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 steatotic 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 elevated serum markers of liver disease, with normal levels of alkaline phosphatase and γ-glutamyl transferase. Four patients presented with symptoms of alcoholic hepatitis, with normal levels of alkaline phosphatase and γ-glutamyl transferase. All patients received a pathologic diagnosis of FNH.
resonance imaging is probably the best noninvasive imaging modality for FNH, with a specificity of 98% and a sensitivity of 79%. 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 al,7 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 hepato-blastoma (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

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 × 3.5 × 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 × 5 × 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 × 7 × 12 cm</td>
<td>CT/MRI</td>
<td>Biopsy and embolization, then left hepatectomy</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 × 6 × 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 × 5.5 × 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 × 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.
a size more amenable to resection or ablate them such that no further therapy is needed. These therapies also could be used for small lesions that are difficult to resect because of their central location. There is efficacy of embolization with diminution in the size of the lesion, and in some cases total ablation is possible. Radiofrequency ablation may be another modality to use in patients with small yet anatomically difficult lesions, as was demonstrated in one of our patients who underwent resection combined with radiofrequency ablation for a satellite lesion (patient 10). The efficacy of radiofrequency ablation alone for small asymptomatic lesions has not been studied.

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