Ultrasound-Guided Fine Needle Aspiration in Differential Diagnosis of Portal Vein Thrombosis in Patients with Hepatocellular Carcinoma

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Abstract

Background and Study Aims: Portal vein thrombosis (PVT) associated with untreated HCC are almost always malignant, still benign portal vein thrombus should be considered as well. This study was designed to study the value of ultrasound-guided fine needle aspiration cytology in the differential diagnosis of portal vein thrombosis.

Patients and Methods: This study included 20 patients with chronic liver disease and hepatocellular carcinoma (associated with portal vein thrombosis). All the patients were subjected to abdominal ultrasonography, color coded duplex sonography of portal vein and ultrasound guided fine needle aspiration cytology of portal vein thrombus.

Results: FNAC was positive for malignant cells in 70% of cases, the presence of either complete thrombus and/or positive intralobular signals were exclusive for malignant nature (p-value was 0.042 & 0.002 respectively). CCDS had a sensitivity of 78.6%, specificity of 100%, positive predictive value of 100%, negative predictive value of 66.7% for the diagnosis of malignant PVT with a total accuracy of 85%.

Conclusion: Ultrasound-guided fine-needle aspiration of portal vein thrombosis is a feasible, accurate and well-tolerated procedure in the diagnosis of the nature of portal vein thrombus associated with hepatocellular carcinoma.

Key Words: Portal vein thrombus – HCC – CCDS.

Introduction

HEPATOCELLULAR carcinoma (HCC) is frequently complicated with malignant portal vein thrombosis that is related to neoplastic infiltration of the portal venous system [1].

Although it has been suggested that portal vein thrombosis (PVT) associated with untreated HCC are almost always malignant, still benign portal vein thrombus (that can develop on top of hepatic cirrhosis as well as following percutaneous ethanol injection into HCC) should be considered as well [2].

Several diagnostic modalities can differentiate benign from malignant portal vein thrombosis, these include combined use of B mode ultrasound and color coded duplex sonography (CCDS), color Doppler power image (CDPI) and pulsed Doppler [3].

The pulsed Doppler is of utmost importance as it can differentiate benign from malignant portal vein thrombosis by probing for pulsatile arterial current in portal vein thrombosis; yet still such arterial frequency spectrum can be detected in some portal vein benign thrombosis (PVBT) [4].

So, the need for an additional diagnostic modality represented in the use of ultrasound guided fine needle aspiration from the portal vein thrombus checking the presence of malignant hepatocytes [5].

So we aimed in this study to assess the value of ultrasound-guided fine needle aspiration in the differential diagnosis of portal vein thrombosis associated with hepatocellular carcinoma.

Patients and Methods

This study included 20 patients with chronic liver disease and hepatocellular carcinoma (associated with portal vein thrombosis) admitted to Tropical Medicine Department, Kasr El Aini Hospital and Cairo University in the period from August 2007 to August 2008.

They were 17 (85%) males and 3 (15%) females. Their ages ranged from 30 to 72 years.

They were chosen according to the following inclusion criteria: Chronic liver disease (Child-Pugh's class A&B) with hepatocellular carcinoma (diagnosed by triphasic spiral CT ± high AFP level (>200ng/ml), portal vein thrombosis detected by
B mode ultrasound and confirmed by color coded duplex sonography, platelet Count $\geq 60,000$ and INR (1.5-2.5).

Cases with multicentric HCC (focal lesions $>3$) or metastatic HCC were excluded from the study.

Prior to FNAC All patients were subjected to full history taking, clinical examination, routine laboratory investigations (CBC, liver function test [Bilirubin total and conjugated, serum albumin, INR], liver enzymes (AST, ALT) and alkaline phosphatase), AFP assays by ELISA technique and abdominal sonographic assessment including (conventional gray scale B mode ultrasonography and Color coded duplex sonography).

Sonographic Assessment was done in the ultrasonography unit, Tropical Medicine Department, Kasr El-Aini Hospital using a machine (Toshiba SSA 340 with a 3.5MHz curved sector transducer).

