Gastroenterology and Hepatology From Bed to Bench.

CASE REPORT

Plexiform neurofibromatosis of the liver: an extremely rare case

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ABSTRACT

Herein, we report an extremely rare case of histopathologically proven neurofibromatosis of the liver. A 15-year-old male, a known case of type I neurofibromatosis (NF1), referred to our hospital with a complaint of right upper quadrant pain. He had a café-au-lait spot and positive family history of NF1 in his mother. Laboratory data was within normal limits, and computed tomography (CT) revealed a large predominantly less attenuated infiltrative liver mass along the porta hepatis with extension to both lobes of the liver. Magnetic resonance imaging showed a large hypo-signal mass in T1-weighted images and hypersignal lesion in T2-sequences with faint enhancement, periportal distribution, and encasing of major branches of the portal vein without evidence of narrowing and invasion. A CT-guided biopsy was taken from both liver lobe lesions, and pathological diagnosis of the biopsy specimens confirmed plexiform neurofibromas of the liver. According to the extensive intrahepatic extension and periportal infiltration, the mass was unrespectable. Radiologists need to be familiar with the typical imaging features of the uncommon hepatic neoplasms. If imaging findings are not typical or diagnostic, a further biopsy should be performed again.

Keywords: Magnetic Resonance Imaging (MRI), Noncommon liver tumors, Neurofibromatosis, Plexiform neurofibroma

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Introduction

Neurofibromatosis type 1 (NF1) (also known as Von Recklinghausen Disease) is the most common phakomatosis, which is a multisystemic and autosomal dominant disorder. The NF1 gene is localized to chromosome 17; however, it can appear anywhere on the body, such as the head, neck, abdominopelvic cavity, and extremities (1, 2). NF1 is usually diagnosed by multiple cutaneous lesions, such as café-au-lait spots, axillary freckling, Lisch nodules, cutaneous neurofibroma, and optic glioma (1). The common gastrointestinal manifestation is a gastrointestinal stromal tumor (1). Among rare and uncommon manifestations is internal neurofibromatosis, which presents in the retroperitoneum, mesenteric cavity, and hepatic hilum as well as around the celiac trunk and within the liver parenchyma (3-6). Neurofibroma of the pancreas and retroperitoneum can present as a sporadic form, albeit rarely (7). Since the imaging features of the uncommon liver neurofibromatosis are less discussed in the literature, we present and review an extremely rare case of histologically proven plexiform neurofibroma involving liver parenchyma and porta hepatis.

Case Report

A 15-year-old Caucasian male, known case of NF1 was referred to our hospital for further assessment. He had a history of 5-year intermittent abdominal pain more prominent in the right upper quadrant. Upon physical examination, multiple cutaneous café-au-lait macules were observed all over the abdominal wall and over both hands. The patient had a positive family history of cutaneous NF1 in his biological mother. Upon admission, he complained of progression of right

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upper abdominal pain. He had a history of receiving many unsuccessful treatments in the past 6 months. Laboratory test results, including liver enzymes tests (SGOT and SGPT), alpha-FP level, and bilirubin, were within normal limits (Table 1).

Table 1. Laboratory findings of an investigated case.

Parameter	Value	Reference Range
Total Bilirubin	0.6 mg/dL	0.1 - 1.3
Direct Bilirubin	0.1 mg/dL	0 - 0.2
Indirect Bilirubin	0.4 mg/dL	0.1 - 0.7
SGOT	33IU/L	Normal Males:<45
SGPT	40 IU/L	Normal Males: <43
ALP	50 IU/L	55 -130

SGOT: serum glutamic-oxaloacetic transaminase
SGPT: serum glutamic pyruvic transaminase
ALP: alkaline phosphatase

