Multidisciplinary Management of Focal Nodular Hyperplasia in Children: Experience With 10 Cases

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Focal nodular hyperplasia (FNH) represents a benign lesion that accounts for 2% of all pediatric hepatic tumors, which are themselves rare.1,2 The pathogenesis of the lesion is presumed to involve hyperplasia rather than a primary neoplastic process, with hepatocytes responding to a congenital vascular anomaly. Focal nodular hyperplasia appears radiographically as a lobulated mass with a central stellate scar. Histologically, a well-circumscribed lesion is seen, surrounded by a thin fibrous layer with a central scar and radiating septa containing bile ducts, blood vessels, and lymphocytes.3 Most lesions are noted as a painless mass or are found incidentally.4-5

Although nonoperative management with observation has been deemed appropriate in adults, a higher percentage of pediatric liver tumors are malignant, requiring diagnostic certainty to be of even higher importance.6 As a result, and because of symptoms from relatively smaller lesions than in adults, surgical resection of FNH is more common in children. In the present report, we review the diagnosis, management, and outcome for children at our institution with a pathologic diagnosis of FNH to provide additional data toward development of a coherent management strategy for this disease.

Methods

Following approval by the institutional review board of the Johns Hopkins Hospital, a review of the medical records of all patients with a pathologic diagnosis of FNH between 1984 and 2008 at Johns Hopkins Hospital was undertaken. Data were collected on age at diagnosis, sex, location and size of lesion, symptoms, associated diagnoses, radiographic findings, treatment options, and clinical outcomes.

Results

A total of 10 pediatric patients were identified between 1984 and 2008 as having a pathologic diagnosis of FNH by either biopsy sample (n = 5) or hepatic resection specimen (n = 5). Seven patients were female, and the mean age was 12.1 years (range, 23 months-19 years) (Table) at the time of diagnosis. Patient 7 presented with nonspecific abdominal or epigastric pain, 4 (patients 2, 3, 5, and 9) presented with painless right upper quadrant masses, 2 masses (patients 8 and 10) were detected incidentally during workup of abdominal or pelvic pain with a nonhepatic source, and 3 masses (patients 1, 4, and 6) were identified in screening for unrelated genetic or oncologic conditions. All 10 patients had prior exogenous estrogen exposure.

Four of the 5 patients who underwent biopsy were monitored conservatively without sequelae after a mean follow-up time of 20 months (range, 3-53 months). One patient who received an initial recommendation for observation de-
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Discussion

There are no standardized treatment guidelines for the treatment of FNH in children. Thus, we undertook a retrospective study of children with FNH at our institution to gather further evidence to support development of a cohesive management strategy. Our review supports observational management of small asymptomatic FNH lesions, with surgical resection reserved for both symptomatic and large asymptomatic lesions amenable to resection.

The demographics of our cohort and the manners of presentation are similar to those of previous work by Reymond et al4 and Yang et al7, although our patients less frequently experienced right upper quadrant pain (20% vs 55% and 61.5%). Selection of our observational group was based on size of the lesion (mean 1.9 cm) and symptoms. None of these patients experienced growth, rupture, bleeding, or malignant degeneration of their observed lesions. We strongly suspect a natural history of negligible tumor growth and possibly regression of FNH lesions of the liver, which suggest the beneficial nature of conservative management. Diagnosis of FNH mainly relies on imaging examinations: ultrasonography, computed tomography, and/or magnetic resonance imaging. Magnetic resonance imaging is probably the best noninvasive imaging modality for FNH, with a specificity of 98% and a sensitivity of 70%. Specific characteristics include uniform isointensity or hypointensity on T1-weighted images, mild hyperintensity with a central scar on T2-weighted imaging, and delayed arterial enhancement. Differentiation of FNH from fibrolamellar hepatocellular carcinoma (hypointense central scar on T2-weighted images) can be based on radiographic characteristics with high accuracy.9 Kamel et al,10 using 16-multi-detector computed tomography and 3-dimensional computed tomographic angiography, reported that imaging alone can be used to accurately diagnose FNH, saving the patient potential risks of biopsy and surgery. Yang et al7 however, found only 6 cases (46.2%) that were correctly diagnosed as FNH preoperatively on the basis of imaging and fine-needle aspiration biopsy. In their review, Nguyen et al3 reported a series of 51 women with preoperative assessment of benign liver disease; of those patients, 18 had a diagnosis of FNH. Of patients in the series, 36 received diagnoses postoperatively of FNH; 12 patients, of hepatic adenoma; and 3, of hepatocellular carcinoma. In our series, 3 of the 10 patients had an unclear image-only assessment. Of the remaining 7, only 2 received correct preoperative diagnoses based on imaging and fine-needle aspiration biopsy. The other lesions preoperatively identified were hepatoablastoma (1 lesion), metastatic Langerhans sarcoma (1), hepatic adenoma (2), and hepatic mass (1). This underscores the necessity of open biopsy to confirm a diagnosis when ambiguity exists in the imaging of fine-needle pathologic data surrounding hepatic lesions. Furthermore, although prior chemotherapy may increase risk for developing FNH,11-15 we are always careful to exclude metastatic or recurrent disease before recommending surveillance alone.

