Hepatic focal nodular hyperplasia in a five-year-old healthy boy: A case report and literature review

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ABSTRACT

Introduction: Focal nodular hyperplasia is unusually seen in a pediatric age group, with few reported cases in the literature. We report the case of a 5-year-old boy not known to have medical illnesses, who was found to have a liver mass, underwent right trisectionectomy. The purpose of this report is to familiarize the healthcare community with similar events, review the literature, and discuss recommendations for future similar cases.

Case Report: A case of focal nodular hyperplasia (FNH) in a 5-year-old healthy boy who was found to have a huge liver lesion on ultrasound imaging due to a vague abdominal pain and distension. The patient underwent surgical excision of the mass due to abdominal pain, distension, and atypical features of FNH in radiological examinations. Histopathological analysis revealed a focal nodular hyperplasia.

Conclusion: Focal nodular hyperplasia considered a benign lesion that has no malignant transformation. The presenting symptoms are variable, usually asymptomatic. Laboratory tests have of little significance. Imaging modalities mainly ultrasound scan initially then magnetic resonance imaging (MRI) are useful to obtain more accurate characteristic features of the lesion. Uncertain diagnostic lesion needs to be biopsied and examined under microscopy. Confirming the diagnosis will follow an acceptable conservative management approach. Surgical resection is the preferred method in uncertain, questionable, or atypical features observed in radiological imaging.

Keywords: Children, Focal nodular hyperplasia (FNH), Hepatic tumors

INTRODUCTION

Focal nodular hyperplasia (FNH) is a non-malignant hepatic tumor that is not of a vascular origin. It is seen in both sexes and throughout the age spectrum, although it is found predominantly in women (in a ratio of 8 or 9:1) between the ages of 20 and 50 years [1]. It comprises up to 2% of liver tumors in children. In large retrospective studies of patients referred for an ultrasound and multidetector computed tomography, the prevalence of FNH was 0.2% and 1.6%, respectively [2, 3]. Focal nodular hyperplasia has various labels: solitary hyperplastic nodule, hepatic hamartoma, focal cirrhosis, hamartomatous cholangihepatoma, and hepatic pseudotumor. The majority of reports have found...
that symptoms or signs directly attributable to FNH are infrequent. The diagnosis of FNH is usually made by demonstrating its characteristic features on imaging tests and excluding other lesions. The latter can typically be accomplished by assessing the context in which FNH is detected and by obtaining specific radiologic and laboratory testing. The natural history of FNH is a stable mass and lacks of complications.

CASE REPORT

A 5-year-old boy, previously well, presented to the emergency department with a history of mild abdominal pain and distention mainly over the right upper quadrant five days prior to his visit. There was a mild right upper quadrant abdominal pain, dull in nature, not radiating, no triggering or relieving factors, not associated with vomiting or change in bowel habit. He had a good appetite and did not lose weight, no associated fever, night sweating, jaundice, or rash. No urine changes in color or frequency, no recent blood transfusion or travel. His mother gave a history of acute gastroenteritis four months prior to his presentation with unexplained elevated aspartate transaminase at that time. He underwent tonsillectomy at the age of four. Parents are second cousins. He has two sisters and one brother, all healthy and well with no history of liver diseases in the family. In the beginning, his parents took him to a general pediatric clinic where an ultrasound abdomen was done and showed a solid hepatic mass in the liver, the family was advised to go to a tertiary hospital for further evaluation. Physical examination revealed a healthy boy, not pale or jaundiced. Abdominal examination: asymmetric abdomen, slightly distended over the right side, no visible dilated veins. Up on palpation: Soft and lax, no area of tenderness. Liver was palpable 4.0 cm below the costal margin, not tender, firm to touch with a smooth surface. There were no other palpable masses, and no ascites. Other systemic exams were unremarkable. The patient was admitted in our pediatric hospital and reviewed by a hepatologist, oncologist, and hepatobiliary surgeons. The following investigations were done: Complete blood count and renal profile were normal, viral polymerase chain reaction screening for cytomegalovirus, Epstein–Barr virus, and serology for hepatitis B surface were negative. Hepatic profile and tumor marker results are shown (Tables 1 and 2).

