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Cell Block Biopsy of Portal Vein Thrombosis for Liver Pre-Transplantation Evaluation

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Abbreviations:

BPVT: benign portal vein thrombosis; CT: Computed Tomography; HCC: hepatocellular carcinoma; INR: international normalized ratio; LT: liver transplantation; LDLT: living donor liver transplantation; MPVT: malignant portal vein thrombosis; MRI: Magnetic Resonance Imaging; RPM: revolutions per minute

1. Abstract

Major vessel invasion in patients with hepatocellular carcinoma (HCC) receiving living donor liver transplantation (LDLT) is one of the major factors for HCC recurrence. Malignant portal vein thrombosis (MPVT) is an absolute contraindication for liver transplantation (LT). However, benign portal vein thrombosis (BPVT) mostly occurs in advanced liver cirrhosis patients with a slowdown of the portal vein flow. The pathological diagnosis is believable to be a tool in the pre-transplantation evaluation. Because of the small caliber of the portal vein and its location behind the common hepatic duct, conventional liver biopsy is difficult to perform in these patients. Fine-needle aspiration cytology has been reported with regard to the differential diagnosis between MPVT and BPVT. Herein, we investigated 8 cases to describe the use of cell block biopsy of portal vein thrombosis (PVT) for the pre-transplantation evaluation in patients on our waiting list for LDLT. The result indicated that cell block biopsy is not only an innovation method for approach portal vein thrombosis, but also a safety and accurate way to identify MPVT or BPVT during the liver pre-transplantation evaluation.

2. Introduction

Major vessel invasion in patients with hepatocellular carcinoma (HCC) receiving living donor liver transplantation (LDLT) is one of the major factors for HCC recurrence [1]. Malignant portal vein thrombosis (MPVT) is an absolute contraindication for liver transplantation (LT). However, benign portal vein thrombosis (BPVT) mostly occurs in advanced liver cirrhosis patients with a slowdown of the portal vein flow. The pathological diagnosis is believable to be a tool in the pre-transplantation evaluation. Because of the small caliber of the portal vein and its location behind the common hepatic duct, conventional liver biopsy is difficult to perform in these patients. Fine-needle aspiration cytology has been

reported with regard to the differential diagnosis between MPVT and BPVT [2,3]. Herein, we investigated 8 cases to describe the use of cell block biopsy of portal vein thrombosis (PVT) for the pre-transplantation evaluation in patients on our waiting list for LDLT.

3. Patients and Methods

3.1. Short Report

From December 2016 to March 2019, 8 patients with HCC (hepatitis B virus-related liver cirrhosis in 5 patients and hepatitis C virus in 3 patients) had been receiving optimal treatments previously and were complicated with PVT. Their mean age was 58.1 years (range, 46–65 years), and all of them were men. All PVTs were documented by Doppler ultrasonography (Figure 1a), computed tomography angiography, and magnetic resonance imaging studies. The right-side portal vein was affected in 4 cases, and umbilical portion of the portal vein was affected in the other 4 cases.

Using a sonography-guided Chiba needle (22-gauge, 15 cm), aspiration was performed via the right intercostal space, and segment 5 of the liver was obliquely punctured to avoid injuring the common hepatic duct in the cases of right PVT. For the cases of PVT at umbilical portion, a vertical puncture was performed via segment 4 of the liver (Figure 1b).

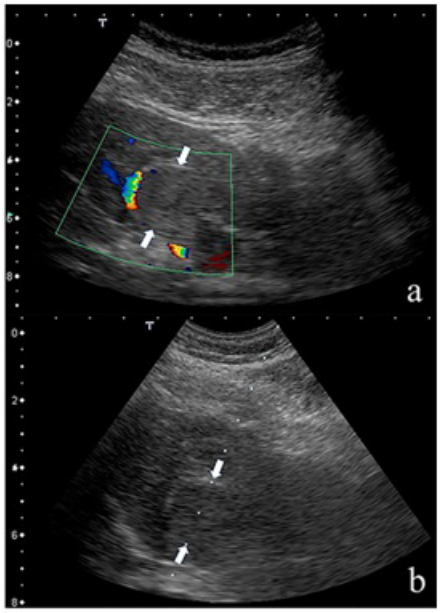

Figure 1: (a) Color Doppler ultrasonogram showing thrombosis (arrows) in the umbilical portion of the portal vein. (b) Ultrasonography-guided Chiba needle aspiration of the umbilical portion of the portal vein along (arrows) the puncture-guided line.