Abdominal ultrasonography examination showed an isoechoic to hypoechoic mass in the porta hepatis throughout the mid-part of the liver with an extension to the right and left lobes of the liver and an approximately generalized mean diameter of 120×80×69 mm. Color Doppler evaluation showed the mass to be hypovascular. For further evaluation, the patient underwent abdominal computed tomography (CT) and, subsequently, abdominal magnetic resonance imaging (MRI) with contrast. The CT scan revealed an infiltrative and multilobulated low-attenuation non-enhancing mass involving both lobes of the liver with predominantly periportal distribution (Figure 1). The portal vein was normally enhanced and mildly narrowed and encased by the mass without obvious intraluminal thrombosis or obstruction. Calcification, necrosis, or hemorrhage within the mass was not observed. MRI showed that the mass was hypointense in T1-weighted images and hyperintense in T2-weighted sequences with periportal distribution (Figure 2). The mass encased the main, right, and left portal vein branches, resulting in a narrowing of the portal branch with no evidence of invasion or thrombosis. Faint enhancement of the tumor was seen after intravenous (IV) injection; however, central and peripheral necrosis was not evident. Sublet target signs within some lesions (central low T2 signal) and some parts of the mass were noted. In addition, a CT guided biopsy was taken from liver lesions, and multiple specimens were taken from the lesions of both liver lobes. According to the pathologic report, the entire specimen of the left lobe as well as V, VI, and VIII segments of the right lobe of the liver were involved, and periportal infiltration was proven. The final pathological examination revealed that the tumor was composed of spindle-shaped cells with a myxoid matrix (Figure 3A and B). These findings were consistent with the diagnosis of plexiform neurofibroma with no evidence of malignant transformation. Due to the extensive intrahepatic involvement and diffuse periportal infiltration, the tumor underwent unresectable conservative treatment along with close clinical follow-up and surveillance imaging.

Discussion

Neurofibroma may be observed anywhere on the body with different sizes and shapes; moreover, it is a major cause of morbidity in afflicted patients. Its common symptom is cutaneous neurofibroma (1); however, plexiform neurofibroma (PN) is a different type of neurofibroma which is usually congenital. The

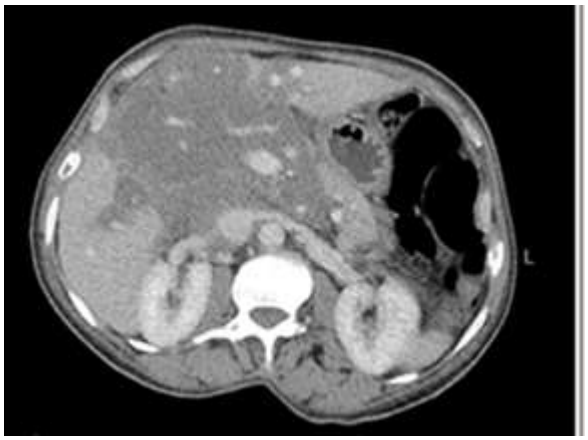

Figure 1. Contrast-enhanced computed tomography showing a low attenuation lesion involving both lobes of the liver in periportal distribution and extending into the hepatic hilum.

