore, despite limitations related to the radiological methods used, a prospective study based on US reported the complete disappearance of 6 FNHs, mostly of small initial size (< 2 cm) and in elderly patients [12]. More recently, a single case report showed complete regression of a giant FNH in a young woman over a period of 7 years [13]. To the best of our knowledge, this is the first reported case of not only complete regression of 2 FNHs, but also concomitant recurrence of a similar lesion in a different liver segment in the same patient.

### TEACHING POINT

Focal nodular hyperplasia is a benign hepatic nodular formation with an unclear pathogenesis, a typical magnetic resonance appearance and no need for specific treatment or follow-up. The possibility of complete regression and reappearance of focal nodular hyperplasia in another liver segment is a rare event, opening new perspectives on its etiopathogenesis, prognosis and management.

### ACKNOWLEDGMENTS

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### QUESTIONS

**Question 1: Which of the following statements about focal nodular hyperplasia (FNH) is incorrect?**

1. FNH is a benign liver lesion.
2. FNH is a non-capsulated hepatic lesion.
3. FNH is a well-defined hepatic lesion.
4. FNH has a moderate risk of malignant transformation. (applies)

5. FNH prevalence in the general population has been estimated at 0.9–3.0%.

### Explanation:

1. FNHs are benign lesions of the liver. [FNH is one of the most common benign liver lesions, second only to haemangiomas, with an estimated prevalence of 0.9-3.0% in the general population.]
2. FNHs are non-capsulated lesions of the liver. [FNH is a well-defined, non-capsulated hepatic lesion with no risk of malignant transformation.]
3. Even if non-capsulated, FNHs are well-defined lesions in the liver. [FNH is a well-defined, non-capsulated hepatic lesion with no risk of malignant transformation.]
4. FNHs are benign liver lesions, with no risk of malignant transformation. [FNH is a well-defined, non-capsulated hepatic lesion with no risk of malignant transformation.]
5. FNHs are the second most common liver lesion, with an estimated prevalence of 0.9-3.0% in the general population. [FNH is one of the most common benign liver lesions, second only to haemangiomas, with an estimated prevalence of 0.9-3.0% in the general population.]

**Question 2: Which of the following statements about focal nodular hyperplasia (FNH) is incorrect?**

1. FNH is common in women aged 20-50 years.
2. The pathogenesis of FNH is not fully understood.
3. The central fibrous scar typical of FNH is a stellate cell response to oxidative stress.
4. Multiple FNHs are common in Budd-Chiari syndrome.
5. FNH is more common in women taking oral contraceptives or in pregnant women. (applies)

### Explanation:

1. FNHs are more common in women of 20-50 years of age. [It is more common in women (up to 90% of cases) of 20-50 years of age and is one of the most common benign liver lesions...]
2. The pathogenesis of FNHs is still unclear. [The pathogenesis is not well understood; by definition, FNH usually occurs in a normal liver due to hepatocellular proliferation in response to abnormal perfusion.]
3. The central fibrous scar of FNHs is produced by stellate cells. [The resulting oxidative stress induces stellate cells to form a typical central fibrous scar.]
4. Multiple FNHs may be seen in patients with vascular liver disease such as Budd-Chiari. [In addition, multiple FNHs are commonly seen in vascular liver diseases such as Budd-Chiari syndrome or congenital vascular disorders.]
5. Oral contraceptives or pregnancy do not correlate with the occurrence of FNHs [Although female hormones have been considered as a possible cause, it is now well established that oral contraceptives or pregnancy do not correlate with the appearance and dimensions of FNH.]

**Question 3: Which of the following is the gold standard for the diagnosis of focal nodular hyperplasia (FNH)?**

1. Ultrasound.
2. Contrast-enhanced computed-tomography (CT) of the abdomen.

3. Contrast-enhanced magnetic resonance imaging (MRI) of the abdomen. (applies)
4. Positron emission tomography (PET).
5. Liver biopsy.

**Explanation:**

1. In the diagnosis of FNH, ultrasound is inferior to MRI in sensitivity and specificity. [MRI is the gold standard for diagnosis of FNH due to its high sensitivity and specificity, especially in combination with hepatobiliary extracellular contrast, and its suitability in women of childbearing age.]

2. In the diagnosis of FNH, CT is inferior to MRI in sensitivity and specificity. [MRI is the gold standard for diagnosis of FNH due to its high sensitivity and specificity, especially in combination with hepatobiliary extracellular contrast, and its suitability in women of childbearing age.]

3. MRI is the gold standard for diagnosis of FNH due to its high sensitivity and specificity. [MRI is the gold standard for diagnosis of FNH due to its high sensitivity and specificity, especially in combination with hepatobiliary extracellular contrast, and its suitability in women of childbearing age.]

