Periportal neurofibromatosis with intrahepatic, retroperitoneal and pelvic involvement: a case report and literature review

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Abstract

Neurofibromatosis type 1 (NF1) is a benign peripheral nerve sheath tumor which primarily cause neurocutaneous manifestations. We presented a rare case of periportal neurofibromatosis with intrahepatic, retroperitoneal and pelvic involvement. The patient underwent US-guided biopsy and a diagnosis of intrahepatic neurofibromatosis was made.

Keywords: Case report, ultrasonography, radiology, neurofibromatosis, Glisson's sheath

Key Clinical Message

Periportal infiltration with well-perfused vessels throughout the hypovascular mass may be characteristic which could be detected by imaging techniques. Biopsy is indispensable and the diagnosis should depend on histopathology results.

Introduction

Neurofibromatosis type 1 (NF1) is a benign peripheral nerve sheath tumor first described by the German pathologist von Recklinghausen in 1882[1,2]. Then further research concluded that inheritance of NF1 was autosomal dominant[3,4]. It is a proliferation of all parts of peripheral nervous system and as a result, it can cause the pain, functional damage, and considerable mortality[5-13]. NFs rarely located in abdomen and the involvement of liver is extremely unusual. We report a rare case of an 18-year-old male patient with a randomly detected histologically proven neurofibroma of liver with wide infiltrations. The patient underwent ultrasound(US), magnetic resonance imaging(MRI), and a positron emission tomography-computed tomography(PET-CT) with maximum standardized uptake values(SUVmax) accessed. The

emphasis of this report is on the image features and the differential diagnosis of NF occurred in unusual locations, along with related literature reviews.

Case presentation

An 18-year-old male patient, who previously underwent the abdominal ultrasonography and computed tomography(CT) for physical examination, was diagnosed as focal liver lesion which was considered as malignancy. For further evaluation and treatment, he was referred to our hospital.

The patient had no obvious clinical manifestations such as jaundice or hepatosplenomegaly, while the extremely dark color of his complexion was noticeable. There was no relevant history of any particular or familial disease. Laboratory findings consisted of normal blood tests and liver function. Serum carbohydrate antigen 19-9, carcinoembryonic antigen and alpha-fetoprotein levels showed negative results. The hepatitis B surface antigen was positive while hepatitis C antibody was negative.

The conventional gray-scale ultrasonography identified heterogeneous hypo-echoic lesion extending along the portal vein, which was measured approximately 14×6.5cm (Fig.1a). Mild dilatation of the portal vein was seen within the lesion, with local narrowing compressed by the encasing mass. In color Doppler flow imaging, the portal vein showed unobstructed (Fig.1b). After the injection of a dose of 1.2ml SonoVue as contrast agent, the portal vein and hepatic artery presented well-perfused and locally compressed. The perivascular lesion started to enhance at approximately 20s and remained heterogeneous hypo-enhanced in comparison with adjacent liver parenchyma (Fig.1c,d).

Upper-abdomen magnetic resonance imaging (MRI) revealed a widely infiltrative mass-like

lesion extending along intrahepatic ducts, with heterogeneous low signal intensity on T1-weighted images and high signal intensity on T2-weighted images. Areas of low signal intensity surrounded by a halo of high signal intensity could be observed clearly on fat-suppressed T2-weighted images, along with curvilinear structures of low T2 signal (Fig.2a,b). After the injection of Gd-EOB-DTPA, the portal vein presented serpentine and locally compressed by surrounding lesion but integrally going through the lesion, which showed hypo-enhancement (Fig.2c). During the hepatobiliary phase, the whole lesion presented low signal. Additionally, an unobstructed intrahepatic bile duct could be detected (Fig.2d).

Positron emission tomography-computed tomography (PET-CT) showed a huge intra-abdominal, low-attenuation mass with slight-elevated FDG uptake (SUVmax 2.2). The mass was encasing the intrahepatic vessels (Fig.3a,b), infiltrating via the Glisson's sheath into the liver and extending inferiorly into the retroperitoneum and abdominopelvic cavity. The adjacent vascular system and relevant abdominopelvic organs could not be separated clearly from the mass tissue. In addition, multiple cutaneous nodules could be observed around the buttock and upper thighs (Fig.3c,d). The FDG-uptake of both internal and cutaneous nodules were minimal.