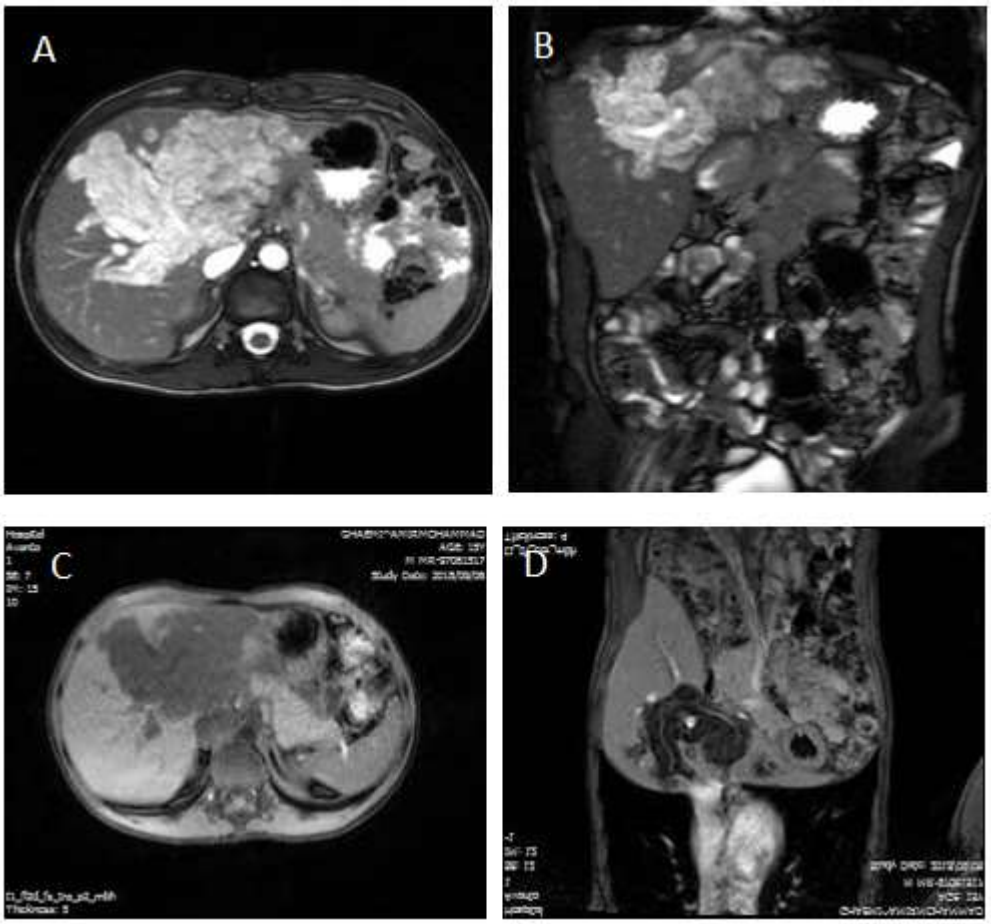

Figure 2. Magnetic resonance imaging of the plexiform neurofibromas involving the liver, A: T1-weighted sequences without contrast, axial view, B and C: axial and coronal views, T2-weighted sequences, D: Coronal T1-weighted images with contrast.

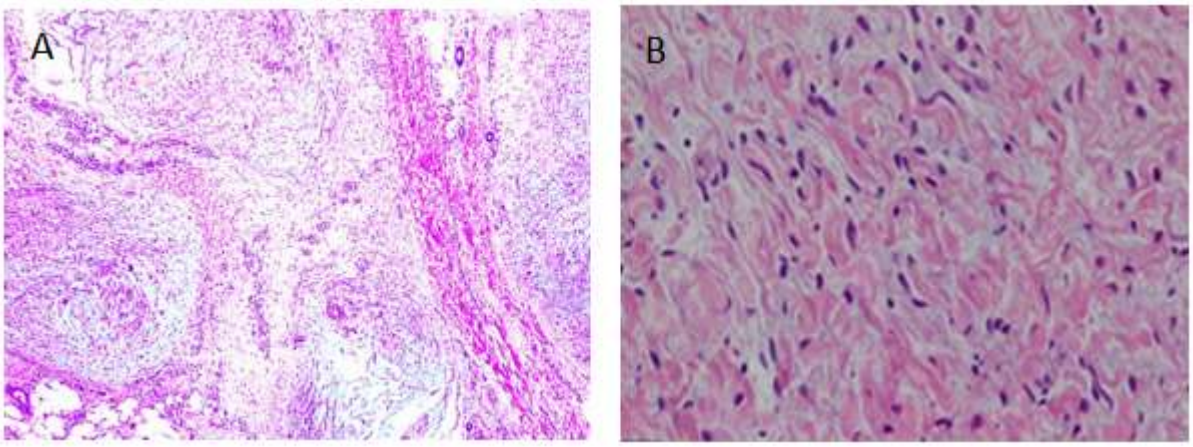

Figure 3. Spindle-shaped cells with entrapped bile ducts (hematoxylin-eosin stain, 100X); B: High-power view of spindle cells arranged against a myxoid background (400 X).

PN is a non-circumscribed, thick, and irregular tumor of the peripheral nerve sheath with benign nature (4). Moreover, superficial PN is often observed with overlying hyperpigmentation or hypertrichosis (1). According to the review of the literature and the results of a case report conducted by Fujisawa et al.,

intraperitoneal presentation of neurofibromatosis is rare and seen mostly in the pediatric group (8). Abdominal involvement is mostly seen in the abdominopelvic wall and retroperitoneum. One uncommon region of neurofibroma is retroperitoneum. Most cases of internal PN remain asymptomatic for many years and are often detected as an incidental finding in imaging investigation (1).

