To evaluate retrospectively the optimized biphasic computed tomographic (CT) findings of focal nodular hyperplasia (FNH) that might facilitate correct diagnosis.

Biphasic helical CT scans were performed in 28 patients with 40 FNH lesions. Hepatic arterial phase (HAP) and delayed venous phase (DVP) images were obtained initially at 20-25 and 120 seconds, respectively. Diagnosis was based on complete resection (n = 9), MRI (magnetic resonance image) (n = 12) or CT (n = 7) follow-up for a minimum of 6 months without evidence of significant change. We evaluated the number, size, location, margins, surface, homogeneity of enhancement, and presence of central scar, mass effect, calcification, or vessels feeding or draining the lesion. Forty tumors (mean diameter, 4.2 cm; range, 1-9.5 cm) were seen. The large lesion group included 18 nodules larger than 3 cm in diameter. Typical imaging features of FNHs included strong, homogeneous contrast enhancement on HAP images and isodensity to the liver or maybe hyperattenuating in hepatic steatosis on DVP images. The large lesion group usually demonstrated subcapsular location, a thin central scar and peritumoral vessels (p < 0.05). The small lesions (≤ 3 cm in diameter) tend to present isoattenuating on non-enhanced scan more than the large lesions (p < 0.05). Our optimized biphasic protocol using HAP and DVP instead of portal venous phase (PVP) scans demonstrated good detectability and characteristic features of FNH. Such familiarity may help to avoid unnecessary imaging, biopsy, or surgery.

Key words: Computed tomography (CT); Focal nodular hyperplasia; Liver

Edmondson introduced the term “focal nodular hyperplasia” (FNH) in 1958 [1]. However, the cause of FNH is not well understood [2, 3]. Congenital vascular malformation and vascular injury have been suggested as the underlying mechanism [3, 4]. Recently, an association with steroids has been disproved [5]. FNH is the second most common benign liver tumor after hemangioma [6]. Distinction between FNH and other hypervascular liver lesions such as hepatocellular adenoma, hepatocellular carcinoma, and hypervascular metastases is critical to proper treatment. The purpose of this retrospective study was to evaluate the CT imaging features of FNH on optimized biphasic scan for confident diagnosis. FNH is usually isoattenuating to the liver on DVP (120 sec and 5-10 min) scan. So we use DVP (120 sec) instead of the later due to almost the same detectability and saving much time.

METHODS

From January 1999 to March 2004, we reviewed the medical records and pathology data bank and identified 46 patients with a diagnosis of FNH. Thirty-five patients had undergone CT. Five patients were excluded because of lack of presurgical CT. Two patients without pathologic proof of FNH were excluded because of insufficient imaging follow-up. The remaining 28 patients were included in our study group.
There were 18 women and 10 men, aged 17-58 years (mean, 32 years) in this study. One patient had a history of breast carcinoma. Two patients had clinical evidence of viral hepatitis B. Eleven FNHs were surgically removed in 9 patients due to fear of malignancy. Other patients underwent MRI (n = 12) or CT (n = 7) follow-up for a minimum of 6 months (range, 6-40 months; mean, 24 months) without evidence of significant change.

Optimized biphasic CT was performed in 28 patients with PQ2000 or PQ 6000 CT scanner (Picker International, Highland Heights, OH, USA) including both hepatic arterial phase (HAP) and delayed venous phase (DVP) imaging through the liver, with delays of 20-25 seconds and 120 seconds, respectively, after initiation of the intravenous bolus injection of 100 ml contrast medium. The injection rate was 2.5-3 mL/sec with use of a power injector. Slice thickness of 8 mm