A- Gray scale B mode ultrasound:

Routine scanning of the liver, gall bladder, spleen and midline area as well as scanning for ascites, abdominal lymphadenopathy or masses was done, with special emphasis on the number, site and size of the focal hepatic lesions. Portal vein was assessed as: Dilated or not and patent or thrombosed, the thrombus was expressed as (Partial or complete) and (main trunk, RT branch or LT branch).

B- Color coded duplex sonography:

Baseline unenhanced color doppler sonographic studies were performed by using a low pulse repetition frequency (750 to 1200Hz) to optimize detection of weak signals. The bandpass filter was set at (0 to 50Hz). The color box was restricted as much as possible to maximize color sensitivity and frame rate. On-screen real-time, B-mode color doppler imaging and spectral analysis were simultaneously displayed.

Portal vein thrombi in the left portal vein were evaluated using an anterior subxiphoid approach, portal vein thrombi in the right or main portal veins were evaluated between the right mammary line and the right posterior axillary line using an intercostal or subcostal approach according to Tanaka et al. [6].

The criterion for diagnosing malignant thrombosis was the detection of pulsatile arterial flow in the thrombus [3].

Lastly Fine Needle Aspiration cytology (FNAC) was obtained from the thrombus in the portal vein, prior to procedure an informed consent was obtained from each patient after explaining technique, possible benefits, complications and coagulation profile of patient was checked.

The procedure was performed with the patient under conscious sedation induced by the intravenous administration of diazepam 10mg. Cleansing the skin with povidone iodine (Betadine) and alcohol was done and local anesthesia was achieved by using 5ml of 2% lidocaine (Xylocaine; Astra).

Fine needle aspiration was performed under real-time US with free-hand technique using a 21-23 gauge lumbar puncture needle, fitted to a 20-ml disposable syringe attached to a metallic syringe holder, when the needle reached the wall of the portal vein, it was strengthened through the wall and into the portal vein thrombus, subsequently the needle was twitched up and down in the portal vein thrombus associated with keeping negative pressure in the syringe, the needle was taken out when the tissue and/or tissue with blood was seen in the syringe. The aspirate was fixed by alcohol 95%.

The specimens were then sent to the cytopathology laboratory for staining by Haematoxylin and Eosin stains and for cytological assessment.

A diagnosis of malignancy was made when the cytology contained cells that showed malignant features (solid trabecular groups of pleomorphic polyhedral cells showing dark nuclei, high N/C ratio and anisonucleosis, surrounded by amphophilic cytoplasm seen in back ground of coagulated blood).

After the procedure, patients were kept in hospital for 4-6 hours with close monitoring of vital signs.

Statistical evaluation:

Data was coded and entered using statistical pakage SPSS for version 15.

Data was summarized using mean, SD and range for quantitative variables and percentage for qualitative variable. Comparison between groups were done using Chi-square and Fisher exact test for qualitative variable and non-parametrical Mann-Whitney Wilcoxon test for quantitative variables not normally distributed.
*p* value less than or equal to 0.05 were considered as statistical significant.

**Results**

This study included 20 patients with HCC and portal vein thrombosis, they were mostly males (85%) with a mean age of 55.6 ± 9.5 years, most of our patients (80%) fit into child Pugh class (B) with small percentage (20%) fitting into child Pugh class (A).

Most of the patients (65%) were discovered accidentally during assessment of HCC cases for treatment, the focal lesions were mostly located in right lobe (70%) with a mean diameter <5cm in 65% of the cases, while the portal vein thrombi mainly involved main trunk in 9 patients (45%) followed in frequency by right branch in 8 patients (40%) Fig. (1) Picture (1).

Color coded duplex ultrasound demonstrated that portal vein thrombi were mostly partial in 12 patients (60%) with positive arterial signals in 11 patients (55%) Table (1) Picture (2).

