Plexiform neurofibroma in the hepatic hilum associated with neurofibromatosis type 1: a case report

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Abstract

We present an extremely rare case of plexiform neurofibroma involving the hepatic hilum. A 24-year old woman who had been diagnosed with neurofibromatosis type 1 was referred to our hospital for evaluation of an abdominal mass found on computed tomography and progressive aggravation of intermittent abdominal pain. Abdominal computed tomography revealed a multilobulated nonenhancing mass involving the celiac trunk and hepatic artery, that extended to the hepatic hilum through the hepatoduodenal ligament. Magnetic resonance imaging showed the lesion extending along the intrahepatic Glisson's sheath. Based on the imaging findings, the patient was diagnosed to have a neurofibroma, although sarcomatous differentiation could not be excluded. The tumor was resected, leaving behind the intrahepatic extension, with the aim of alleviating the abdominal pain and preventing obstructive jaundice. Histopathological examination revealed the diagnosis of plexiform neurofibroma. At present, three years after the surgery, the patient remains symptom-free, without any evidence of recurrence.

Introduction

Plexiform neurofibroma, which is considered pathognomonic of neurofibromatosis type 1 (NF-1), usually occurs in the neck, pelvis, and extremities. Plexiform neurofibroma in the hepatic hilum is an unusual manifestation of NF-1 and is extremely rare. We present the case of a 24-year old woman with NF-1 diagnosed to have plexiform neurofibroma involving the celiac trunk, the common hepatic artery, the hepatoduodenal ligament and the hepatic hilum that showed extension along the intrahepatic Glisson's sheath.

Case Report

A 24-year old woman who had been diagnosed with NF-1 during childhood was referred to Fujita Health University Hospital in September 2004 for evaluation of an upper abdominal mass found on abdominal computed tomography (CT) at another hospital and progressive aggravation of intermittent upper abdominal pain. There was no relevant family history. Physical examination revealed numerous café-au-lait spots and cutaneous tumors. In addition to the skin lesions, there was a history of surgical treatment for scoliosis. All laboratory test results obtained at admission were all within normal limits. Abdominal CT revealed a multilobulated low-attenuation nonenhancing mass involving the celiac trunk and the common hepatic artery, extending to the hepatic hilum through the hepatoduodenal ligament (Figure 1). Hepatic angiography showed a normal caliber of the hepatic artery without any irregularity, and portography as visualized through the superior mesenteric artery revealed a patent portal vein without encasement. On magnetic resonance imaging (MRI), the lesion was visualized as a hypointensity on T1-weighted images and as a hyperintensity on T2-weighted images, and was found to extend along the intrahepatic Glisson's sheath (Figure 2). On magnetic resonance cholangiopancreatography (MRCP), the common bile duct and the left hepatic duct were slightly depressed, without dilatation of the intrahepatic bile duct. Based on these imaging findings, the patient was diagnosed to have a neurofibroma, although sarcomatous differentiation could not be excluded.

Although MRI findings suggested that the

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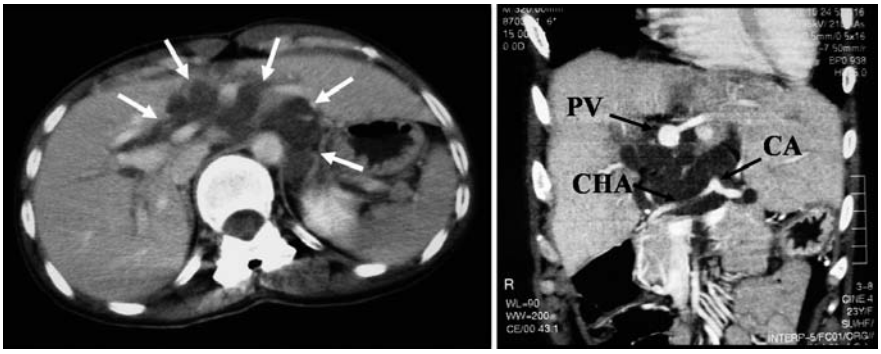

Figure 1. Contrast-enhanced computed tomography showing a low-attenuation lesion involving the celiac axis (CA), the common hepatic artery (CHA), and the portal vein (PV), and extending into the hepatic hilum (arrows).