Patients with symptomatic large, unresectable FNH lesions pose a unique problem. Embolization and vascular occlusion studies16-18 have shown promise in the treatment of difficult lesions. These approaches may shrink lesions to manageable size. However, this approach must be considered carefully, given the potential morbidity and the high rate of complications, including liver failure, occurring in patients who have undergone embolization.

Table. Clinical Characteristics, Treatment, and Outcomes of 10 Pediatric Patients With Focal Nodular Hyperplasia

<table>
<thead>
<tr>
<th>Patient No./Sex/Age</th>
<th>Presenting Symptoms/Initial Diagnosis</th>
<th>Size (Location)</th>
<th>Radiologic Test</th>
<th>Treatment</th>
<th>Outcome (Follow-up, mo)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/M/23 mo</td>
<td>None/Langerhans sarcoma screening</td>
<td>0.8 cm</td>
<td>CT</td>
<td>Biopsy (OSH)</td>
<td>AS/NCIS (16)</td>
</tr>
<tr>
<td>2/M/3 y</td>
<td>Painless right upper quadrant mass/hamartoma</td>
<td>5 x 3.5 x 5 cm</td>
<td>CT/MRI</td>
<td>Resection of medial segment</td>
<td>AS (36)</td>
</tr>
<tr>
<td>3/F/5 y</td>
<td>Painless right upper quadrant mass/hepatoblastoma</td>
<td>7 x 5 x 4 cm</td>
<td>CT</td>
<td>Trisegmentectomy</td>
<td>AS (36)</td>
</tr>
<tr>
<td>4/F/10 y</td>
<td>Neuroblastoma screening/hepatic adenomatosis</td>
<td>3 cm</td>
<td>MRI</td>
<td>Biopsy (OSH)</td>
<td>AS/NCIS (6)</td>
</tr>
<tr>
<td>5/F/13 y</td>
<td>Painless right upper quadrant mass/focal nodular hyperplasia</td>
<td>13 x 7 x 12 cm</td>
<td>CT/MRI</td>
<td>Biopsy and embolization, then left heptectomy</td>
<td>AS (54)</td>
</tr>
<tr>
<td>6/F/16 y</td>
<td>Ataxia-telangiectasia screening/unknown</td>
<td>Unknown</td>
<td>Unknown</td>
<td>Resection of left lobe (OSH)</td>
<td>Unknown</td>
</tr>
<tr>
<td>7/F/17 y</td>
<td>Nonspecific abdominal pain/unclear</td>
<td>7 x 6 x 5 cm</td>
<td>CT/MRI</td>
<td>Biopsy (OSH)</td>
<td>AS/NCIS (11)</td>
</tr>
<tr>
<td>8/M/18 y</td>
<td>Heart failure-related liver dysfunction/unclear</td>
<td>Unknown</td>
<td>CT</td>
<td>Biopsy (OSH)</td>
<td>AS/NCIS (53)</td>
</tr>
<tr>
<td>9/F/18 y</td>
<td>Nonspecific chest pain/focal nodular hyperplasia</td>
<td>7 x 5.5 x 4 cm</td>
<td>CT</td>
<td>Resection of caudate lobe</td>
<td>AS (6)</td>
</tr>
<tr>
<td>10/F/19 y</td>
<td>Right lower pain from ovarian cyst, incidental finding/adenoma</td>
<td>2.7 x 2.2 cm</td>
<td>CT/MRI</td>
<td>Resection of segment 7 and ablation of segment 4</td>
<td>AS/NCIS (23)</td>
</tr>
</tbody>
</table>

Abbreviations: AS, asymptomatic; CT, computed tomography; MRI, magnetic resonance imaging; NCIS, no change in size; OSH, outside hospital.
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In summary, the present study supports a management paradigm of conservative observational management of small asymptomatic FNH lesions, with surgical extirpation reserved for symptomatic and possibly large asymptomatic lesions amenable to resection. Embolization and vascular occlusion are modalities new to the field but offer a less morbid outcome and possible advantage in dealing with unresectable or large (symptomatic and asymptomatic) lesions. It is unclear at this time whether embolization confers any additional benefit to surgical ablation or even to observational management of small asymptomatic lesions; this approach requires additional study.

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REFERENCES