### Table 1. Characteristic CT Findings of the 40 FNH Lesions According to Size

<table>
<thead>
<tr>
<th>Finding</th>
<th>Small (≤ 3 cm)</th>
<th>Large (&gt; 3 cm)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smooth surface</td>
<td>22 (100)</td>
<td>17 (94)</td>
<td>0.239</td>
</tr>
<tr>
<td>well-defined margins</td>
<td>22 (100)</td>
<td>18 (100)</td>
<td></td>
</tr>
<tr>
<td>Subcapsular location</td>
<td>9 (41)</td>
<td>15 (83)</td>
<td>0.004</td>
</tr>
<tr>
<td>CT attenuation</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypo- on NE scan</td>
<td>7 (32)</td>
<td>10 (56)</td>
<td>0.317</td>
</tr>
<tr>
<td>Iso- on NE scans</td>
<td>14 (64)</td>
<td>7 (39)</td>
<td>0.025</td>
</tr>
<tr>
<td>Hyper- on HAP scans</td>
<td>22 (100)</td>
<td>18 (100)</td>
<td></td>
</tr>
<tr>
<td>Homogeneous on HAP scans</td>
<td>22 (100)</td>
<td>18 (100)</td>
<td></td>
</tr>
<tr>
<td>Iso- on DVP scans</td>
<td>21 (95)</td>
<td>15 (83)</td>
<td>0.182</td>
</tr>
<tr>
<td>Central scar</td>
<td>1 (5)</td>
<td>15 (83)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Peritumoral vessels</td>
<td>0 (0)</td>
<td>13 (72)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Hypo- = Hypoattenuating; Iso- = isoattenuating; Hyper- = Hyperattenuating; NE = nonenhanced; HAP = hepatic arterial phase; DVP = delayed venous phase.

**Figure 1.** Typical FNH on biphasic CT scans. **a.** On nonenhanced image, the hypodensitively central scar (long arrow) is not obvious in the slightly hypodensitively FNH (arrow). **b.** On HAP image, FNH (arrow) enhances brightly and homogeneously except for the central scar and thin septa (long arrow). **c.** On DVP image, FNH (arrow) is isoattenuating to liver. Increased attenuation of the central scar (long arrow) causes it difficult to differentiate from periphery.

**Figure 2.** FNH with hepatic steatosis on biphasic CT scans. **a.** On nonenhanced image, central scar (long arrow) is not definite and most of the FNH (arrow) is hyperattenuating to liver. **b.** On HAP image, FNH (arrow) enhances brightly and homogeneously except for the central scar (long arrow). **c.** On DVP image, FNH (arrow) is still hyperattenuating to liver, and the central scar (long arrow) is faintly hyperattenuating (arrow).
and pitch of 1-1.5 depending on the liver size were used for helical imaging.

The CT images were reviewed retrospectively by two experienced gastrointestinal radiologists. We evaluated the number, size, surface (smooth or lobulated), margin (sharply or ill defined), location (subcapsular or deeper) and central scar of the FNH lesions. A lesion was considered small if it was smaller than 3 cm in maximal diameter. A central scar was considered large if it had a thickness larger than 1 cm. The presence of enlarged vessels feeding or draining the mass, as well as that of peripheral, or central arteries, was assessed. The attenuation of the lesion was judged relative to that of the surrounding liver on nonenhanced scans, HAP and DVP images. Comparisons of the findings between the small lesion group and the large lesion group were made using the χ²-square test. A level of < 0.05 was considered significant for the test.

RESULTS

Each radiologist identified 40 lesions in 28 patients. Twenty-two patients (77%) had a single lesion, while 6 patients had multiple FNH lesions: One patient had 6 lesions, two patients had three lesions, and the other 3 patients had two lesions. The lesions had a mean maximal diameter of 4.2 cm (range, 1-9.5 cm). Twenty-two lesions were 3 cm or smaller in diameter while 18 lesions were larger than 3 cm.

A summary of characteristic CT findings is shown in Table 1. The surface of the FNH was smooth in 39 (97%) of 40 lesions and lobulated only in 1 (3%) lesion which was larger. The margins were well-defined in all 40 lesions (100%) (Fig. 1). The lesions were predominantly in a subcapsular location in 24 (60%) (Fig. 2). Among them, the large lesion group (83%) was more subcapsular than the small lesion group (41%) (P < 0.05). Fewer lesions were deeper within the liver in 16 (40%) (Fig 1). Sixteen (40%) FNH lesions exerted a mass effect and displaced adjacent blood vessels. Fat and calcification were not identified within any FNH lesion in our series.

Of the 40 lesions seen on nonenhanced CT images, the FNHs were hypotenuating to the liver in 17 (43%), isoattenuating in 21 (52%), and hyperattenuating in 2 (5%). Isoattenuating was more in the small lesion group (64%) than the large lesion group (39%) (P < 0.05). The two hyperattenuating lesions were found in a fatty liver with abnormally low attenuating liver parenchyma. On HAP images, all 40 FNHs (100%) were hyperattenuating to the liver. On the DVP images, none were hypotenuating, 36 (90%) were isoattenuating (Fig. 1), and 4 (10%) were hyperattenuating (Fig. 2) which were also found in the patient with a fatty liver. All 40 (100%) lesions enhanced homogeneously except the components of central scar.