Then abdominal ultrasound (US), computed tomography (CT)-chest, abdomen, pelvis (CAP), and magnetic resonance imaging (MRI) were done (Figures 1–3). They concluded that there was a huge solid vascular mass where neoplasia cannot be ruled out in radiological examination. Two liver biopsies were requested, the first was insufficient, the second biopsy revealed a picture of chronic cholangiopathy with bridging fibrosis and early cirrhosis, there was no malignancy. As a result of these, the surgical option was carried out because of abdominal pain and discomfort. Extended right hemihepatectomy was done, a gross appearance of the mass is shown (Figure 4).

Under microscopic examination, the overall pathology was in keeping with the features of focal nodular hyperplasia induced by abnormal vascular malformation (Figures 5A–C and 6A–C).

Post-operative period was uneventful, he was well and discharged on 5th day after surgery in a good condition. He was followed up in the clinic after two weeks, one month, two months, and six months.

Table 1: The hepatic profile results

| GGT  | Alanine transaminase | Alkaline phosphatase | Albumin | Direct bilirubin | Total bilirubin |
|------|----------------------|----------------------|---------|------------------|----------------|
| 298 U/L | 259 U/L then 365 U/L | 311 U/L | 47 g/L | 2.0 umol/L | 3.0 umol/L |

Table 2: The tumor markers results

| Serum ferritin | Serum urate | LDH | Alpha fetoprotein |
|---------------|-------------|-----|-------------------|
| 27 ng/mL | 269 umol/L | 233 U/L | 1.2 kIU/L |
three months, six months and a year, no pathology was noted by US scanning and normal vasculature (Figure 7).

Figure 3: Magnetic resonance imaging of the abdomen revealed a solid mass noted on segment IV extending to the anterior segment of the right hepatic lobe. It measured about 11.5 × 9.6 × 9.0 cm. The mass was slightly hypotense to isotense on T1 and hypointense on T2. Post-contrast, the mass took more enhancement than the liver in the arterial phase with multiple hypodense septa and enhanced nodule. On delay phases, there was a washout of the enhanced mass and also the nodule. More enhancements of the delayed phases of the septa. The impression was “Large mass of the liver likely malignant, fibrolamellar type of HCC or HCC on non-cirrhotic liver has to be considered”.

Figure 4: Gross appearance of the mass. Specimen weighing 640 grams and measuring 140×110×90 mm.

Figure 5: (A) Low power showing the degree of fibrosis separating the benign liver tissue (H&E, ×2). (B) Masson trichome is illustrating the degree of fibrosis (MT, ×2). (C) This photo is illustrating the abundance of thick walled vessels with intimal thickening and replication of elastic lamina (elastic stain ×10).

Figure 6: (A) The periportal hepatocyte showed prominent cytoplasmic ballooning (H&E, ×20). (B) The hepatocyte with increased copper associated protein (copper ×20). (C) Focal florid ductular reaction is noted (H&E, ×20).

Figure 7: Follow-up ultrasound scanning, with no recurrence detected along with normal hepatic parenchyma.

DISCUSSION

Focal nodular hyperplasia is most often solitary (80–95%), and usually less than 5 cm in diameter. Only 3% are larger than 10 cm, although FNH as large as 19 cm has been reported [4]. It has a sharp margin with no capsule and may be pedunculated. The characteristic finding is the presence of a central stellate scar containing an inappropriately large artery with multiple branches radiating through the fibrous septa to the periphery. These branches divide the mass into multiple small nodules or cords of normal appearing hepatocytes. The scar-like tissues within FNH nodules are composed of abnormally large portal tracts including large feeding arteries, portal veins, and bile ducts [5]. It is now generally accepted to be a hyperplastic (regenerative) response to hyper perfusion by the characteristic anomalous arteries found in the center of these nodules.
The natural course of FNH was described in one case with hepatic capsular retraction following regression of the mass. Department of radiology, Antalya training and research hospital-Turkey, published an article in 2017 which was described about an 11-year-old child who had a giant hepatic FNH with follow-up period of 12 years using the US, CT, and liver enzymes after they established the diagnosis by a pathological examination, they did not use MRI because it was 0.35-T open shield system and was not suitable for abdominal imaging. In reviewing the literature, the natural course of FNH is variable. Apoptosis is a possible explanation for regression as they found that feeding artery is clearly visible on CT 2013 but not in the CT 2015, therefore they proposed that regression is due to ischemia caused by compression between the enlarging lesion and normal hepatic parenchyma which trigger the apoptosis. They found a correlation between the size of the mass and Gamma-glutamyltransferase (GGT) level, with a conclusion to go for surgery once the size and GGT level is decreased in both [6].