3.2. Cell Block Biopsy Technique

Under the sonographic guidance, the 22-gauge Chiba needle pierces through in the porta vein. The tip of the needle was aspirated back and forth in the portal veins and the material of the blood clot was obtained, the specimen was immediately fixed using the formalin, and 3 minutes after centrifugation at 3000 rpm, dressed in liquid paraffin during the embedding process, then paraffin block sliced at a thickness of 0.6-µm, and finally stained using hematoxylin and eosin (Figure 2a), as described in our previous study [4].

4. Result

Seven MPVTs were identified by the cell block histological study and withdrawn for further LT. Only one BPVT was diagnosed and that patient received LDLT subsequently. In the case of BPVT, calcification occurred in areas of tumor necrosis, and through very careful pathological explanations, there were no visible residual malignant cells in the resected liver. Portal vein thrombosis with fibrous obliteration and clustering destroyed red blood cells were defined as benign thrombosis in the portal vein by the pathological evaluation of the resected liver (Figure 2b). There was no evidence of HCC recurrence for 6 months of follow-up until now. In our case series, no complication associated with sonographic guided 22-gauge Chiba needle puncture of the PVT was observed.

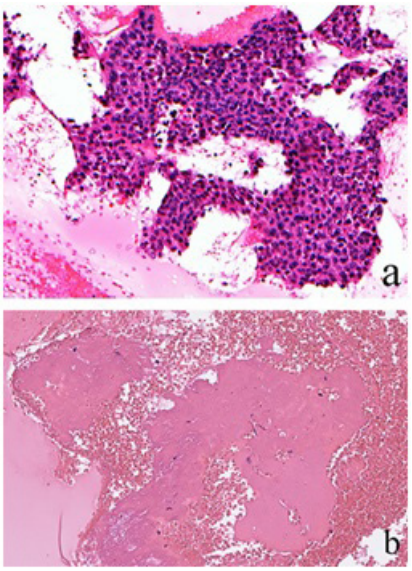

Figure 2: (a) Histopathological findings of the cell block biopsy showing neoplastic tissue fragments comprising polygonal cells bearing hyperchromatic and pleomorphic nuclei and granular cytoplasm (hematoxylin and eosin stain, magnification 20X). They are arranged in a trabecular pattern with intervening sinusoidal spaces and a poorly developed reticulin framework; therefore, hepatocellular carcinoma is diagnosed with moderate differentiation. (b) Portal vein thrombosis with fibrous obliteration and clustering destroyed red blood cells defines as benign thrombosis in the portal vein of the resected liver (hematoxylin and eosin stain, magnification 20X).

5. Discussion

A LDLT is consisted of two major surgical procedures simultaneously for both the donor and the recipient. Patients combined HCC with MPVT have a very poor prognosis for transplant surgery, and traditional liver transplantation is a contraindication for such patients. Because of the rapid progression and recurrence