4. The diagnostic pathway for focal nodular hyperplasia does not include PET. [MRI is the gold standard for diagnosis of FNH due to its high sensitivity and specificity, especially in combination with hepatobiliary extracellular contrast, and its suitability in women of childbearing age.]

5. In the diagnosis of FNH, biopsy is only necessary in equivocal cases. [Biopsy is only necessary in equivocal cases, especially when the size is greater than 3 cm.]

**Question 4: Which of the following statements about the diagnosis of focal nodular hyperplasia (FNH) on contrast-enhanced magnetic resonance imaging (MRI) is incorrect?**

1. Typical FNH shows an isointense signal peripherally on T1 scan.
2. Typical FNH central scar shows hyperintensity on T1 scan. (applies)
3. Typical FNH central scar shows hyperintensity on T2 scan.
4. Typical FNH shows peripheral enhancement in the arterial phase on T1 scan.
5. Typical FNH maintains peripheral enhancement in the delayed phase on T1 scan.

**Explanation:**

1. FNHs typically show an isointense signal peripherally on T1 scan. [Typical FNH shows an isointense signal peripherally with central hypointensity on T1 scan, while the central scar shows a hyperintense signal on T2 scan.]

2. FNHs central scars typically show hypointensity on T1 scan. [Typical FNH shows an isointense signal peripherally with central hypointensity on T1 scan, while the central scar shows a hyperintense signal on T2 scan.]

3. FNHs central scars typically show hyperintensity on T2 scan. [Typical FNH shows an isointense signal peripherally with central hypointensity on T1 scan, while the central scar shows a hyperintense signal on T2 scan.]

4. FNHs typically show peripheral enhancement in the arterial phase on T1 scan. [On T1-contrasted images, FNH shows peripheral enhancement in the arterial phase that persists in the delayed/hepatobiliary phase.]

5. FNHs typically maintain peripheral enhancement in the delayed phase on T1 scan. [On T1-contrasted images, FNH shows peripheral enhancement in the arterial phase that persists in the delayed/hepatobiliary phase.]

**Question 5: Which of the following statements about the management of focal nodular hyperplasia (FNH) is correct?**

1. FNHs usually grow in size over time, and therefore always require surgery.
2. FNHs usually grow over the years, but surgery is only required when the size exceeds 3 cm.
3. FNHs always require surgery in women taking oral contraceptives or who are pregnant.
4. FNHs usually remain stable over time, no treatment is recommended. (applies)
5. FNHs usually decrease in size over time, until complete spontaneous regression.

**Explanation:**

1. FNHs usually remain stable over time, no treatment is recommended. [Most FNH remain stable over time and therefore no follow-up or treatment is usually recommended, although caution is advised in women on OCP treatment.]

2. FNHs usually remain stable over time, no treatment is recommended. [Most FNH remain stable over time and therefore no follow-up or treatment is usually recommended, although caution is advised in women on OCP treatment.]

3. Although caution is advised in women with FNH who take oral contraceptives, surgery is not recommended. [Most FNH remain stable over time and therefore no follow-up or treatment is usually recommended, although caution is advised in women on OCP treatment.]

4. No treatment is recommended for FNHs, which usually remain stable over time. [Most FNH remain stable over time and therefore no follow-up or treatment is usually recommended, although caution is advised in women on OCP treatment.]

5. FNHs usually remain stable over time. [Most FNH remain stable over time and therefore no follow-up or treatment is usually recommended, although caution is advised in women on OCP treatment.]

**Authors' contributions**

V. Poletti and G. Migliorisi performed the literature search and drafted the manuscript. R. Ceriani, V. Pedicini, A. Aghemo critically revised, and gave final approval to the draft. All authors have read and agreed to the published version of the manuscript.

**Disclosures**

The authors declare no conflict of interest.

### Consent

Did the author obtain written informed consent from the patient for submission of this manuscript for publication? Yes. Images were obtained with patient permission accordingly to current National Privacy Regulations.