A Japanese girl found to have hypergalactosemia during newborn screening when she was four months old. The abdominal US and pre-rectal portal scintigraphy showed intrahepatic portosystemic shunt (PSS) of the right lobe as a cause of the hypergalactosemia, then she had elevated hepatic enzymes and small hypoechogenic hepatic lesions were discovered upon US images at age 12 months. Computed tomography and MRI showed hypervascular mass with spoke wheel arterial flow and central stellate scar, typical imaging feature of FNH. Osaka city university graduate school of medicine, Japan published this article and concluded that congenital intrahepatic PSS should be evaluated on abdominal contrast enhanced US and observed over time because of its potential to develop into hepatic FNH [7].

A review of the medical records of children diagnosed as having FNH between 1999 and 2013 at West China Hospital of Sichuan University was undertaken and 79 patients were identified, 68 patients without a history of malignancy and 11 patients with a history of malignancy. Major symptoms are summarized in Chart 2 and the imaging findings of FNH between the two groups are demonstrated (Table 3) [8].

| Imaging modality | Imaging features | Without malignancy | With malignancy | Total |
|------------------|------------------|--------------------|----------------|-------|
| **US**           |                  |                    |                |       |
| Well-circumscribed mass | n=61             | 38 (62.3%)         | 6 (54.5%)      | 44 (61.1%) |
| Homogeneous mass | 24 (39.3%)       | 5 (45.5%)          | 29 (40.3%)     |
| Central scar    | 25 (41.0%)       | 2 (18.2%)          | 27 (37.5%)     |
| **CT**           |                  |                    |                |       |
| Non-contrast-enhanced examination: hypodense | n=42             | 17 (40.5%)         | 2 (40.0%)      | 19 (40.4%) |
| Non-contrast-enhanced examination: isodense | 25 (59.5%)       | 3 (60.0%)          | 28 (59.6%)     |
| Arterial phase: enhances homogeneously (hyperdense) | 26 (61.9%)       | 3 (60.0%)          | 29 (61.7%)     |
| Central scar    | 24 (57.1%)       | 2 (40.0%)          | 26 (55.3%)     |
| **MRI**          |                  |                    |                |       |
| T1-W imaging: hypointense | n=39             | 14 (35.9%)         | 2 (25.0%)      | 16 (34.0%) |
| T1-W imaging: isointense | 25 (64.1%)       | 6 (75.0%)          | 31 (66.0%)     |
| T2-W imaging: isointense | 9 (23.1%)        | 3 (37.5%)          | 12 (25.3%)     |
| T2-W imaging: hyperintense | 30 (76.9%)       | 5 (62.5%)          | 35 (74.5%)     |
| Enhance with contrast | 31 (79.5%)       | 6 (75.0%)          | 37 (78.7%)     |
| Central scar    | 21 (53.8%)       | 1 (12.5%)          | 22 (46.8%)     |
A retrospectively examined diagnostic workup, treatment, and outcome of 18 patients aged 1–15 years, with FNH, was observed in the pediatric surgery department at the University of Padova-Italy, between 1988 and 2008. Clinical presentation was 27.8% vague abdominal pain and 72% were asymptomatic. They interestingly observe a high incidence of FNH after a malignancy 33%. Ultrasound, CT, MRI imaging accurately described the lesion, in the contrast opportunity of performing a biopsy was decided in most patients. In their study, currently recommended therapy for FNH is conservative monitoring and follow-up, but other approaches are acceptable. No recurrence was observed after complete surgical resection of the mass in two patients. Previously treated patients for cancer have been found to be unpredictably prone for FNH with higher association described following neuroblastoma or after hepatotoxic drugs related to veno-occlusive disease. In this study, they found a correlation between FNH and cytotoxic regimens together with bone marrow transplantation, and it involves multiple sites in the liver [9].