US-guided percutaneous liver biopsy was performed after the patient's consent. The pathological section of the biopsy sample showed integrated hepatic vessels surrounded by loosely arranged spindle-shaped cells which are adjacent to normal hepatocytes (Fig.4a,b). The histological features favored neurogenic tumors. The immunohistochemical results also presented positive expression for S100 (Fig.4c) and Sox10 (Fig.4d) , along with 1% markup rate of Ki67 protein. No signs of malignant elements were seen in the biopsy sample. Due to the tumor's wide extension and unclear boundaries with adjacent organs, surgical treatment was not offered.

A follow-up after 4 months was operated and there was no much change in MRI images.

Discussion

Neurofibromatosis type 1 (NF1) is a benign peripheral nerve sheath tumor, which is autosomal dominant and multisystemic. NF1 primarily cause neurocutaneous manifestations, most of which include cafe-au-lait spots, skin fold freckles, neurofibroma, optic nerve gliomas and lisch nodules on iris[1,2]. NFs rarely located in abdomen and the involvement of liver is extremely unusual. It is a proliferation of all parts of peripheral nervous system and it has a tendency to transform into malignancy, which is referred to as malignant peripheral nerve sheath tumors(MPNSTs)[3,4]. The incidence for NF developing into malignancy is not high but once MPNST formed, it would metastasize widely and often causes early death[3,4].

In this case, abdominal US, MRI and PET-CT presented conglomerated nodules encasing the intrahepatic tracts and integrated intrahepatic vessels diffusion in the lesion. The tumors' growth via the Glisson's sheath was consistent with NF's proliferative characteristics, one of which was tend to grow along the length of nerve fibers accompanying vessels and ducts[5-7]. Compared with several previous reports of the hepatic neurogenic tumors, which were biopsy-proven as plexiform neurofibromatosis(PNF) by surgery, those cases shared many common characteristics with our case[5,6,8-13]. According to the report of a mesenteric plexiform neurofibroma analyzed by Matsuki et al., the MRI characteristically presented multiple ring-like structures in T2-weighted images, which performed in our case as central flow-void in liver surrounded by bright structures. We persumed it as the cross section view of perivascular lesion[9]. Meanwhile, curvilinear hypo-intensity structures on T2 images, which were probably caused by bundles of lemnocytes and collagen fibres, could not be ignored. Those were also described as central target sign and

whorled appearances in Delgado et al.'s research of 5 hepatic and pancreatic PNF patients[8]. The radiology performances mentioned above were highly specific and characteristic. However, the pathological samples of our case were obtained by US-guided percutaneous needle biopsy, of which the visible pathohistological structure is limited. There was no signs of fascicles spindle-shaped cells, only loosely arranged cells could be observed. Surgical treatment was not offered because of the wide extension and unclear boundaries with adjacent organs. In addition, the patient showed no obvious symptom and the pathohistological results revealed no malignant elements. The diagnosis of PNF still cannot be excluded.

The contrast-enhanced US and MRI images both showed slight enhancement in either the arterial or the portal phase, which demonstrated hypovascularity of the lesion. In spite of the unvaried 4-month follow-up MRI images, the NFs still have a chance to develop into MPNSTs[1,3,4]. According to previous researches, a larger size(>5cm) with obscure margins, the presence of calcification, hypervascular and inhomogenous areas in the lesion may increase the suspicion of malignancy[11,15]. Azizi's research concluded that the value of SUVmax over 3.15 may increase the possibility of malignant transformation, but assessed by SUVmax alone is not reliable for its greatly overlapped[10]. In our case, the SUVmax of the periportal lesion is 2.2 and the SUVmax of internal and cutaneous nodules are within the normal limit.

Although neither destruction of adjacent organs nor embolus in vessels could be observed, as the tumor proliferated along all parts of peripheral nervous system, symptoms caused by the space-occupying compression should be paid real attention to. On account of the young age together with no specific related clinical and familial history, size of the mass had no obvious change and the patient had been asymptomatic until the second visit. However, it was underlined

that NFs involving the hepatic hilum could result in portal hypertension and related tests are highly recommended[13]. Although the bile duct presented unobstructed on the hepatobiliarial phase of CE-MRI, a risk of obstructive jaundice should not be neglected. Additionally, MRI showed obscure boundries between the mass and gallbladder, pancrea and colonic wall.