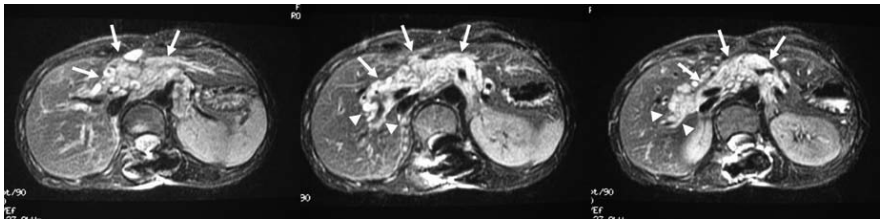

Figure 2. Abdominal MRI (T2-weighted image) showing a hyperintense tumor involving the hepatoduodenal ligament and the hepatic hilum (arrows), extending along the intrahepatic Glisson's sheath (arrow heads).

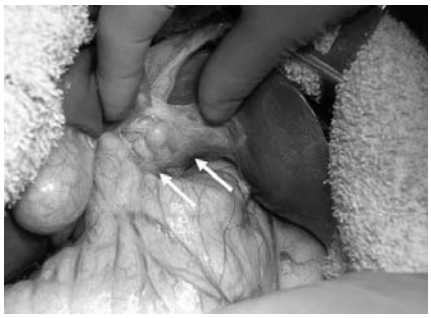

Figure 3. Laparotomy revealed a whitish firm tumor involving the hepatoduodenal ligament and the hepatic hilum (arrows).

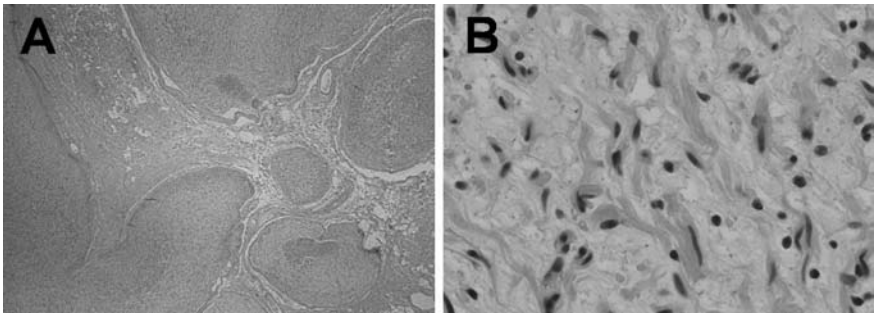

Figure 4. (A) Multiple nerve fascicles are expanded by proliferation of tumor cells embedded in a prominent myxoid matrix. (HE stain, x 40). (B) At high magnification, the tumor was chiefly composed of elongated spindle-shaped cells having wavy nuclei, with a myxoid matrix. (HE stain, x 400).

tumor was unresectable owing to its intrahepatic extension, the tumor was removed in February 2005, leaving behind the intrahepatic extension, with the aim of alleviating the abdominal pain and preventing obstructive jaundice. Laparotomy revealed a whitish firm tumor involving the celiac trunk, the common hepatic artery, and the hepatoduodenal ligament, extending through the hepatic hilum (Figure 3). Since skeletonization of the hepatoduodenal ligament was feasible, the tumor was resected piecemeal, without any need for combined resection of the vessels or ducts.

On examination of the cut surface, the tumor was whitish, firm, solid, and partially encapsulated. Pathological examination revealed expansion of the nerve fascicles, with a multilobulated appearance. The tumor was chiefly composed of elongated spindle-shaped cells having wavy nuclei, with a myxoid matrix (Figure 4A and B). Mucinous change in the stroma was prominent. These findings were consistent with the diagnosis of benign plexiform neurofibroma. No evidence of malignant transformation was seen.

The post-operative course was uneventful. At present, three years after the surgery, the patient remains symptom-free, and shows no evidence of recurrence.