CT demonstrated a central scar in 16 lesions (40%). The size of the central scar was described as small in 11 lesions (69%) (Fig. 2) and large in 5 lesions (31%) (Fig. 1). Central scar and peritumoral vessels were less frequently identified in the small lesion group (40%) than in the large lesion group (60%) (P < 0.05) (Fig. 3). These vessels were believed to represent feeding arteries or early draining veins.

Of the 28 patients with FNH, five (18%) had an associated hemangioma. These hemangiomas were single in four patient and five in one, ranging from 1 to 1.5 cm. One patient with five hemangiomas also had six FNHs. These hemangiomas usually showed peripheral nodular enhancement on HAP images and persistent enhancement on DVP images.

DISCUSSION

In the era before the advent of helical CT scanner, it was more difficult for radiologists to distinguish
among various hepatic tumors. The availability of helical CT has changed the radiologist’s approach to hepatic imaging from lesion detection to tumor characterization. The prevalence of FNH was found to be 0.9% in a study of 2,500 consecutive autopsies, indicating that FNH will be encountered more frequently as imaging methods improve. [7]. With the faster CT scanners it is now possible to scan through the entire liver during the HAP, portal venous phase (PVP), and DVP for hepatic tumor detection and lesion characterization. Reviewing the literature, there are two major protocols of helical CT to detect hepatic lesion, including the biphasic study with HAP and PVP, and the multiphasic study with additional DVP [8-16]. We optimized our protocol of biphasic study for hepatic scanning by including nonenhanced image, HAP and DVP instead of PVP. The delay time of DVP in our series was 120 sec instead of 5-10 mins in other studies [9, 10, 13, 15]. We found our protocol also had a good detection rate for FNH. It’s also advantageous in decreasing the patient’s radiation dose and shortening the examination time.

FNH is a benign neoplastic or tumorlike lesion of the liver that is rarely encountered. Although atypical imaging features are the exception rather than the rule with FNH, it is sometimes difficult to differentiate FNH from other hypervascular tumors [10]. Our experience suggests that most FNHs are easily recognized on CT scans when proper CT techniques are chosen and when the size of the FNH and the status of the surrounding liver are taken into account.

Brancatelli et al. and Carson et al. found that FNH was isoattenuating (48% and 57%), hypoattenuating (42% and 40%), and hyperattenuating (9% and 3%) on nonenhanced CT images, retrospectively [9, 13]. In our study, FNH was isoattenuating (52%) or slightly hypoattenuating (43%). FNH was only hyperattenuating to the nonenhanced liver (5%) when there was hepatic steatosis. Our findings are similar to those of previous findings. We also found that the small foci tend to present isoattenuation more than the larger foci (p < 0.05). Of the six patient with hepatic steatosis on nonenhanced CT, the CT attenuation was hypo-, iso- or hyper-attenuating in two patients, respectively. These hypoattenuating and isoattenuating foci were due to fatty infiltration of the FNH found in the pathology, which was the same finding as that of Mortele et al [7].

FNH is usually isoattenuating to the liver on DVP scan, which accounts for the rarity of this diagnosis in the pre-helical CT era. Only four lesions were hyperattenuating to the liver on DVP scan. They were all hepatic steatosis which causes low attenuation back-ground of the liver and relatively high attenuating FNH. We might have misinterpreted FNH as hemangioma without considering the effect of fatty liver. In Brancatelli’s study, more FNHs appeared as isoattenuating on delayed phase (88%) rather than on PVP scan [9]. In our study, isoattenuating foci were found in 90% on delayed phase. The findings also support the use of DVP scan instead of PVP scan when biphasic study is performed on helical CT scanner.

Homogeneous bright enhancement and a central scar are the most reliable CT signs of FNH. All of our FNH lesions were hyperattenuating on HAP scans. A central scar was identified on CT images in 16 (40%) of the 40 FNH lesions. The scar was almost always visualized as being hypoattenuating to the remainder of the FNH on all phases. Brancatelli et al. found that in delayed scans (5-10 minutes delay time), the retention of contrast material within the fibrous scar made it isoattenuating (15%) or even hyperattenuating (81%) [9]. The difference could be explained that our delay time (2 minutes) in DVP was not longer enough as compared with that (5-20 minutes) in Brancatelli’s series.