Initially, this patient was considered as lymphomas for the radiological features, while the hypovascularity and low uptake of FDP are inconformity[16]. Therefore, histological biopsy is still indispensable for exclusion. We also noticed that, although this patient had no signs of café-au-lait macules, a generalized hyperpigmentation on his skin and multiple cutaneous nodules around the buttock and upper thighs observed by CT are also highly suggestive of NF1[1]. Due to the charateristics of the proliferaion and low-attenuation, several neurogenic and periportal tumors should also be considered, such as schwannomas and angiosarcomas[11,14].

Conclusion

We presented an unusual case of periportal neurofibromatosis with intrahepatic, retroperitoneal and pelvic involvement. Periportal infiltration with well-perfused vessels throughout the hypovascular mass may be characteristic which could be detected by imaging techniques. However, considering the rareness of intrahepatic PNF, imaging alone is not sufficient for differential diagnosis, particularly in patients with no signs of NF1. Biopsy is indispensable and the diagnosis should depend on histopathology results. Although the possibility of malignant transformation of NF1 is little, severe space-occupying compression of surrounding organs should be paid real attention to. Considering the active proliferative character, NF1 growing along the Glisson's sheath may lead to portal hypertension or obstructive jaundice. Above-mentioned makes a close follow-up indispensable.

Acknowledgement: This study was funded by the National Natural Science Foundation of China (81671701).

Conflict of interest

None declared.

Author attributions

Dan-qing Huang: Drafted the work and substantively revised it. Min Tang: Analyzed and interpreted the MRI images. Ai-mei Li: Analyzed and interpreted the PET-CT images. De-cai Yu: Offered suggestions for treatment. Jun Chen: Analyzed and interpreted the histological features and immunohistochemical results. Min Wu, Wen-ping Wang and Wen-tao Kong: Analyzed and interpreted the US images and offered suggestions on revision. All authors read and approved the final manuscript.

Ethical Statement

The patient provided consent for the publication of his case and the use of images from his medical record.

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Figure Legends

Fig.1 Abdominal ultrasonagraphy. (**a**)Conventional US showed massive intrahepatic heterogeneous hypo-echoic lesion(arrows) with irregular shape and unclear margin measured approximately 14×6.5cm. (**b**)The well-perfused portal vein(arrows) diffusion through the lesion could be observed on CDFI. (**c**)CEUS demonstrated hypo-enhancement of the perivascular lesion(arrowheads) at portal phase(38s after contrast agent injection), with integrated preservation of the portal vein(open arrow) and hepatic artery(solid arrow). (**d**)The periportal lesion(arrowheads) remained hypo-enhanced at delayed phase. The portal vein(open arrow) presented well-perfused.

Fig.2 Upper-abdomen magnetic resonance imaging(MRI). (**a**)Coronal T2-weighted image shows a widely infiltrative high signal intensity mass-like lesion(arrowheads) extending along intrahepatic ducts into liver, and proliferating inferior to mesentery(arrows). Central target sign and whorled appearance could be observed. (**b**)Axial SPAIR shows extensive tumor involvement in the pancrea(arrows). Multiple cutaneous nodules(arrowheads) could also be observed. (**c**)CE-MRI demonstrates low signal intensity of tumor at portal phase(65s after EOB injection). The portal vein presents serpaentine and compressed by surrounding tumor(arrowheads). (**d**) An unobstructed intrahepatic bile duct(arrow) could be detected at hepatobiliary phase(15min after injection).

Fig.3 Positron emission tomography-computed tomography(PET-CT). (**a,b**)PET-CT showed a wide-extened intra-abdominal mass with slight-elevated FDG uptake(solid arrows). The portal vein(open arrow) integrately distributes through the lesion. Multiple cutaneous nodules could be

observed around waist and buttock(arrowheads in **c** and **d**). The mass extends inferiorly into the retroperitoneum and pelvic cavity(arrows in **d**). The FDG-uptake of both internal and cutaneous nodules were minimal.

Fig.4 Histological features and immunohistochemical results. (**a**) Loosely arranged spindle-shaped cells with integrated hepatic vessels distribution (open arrows) and are adjacent to normal hepatocytes (arrowheads)(H&E stain, 40x magnification); (**b**) At higher magnification, the sample represents spindle-shaped cells with small, wavy nuclei(H&E stain, 100x magnification). Positive expression for (**c**)S100 and (**d**)Sox10.