Although the sporadic case is very rare, Poon et al. reported a sporadic case of histopathologically proven neurofibroma in porta hepatis, which is an uncommon presentation (7). These are benign nerve sheath tumors, which tend to grow along the length of a nerve involving the fascicles and branches (9). It should be noted that neurofibromatosis is a benign tumor; however, it has a high potential for malignancy (10).

The MRI characteristic of PN is the same as organs and depends on content mass, such as collagen myxoid matrix or fat. PN of the liver is rare in the gastrointestinal tract, and the common presentation is periportal infiltrative mass; however, an uncommon pattern of tumor is a multilobulated mass in imaging.

Hoshimoto et al. reported a 24-year-old female with intermittent upper abdominal pain. Imaging showed a multilobulated mass in the porta hepatis and around the celiac trunk and common hepatic artery. After resection, histopathologic examination revealed neurofibroma without malignant transformation (3). The tumor grows along the intrahepatic nerve fibers and accompanies the hepatic ducts and vessels. Other similar studies have reported the periportal distribution of PN and the preservation of normal vessels using CT (4, 5).

Roduriguez et al. reported a case of diffuse periportal and intrahepatic plexiform neurofibroma as diffuse non-enhancing periportal lesion surrounding spaces named "periportal collar signs" (11). Generally, hepatic neurofibroma shows T1 and T2 hypointensity with an area of heterogeneity. Nodular appearance is observed in the T2 sequences in peripheral neurofibromatosis; however, to the best of our knowledge and according to other studies, it is not seen in the liver (12). In the same vein, Malagari et al. have reported 13 cases of liver neurofibromatosis during the last 10 years (12). They discussed the appearance of CT portography and angiography in the liver neurofibromatosis; moreover, Kumail Khandwala has reported 15 cases to date (5).

In CT portogram, the perivascular involvement is a common finding; however, they emphasized that post-contrast images showed no hypervascularity in hepatic neurofibromatosis.

Portal hypertension is not a common finding; however, Lee reported a known case of esophageal varices and echogenic conglomerated nodule in the porta hepatis encasing the hepatic artery, superior mesenteric artery, celiac trunk, and portal branch, resulting in narrowing and encasement of a portal vein leading to portal hypertension (13). MRI and CT scan generally reveal no enhancement (12). However, minimal enhancement is reported in a retrospective study conducted by Delgado et al. on a group of patients over the age of 12 years (12). They found five known cases of neurofibromatosis involving the liver and pancreas. They further emphasized that the hallmark of the liver lesion was periportal distribution, and the growth was mainly within the head of the pancreas. All patients were asymptomatic without the need for medical treatment or surgery; however, the tumor was stable in all cases over 3-8 years of follow-up. There are some differential diagnoses for low attenuation infiltrative mass in the liver, including mixed epithelial and mesenchymal tumors as well as lymphoma; however normal vascular distribution in neurofibromatosis could differentiate between these two entities (12, 14, 15).

Surgical resection of internal organ neurofibromas is a challenging problem because of the infiltration of surrounding tissue and nerves (16). There is also controversy about the resection of small neurofibromas, as recurrence and regrowth of the tumor are more probable (1).

In summary, PN of the liver is an extremely rare tumor observed mostly in patients with NF1, periportal distribution, and preservation of vascular distribution. The mass is infiltrative and hypoechoic in the ultrasound as well as on the MRI and CT scan. Moreover, the tumor shows low attenuation in abdominal CT, low signal intensity on T1-weighted images, and hyperintensity in T2-weighted and post-contrast images. Additionally, no or minimal enhancement, calcification, necrosis, and hemorrhage were observed in the biopsy to confirm the diagnosis.

Conclusion

Radiologists should be familiar with the typical and atypical imaging features of uncommon hepatic neoplasms. A further biopsy must be performed if imaging features are not typical.

Conflict of interests

The authors declare that they have no conflict of interest.

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