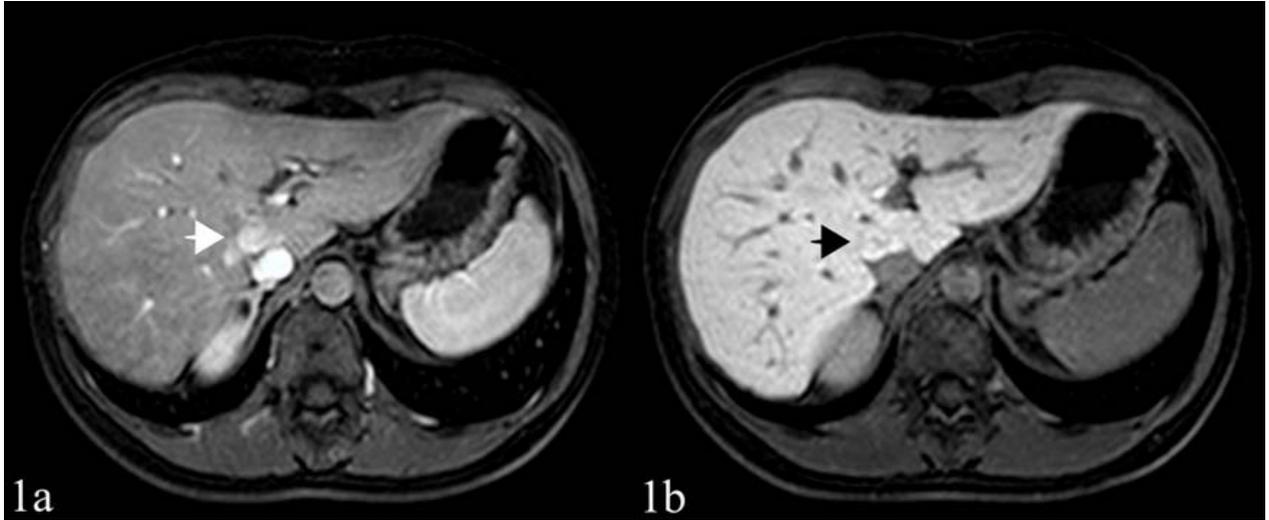
### Human and animal rights

Not applicable.

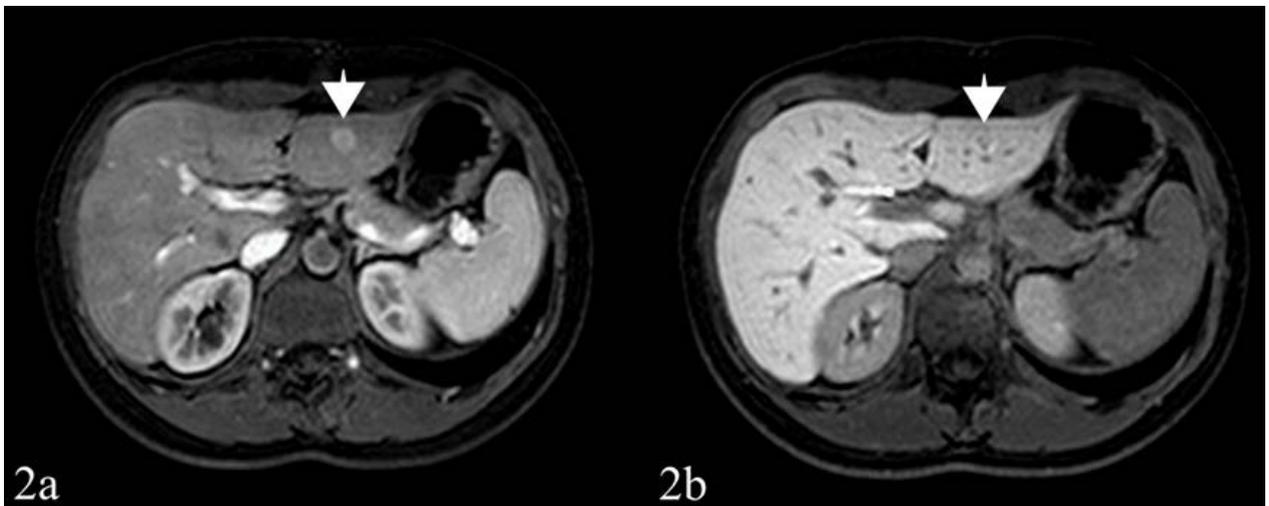
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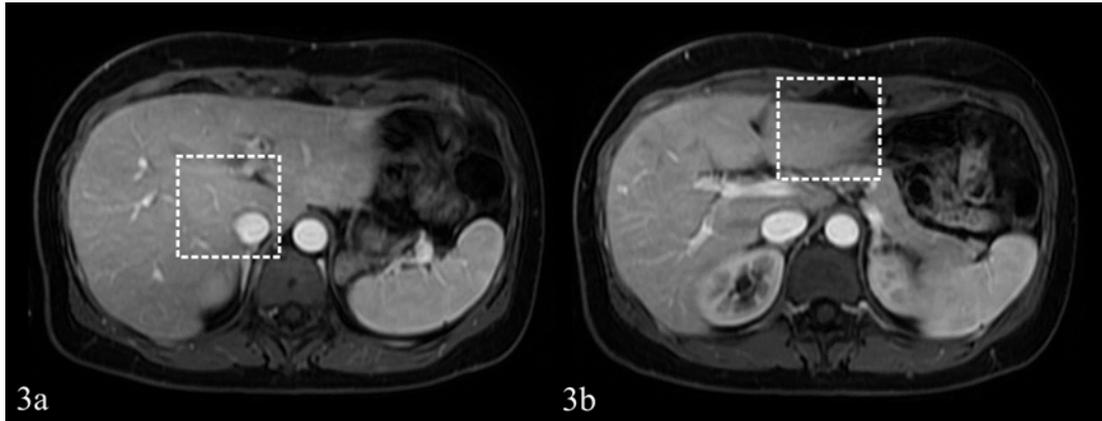
FIGURES