Detection of a central scar was clearly related to the size of the FNH. A central scar was less identified in small group than in large group (P < 0.05). Other features of FNH also appear to be related to its size. Smaller lesions rarely have subcapsular location and peritumoral blood vessels than larger lesions (p < 0.05). Enlarged vessels on the surface of an FNH lesion and penetrating to the central scar are a well-recognized pathologic feature of FNH, and demonstration of such vessels on CT scans should not be regarded as suggestive a sign of malignancy [6]. Additional common features of FNH in our series were smooth (nonlobulated) contour (97%) and well-defined margins (100%). Most studies found that FNH usually has a well-defined margin [3, 6, 10, 13]. Only Brancatelli et al. reported that the margin of most foci (72%) were ill-defined [9]. Some authors ever reported atypical finding of FNH in a minority of lesions [10].

Oral contraceptives is not responsible for the development of FNH, but probably stimulates its growth. Mathieu et al. reported that regardless of whether oral contraceptives or other steroids are being used, most FNH appear to remain stable in size and number, while a few can be expected to show modest interval growth or decrease in size [5]. In our series, one female patient, who had not used oral contraceptives, had two FNH lesions that increased from 4.0 to 5.4 and 3.0 to 4.5 cm in diameter, respectively, after one year. Because of fear of malignancy, the patient
decided to accept the resection. We followed up this patient and there has been no recurrence for 2 years. Another obvious difference between other studies and ours is that the male-to-female ratio of our study (5:9) was higher than that of other studies (1:8) [9, 18]. This may be due to the small number of patients in our study. We also regard calcification as a rare finding in FNH. Caseiro-Alves et al. reported five FNH lesions with calcification in a series of 295 patients, and another isolated case was recently reported [12, 13]. However, no calcification was found in any of our patients.

In our series, 5 (17%) had concomitant hemangioma, including one patient with six hemangiomas. Nguyen et al. reported a surgical pathologic series of 305 FNH lesions in 168 patients and found cavernous hemangiomas in 6.5% of the patients with FNH, which was lower than the percentage in ours, and somewhat higher than the incidence of 2.3% in another article [6]. The association of FNH with hemangioma may support the theory that hepatic vascular derangement predisposes to the development of FNH.

The differential diagnosis for FNH includes other hypervascular tumors such as adenoma, fibrolamellar and conventional hepatocellular carcinoma (HCC), small hemangiomas, and hypervascular metastases. Adenomas occur predominantly in women of child-bearing age, and their presence is strongly associated with the use of oral contraceptives. Adenomas usually enhance less brightly than FNH [14, 15]. They also often demonstrate spontaneous tumor hemorrhage, fat component, central necrosis and calcification.

Fibrolamellar HCC usually appears as a large vascular mass that has surface lobulations. A central scar, often with calcification, can be identified in approximately half of the patients. Obvious signs of malignancy such as lymphadenopathy (65%), metastases, and biliary and vascular invasion are found in the majority of cases [14].

Conventional HCC usually enhanced heterogeneously but FNH has strong and homogenous enhancement on HAP images. On DVP and PVP images, HCC is more likely hypoenhancing to the normal liver while FNH is usually homogeneous and isoattenuating on non-enhanced scan than the lesions larger than 3cm in diameter usually demonstrated subcapsular location, a thin central scar and peritumoral vessels. The small lesions (≤3 cm in diameter) tend to present isoattenuating on non-enhanced scan than the large lesions. Our optimized biphasic protocol using HAP and DVP scans demonstrated good detectability and characteristic features of FNH.

**REFERENCES**

肝臟局部結節增生在最佳化雙相電腦斷層攝影的影像表現

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分析本院肝臟局部結節增生病人在最佳化雙相電腦斷層攝影的影像表現，找出幫助正確診斷的特徵。從1999年到2004年總共蒐集了28位病患共有40個病灶，接受雙相電腦斷層掃描，包含動脈相與延遲靜脈相。我們分析病灶的數目、大小、位置、邊緣、顯影表現、是否呈現中心疤痕組織、供應或引流的血管等特徵。40個病灶中，直徑大小從1到9.5公分，平均4.2公分，22 個小於3公分。典型肝臟局部結節增生的特徵是在動脈相中有非常的高度顯影、在延遲靜脈相中與肝臟同等顯影或因脂肪肝而顯影高於肝臟。大於3公分的病灶較常位於肝臟邊緣，有中心疤痕組織，附近有供應或引流的血管等特徵。不大於3公分的病灶在未注射顯影劑時較常與肝臟呈現相同亮度。最佳化雙相電腦斷層顯示肝臟局部結節增生的特徵，可以給予正確有效的診斷，熟悉這些影像表現可避免不必要的影像檢查、病理切片、開刀。

關鍵詞：電腦斷層；局部結節增生；肝臟