Discussion

NF-1, also known as von Recklinghausen's disease, is a systemic, autosomal dominant neurocutaneous syndrome occurring at a prevalence of one case in 3,000 live births.[1] It is caused by mutations of the *NF1* gene, which is located on chromosome 17q11.2.[2] Although many cases are heritable, approximately 30-50% of cases arise from spontaneous mutations.[1] NF-1 is characterized by *café-au-lait* spots, cutaneous neurofibromas, bone malformations, Lisch nodules, and sometimes, malignant tumors.[1] The average life expectancy of patients with NF-1 is probably reduced by 10-15 years, and malignancy is the most common cause of death.[2] The most characteristic tumors in patients with NF-1 are neurofibromas which arise from cells of the nerve sheath and consist of a mixture of Schwann cells, fibroblasts, perineurial cells, and mast cells.[3] Plexiform neurofibroma is a benign nerve sheath tumor, which is virtually pathognomonic of NF-1. It consists of the same cell types as a cutaneous fibroma but has an expanded extracellular matrix, and its presence is one of the clinical criteria for the diagnosis of NF-1.[3] The incidence of plexiform neurofibroma in patients with NF-1 has been reported to be 15-30%.[4,5] It may be present superficially or be located internally, and consists of proliferation of cells in the nerve sheath extending across the length of a nerve, involving multiple fascicles and branches.[6] Although it tends to grow slowly, growth spurts are seen, particularly in early childhood and during puberty or pregnancy.[6] Plexiform neurofibromas are at an increased risk of developing into malignant peripheral nerve sheath tumors (MPNSTs). MPNSTs arise predominantly from pre-existing plexiform neurofibromas and metastasize widely and often presage a poor outcome.[3] The lifetime risk of MPNSTs in patients with NF-1 is estimated to be about 10%.[7]

On CT, plexiform neurofibromas are visualized as multilobulated low-attenuation masses, usually within a major nerve distribution.[8] On MRI, the tumors are seen as conglomerate hyperintense masses consisting of innumerable neurofibromas with central hypointense regions, known as the "target sign" on T2-weighted images.[8] However, malignant transformation of internal plexiform neurofibromas into MPNSTs is difficult to assess by imaging alone. Thus, the diagnosis of MPNSTs requires biopsy, but there is substantial potential for sampling error in large plexiform neurofibromas.[6] Although plexiform neurofibromas occur predominantly in the head or neck in NF-1 patients,[5] in approximately 40% of patients with NF-1, lesions are detected by abdominal or pelvic CT.[9] Internal plexiform lesions in the abdomen or pelvis are commonly located in the paraspinal space, sciatic nerve, or perirectal space.[9] Therefore, extension of a plexiform neurofibroma involving the retroperitoneum and hepatoduodenal ligament into the hepatic hilum is an unusual manifestation in cases of NF-1. A search of PubMed using the terms "liver", "hilum", "hilar", or "porta hepatis", and "neurofibroma" revealed only 9 cases of plexiform neurofibroma in the hepatic hilum reported to date in the English language literature.[10-17] All of the 10 cases, including the present case, showed retroperitoneal involvement or intrahepatic extension along the Glisson's sheath. Therefore, the imaging features of the present case are closely similar to those of the previously reported cases. Rodriguez *et al.* reported a case with diffuse intrahepatic periportal plexiform neurofibroma and described the non-enhancing low-attenuation lesions surrounding central and peripheral periportal spaces as the "periportal collar sign", which was initially described as a finding of rejection in liver transplantation.[18]

Internal plexiform neurofibromas can persist for many years without causing clinical problems and they usually remain undetected until incidental detection by an imaging study or following the development of clinical symptoms.[6] When patients have substantial neurological deficits or disfigurement, removal of plexiform neurofibromas poses challenging problems because of infiltration by the tumors of the surrounding tissues and nerves,[19] although the current treatment of first choice for plexiform neurofibromas remains surgery. Therefore, there is controversy regarding the optimal timing for surgical intervention. Some authors advocate early surgery to prevent the development of major cosmetic and functional impairment, whereas there is a counter argu-

ment that even small plexiform neurofibromas can rarely be removed entirely and regrowth after surgery may occur.[6] Although in the present case, based on the MRI findings, the tumor was deemed as difficult to remove in its entirety owing to its intrahepatic extension, removal of the tumor was nonetheless attempted in an attempt to alleviate the abdominal pain and prevent obstructive jaundice. To the best of our knowledge, this is the first reported case of plexiform neurofibroma in the hepatic hilum in which successful resection was carried out.

In conclusion, we have reported an unusual case of plexiform neurofibroma, unique in terms of its location at the hepatic hilum. Thus, the presence of this tumor at this uncommon location should also be borne in mind, especially in complaints of abdominal discomfort, and it is essential to periodically monitor patients with NF-1 for the development of this tumor because of the possibility of serious clinical presentations and malignant transformation.

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