**Figure 1:** 26-year-old female with focal nodular hyperplasia (FNH) in segment 1 (2011).  
**1a findings:** Axial T1 gadoxetate-enhanced MRI of the abdomen in the arterial phase demonstrates a 15x15x14 mm FNH with homogeneous hyperenhancement in segment 1.  
**1b findings:** Axial T1 gadoxetate-enhanced MRI of the abdomen in the 20-min hepatobiliary phase confirms a 15x15x14 mm FNH with homogeneous isointense uptake in segment 1.  
**Technique:** Magnetom Aera 1.5T, Siemens Healthineers.



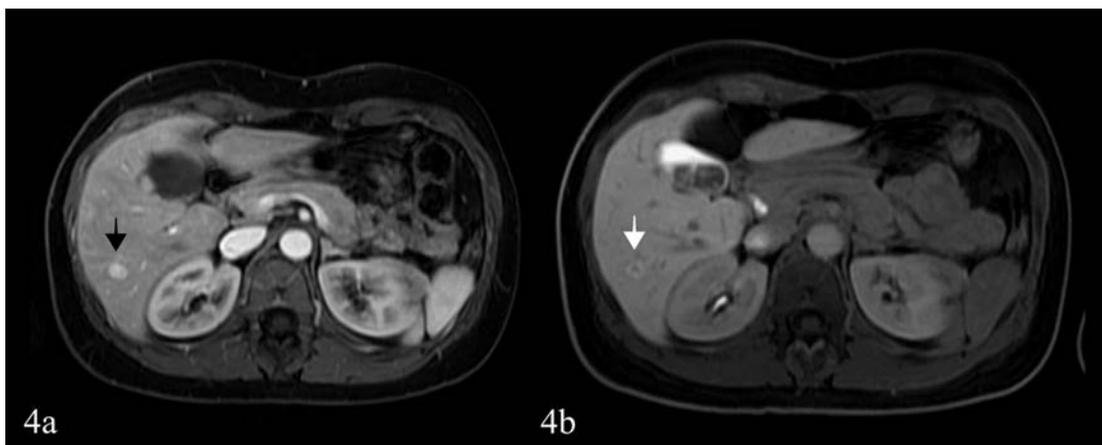
**Figure 2:** 26-year-old female with focal nodular hyperplasia (FNH) in segment 3 (2011).  
**2a findings:** Axial T1 gadoxetate-enhanced MRI of the abdomen in the arterial phase demonstrates a 12x11x12 mm FNH with homogeneous hyperenhancement in segment 3.  
**2b findings:** Axial T1 gadoxetate-enhanced MRI of the abdomen in the 20-min hepatobiliary phase confirms a 12x11x12 mm FNH with homogeneous isointense uptake in segment 3.  
**Technique:** Magnetom Aera 1.5T, Siemens Healthineers.



**Figure 3:** Same patient with focal nodular hyperplasia (FNH), now 38-years-old (2023).

**Findings:** Axial T1 gadoxetate-enhanced MRI of the abdomen in the arterial phase demonstrates the disappearance of the 15x15x14 mm FNH in segment 1 (**3a**) and the 12x11x12 mm FNH in segment 3 (**3b**).

**Technique:** Magnetom Aera 1.5T, Siemens Healthineers.



**Figure 4:** Same patient with focal nodular hyperplasia (FNH), now 38-years-old (2023).

**4a findings:** Axial T1 gadoxetate-enhanced MRI of the abdomen in the arterial phase demonstrates a 10x10x10 mm FNH with homogeneous hyperenhancement in segment 6.

**4b findings:** Axial T1 gadoxetate-enhanced MRI of the abdomen in the 20-min hepatobiliary phase confirms a 10x10x10 mm FNH with homogeneous isointense uptake in segment 6.

**Technique:** Magnetom Aera 1.5T, Siemens Healthineers.

**KEYWORDS**

Focal nodular hyperplasia; Benign hepatic lesions; Liver lesions; Central fibrous scar; Stellate cells

**ABBREVIATIONS**

FNH = Focal Nodular Hyperplasia  
OCP = Oral Contraceptive pill  
US = Ultrasound  
MRI = Magnetic Resonance Imaging

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