of the disease, the American Association for The Study of Liver Disease recommends that HCC with macro-vascular invasion patients are not be suitable for liver transplantation. The indications of cell block biopsy are to obtain a tissue-proof of the portal vein thrombosis, and to determine whether this could be a candidate for liver transplantation [5]. Advances in imaging modalities have obviated the need for tissue confirmation in most HCCs. Such as CT scan, MRI and contrast sonography have been reported with regard to the differential diagnosis between MPVT and BPVT. In fact, imaging diagnosis is not superior to histological diagnosis in practical clinical applications. As liver transplant is a major and highly invasive procedure, with certain risk for both donors and recipients, differentiating MPVT and BPVT merely rely on imaging modalities might inevitably lead to the concern of false-negative result during the preparation and evaluation phase of liver transplantation procedure. As a result, it required a reliable way for surgeons to make histological diagnosis of PVT before a living donor liver transplantation. Aspiration biopsy was performed as similar as aspiration cytology. The use of immediate cytologic staining reduces the number of passes in each lesion with absence of insufficient sampling [6]. Different from the cytological diagnosis of aspiration biopsies, portal vein thrombosis cell block biopsies were a histological diagnosis for fine needle aspiration procedures. The main step was to use formalin firstly to fix the aspirated bloody specimens, then used 3000 rpm of high-speed centrifugal to recombine the tumor structure, so that it was easy to maintain the typical architecture of HCC and the structure of the trabecular pattern, and then with the general paraffin block on the thickness of 0.6-μm of pathological slice, and stained using hematoxylin and eosin for the conventional pathological preparation and interpretation. Such interpretation is certainly much better than the general cytological diagnosis [4].

In the LT setting, Menghini needle biopsy was used to identify the liver parenchyma and tumor pathology in our LT program [5]. Because of the small caliber of the portal vein lumen, even the one-fire biopsy gun or Menghini needle was not appropriate for approaching the portal vein. If the biopsy needle penetrates from the liver parenchyma to the portal vein, mixture of liver parenchyma, red blood cells, vasculature and thrombotic tissues in disoriented order may confound the pathological interpretation, as it will be unclear whether the tissue was obtained from the parenchyma or from inside of the portal vein. However, when using the cytology study, it is difficult to identify well-differentiated cell grading of HCC. The specific trabecular cellular arrangement is a typical finding for diagnosing HCC. High-force centrifugation should be performed again to evaluate the trabecular pattern from the separated single cells in our current study.

The equipment of cell block biopsy is a 22-gauge Chiba needle with far fewer side effects than traditional 15-gauge biopsy guns or Menghini needles. The application of fine needle cell block biopsy for portal venous thrombosis is never a problem of tumor dissemination due to its benign property. In contrast, malignant portal venous thrombosis with the risk of high rate of tumor seeding and dissemination potential has a fairly high degree of distant metastasis in itself, increasing tumor dissemination secondary to spillage into abdominal cavity. so there is no evidence of increased tumor dissemination. In the case of HCC with portal vein thrombosis, the basic requirements for a safe fine needle cell block biopsy are as following: prothrombin time less than 1.2 INR and platelet count more than 80/mm^3. Vitamin K1 supplements, fresh frozen plasma and platelet transfusions should be given if needed to correct clinically significant coagulopathies. In addition, cases concurrent of ascites cannot be performed for portal vein puncture. Finally, after the fine needle cell block biopsy, the puncture site needs to use an elastic belt to combine 2 kg sandbag compression for 4 hours to prevent post-procedure bleeding [5]. On the other hand, the portal veins themselves are buried in liver parenchyma because liver tissue is a sinusoidal structure. If a fine needle puncture causes bleeding from the portal vein, the blood also runs into the hepatic sinusoid and then drains into the hepatic vein. By additional sandbag external compression, we have not experienced definite bleeding complications. Based on the ultrasonographic view, the location of the common hepatic duct was in front of the right portal vein; therefore, we were able to puncture the abdominal surface obliquely at 45 degrees to avoid common hepatic duct injury.

6. Conclusions

In conclusion, cell block biopsy is not only an innovation method for approach portal vein thrombosis, but also a safety and accurate way to identify MPVT or BPVT during the liver pre-transplantation evaluation.

7. Declarations

7.1. Ethics: The study protocol conformed to the ethical guidelines of the Declaration of Helsinki and was approved by the ethics review committee of Chang Gung Memorial Hospital (number 201900568B0). Written informed consent and consent for publication was obtained from the parent of the participant. None of the transplant donors or recipients was from a vulnerable population.

7.2. Competing interests: The authors have no competing interests to declare.

7.3. Funding Statement: The authors have no source of support or funding to report.

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