A unique pedunculated FNH was found in a healthy toddler who underwent surgical excision of liver mass due to a concern of atypical hepatoblastoma or highly differentiated hepatocellular carcinoma, atypical radiological feature and child age, even though MRI showed spoke wheel which retrospectively represented the central scar but pediatric liver tumors are typically not pedunculated, Texas A&M Health Science college of medicine concluded to routinely using hepatobiliary phase imaging with gadoxetate disodium MRI scan for all pediatric liver masses as it causes the lesion to appear hyperintense relative to the surrounding hepatic parenchyma on delayed hepatobiliary phase imaging and it is partially excreted through the biliary system which is particularly useful and sufficient evidence to diagnose FNH [10].

An extremely rare huge FNH in a 6-year-old boy was published by the first affiliated hospital of Nanjing Medical University-China. Two years ago, the child had this mass, CT imaging follow-up revealed enlargement of the mass from 6.5×5.4 to 10.5×9.9 cm in the right hepatic lobe. A biopsy was not conclusive to establish the diagnosis. Due to uncertain diagnosis by histology and previously reported FNH lesions associated with hepatocellular carcinoma, they found liver biopsy or resection might be necessary to establish the diagnosis effectively. Thus, they proceed for surgical resection after indeterminate biopsy and gradually enlarged liver mass with a follow-up period of two years [11].

A retrospective review of children less than 18 years of age diagnosed with FNH at a single institution was conducted from 2000 to 2013. Total of 33 children “11 months–18 years”, 21 cases were diagnosed by imaging and had no further intervention. Twelve patients had a definitive tissue diagnosis of FNH which was focus of their study. Ten patients had biopsy and two required surgical resections. 10 years old girl found to have tumor that was consistent with fibrolamellar hepatocellular carcinoma (HCC) by MRI scan in which she required a segmentectomy. A 17-year-old found to have a liver mass incidentally during his pre-kidney transplant work-up, decision was made to excise the liver mass. Other patients had either stable or reduction in the size of the mass. One patient had complete regression of the mass. In one patient they use hepatocyte specific gadolinium MR contrast, gadoxetate disodium, facilitated the diagnosis of FNH in delayed sequence acquired at 20 minutes. US-guided needle biopsy was the preferred method of biopsy, reserving laparoscopic surgical biopsy for those with insufficient tissue. Follow-up is advised in order to monitor the size of the mass. They concluded that, biopsy is not recommended in young children. However, patients without underlying conditions and no evidence of malignancy, need highly specialized center in order to develop trial to observe these patients without biopsy [12].

CONCLUSION

Pediatric focal nodular hyperplasia, usually adequately diagnosed with magnetic resonance imaging and or needle biopsy of the lesion. Surgical team members, as well as the radiologist, need to carefully read and identify important radiological features of focal nodular hyperplasia. The hepatobiliary surgeon is a key individual in the team caring for a patient with liver mass. Based on literature and previous reports, the recommendation is to manage them mainly conservatively, or surgically as indicated with either atypical radiological features or inadequate histopathological investigation. Surgical treatment is the best choice for those with symptomatic, uncertain, having atypical features on imaging, and insufficient biopsy sampling. When congenital intrahepatic portosystemic shunt (PSS) is detected, follow-up with ultrasound imaging is advisable.

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Author Contributions

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Helayel Almodhaiberi – Conception of the work, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Authors declare no conflict of interest.

Data Availability

All relevant data are within the paper and its Supporting Information files.

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