FNAC was done with no complications and was positive (malignant) in 14 patients (70%) Picture (3) and was negative (benign) in 6 patients (30%), upon comparing benign and malignant portal vein thrombosis as regards color coded duplex sonographic data of portal vein thrombus, we demonstrated that color coded duplex sonographic detection of either complete thrombus and/or positive arterial signals was exclusive for malignant PVT (*p*-value was 0.042 & 0.002 respectively) Table (2) Yet there was no relation between the incidence of positivity for arterial signals and either the distribution of portal vein thrombus (main trunk, Rt branch, Lt branch) or the pattern of portal vein thrombus (partial or complete) in malignant cases (*p*-value was 0.382 & 0.538 respectively).

Finally, on taking FNAC as the gold standard for diagnosis of malignant PVT, we demonstrated that CCDS had a sensitivity of 78.6%, specificity of 100%, positive predictive value of 100%, negative predictive value of 66.7% with a total accuracy of 85%.

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**Fig. (1):** Distribution of the portal vein thrombus by ultrasound.

**Picture (1):** Ultrasound shows a thrombus in the left branch of portal vein.

**Picture (2):** Color coded duplex sonography showing pulsatile arterial signals in portal vein thrombus.

**Picture (3):** FNAC of portal vein thrombus showing malignant cells.
Table (1): Color coded duplex sonographic assessment of portal vein thrombus.

<table>
<thead>
<tr>
<th>Color coded duplex sonographic assessment of portal vein thrombus</th>
<th>No.</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Partial</td>
<td>12</td>
<td>60</td>
</tr>
<tr>
<td>Complete</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td>Positive for arterial signals</td>
<td>11</td>
<td>55</td>
</tr>
<tr>
<td>Negative for arterial signals</td>
<td>9</td>
<td>45</td>
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Table (2): Color coded duplex sonographic data of malignant and benign portal vein thrombus.

<table>
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<tr>
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<th>Benign No.=6</th>
<th>Malignant No.=14</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
</tr>
<tr>
<td>Partial</td>
<td>6</td>
<td>100</td>
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<tr>
<td>Positive for arterial signals</td>
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<td>11</td>
</tr>
<tr>
<td>Negative for arterial signals</td>
<td>6</td>
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Discussion

In this study PVT was diagnosed successfully using B mode ultrasound during routine assessment of HCC cases prior to percutaneous ablation therapies in 13 (65%) patients or following treatment of HCC in 7 (35%) patients. Further differentiation into malignant and benign thrombus was done using color coded duplex sonography that yielded pulsatile arterial signals in 55% of cases with a sensitivity and specificity of 78.6% & 100% respectively as compared to FNAC (the gold standard for diagnosis) that was positive for malignancy in 14 (70%) of the cases.

Regarding the value of B mode ultrasound in assessment of PVT, similar to our results Tarantino et al. [7] was able to identify PVT by B mode ultrasound in all of the cases included in his study (54 patients) either synchronizing with HCC nodules (15/54 cases) or during follow-up of the remaining HCC cases (39/54). Similar results were obtained from Other authors [5,8], the later reported that B mode ultrasound has been considered the first choice for the diagnosis of PVTT because of its high sensitivity and specificity.

Regarding the value of color coded duplex sonography, the current study yielded a sensitivity and specificity of color coded duplex sonography for the diagnosis of malignant PVT 78.6% & 100% respectively.

Comparable to our results, high sensitivities (92, 89%, 90.5%, 80%) and specificities (100%) of color coded duplex sonography in the distinction of a thrombus nature by the presence or absence of thrombus vascularity have been reported by other investigators [4,6,9,10].

On the other hand, others [3,7,11] reported sensitivities of 62%, 57% & 20% respectively though using sophisticated up-to-date CDUS machines. These discrepancies could be due to small size of PVTs, the fact that CDUS overwrite the gray scale image with subsequent misinterpretation of the source of the signals and lastly to the fact that nearby moving structures or vessels can cause artifacts [12,13].

Ultrasound-guided fine-needle aspiration cytology of portal vein thrombosis is a feasible, accurate, safe, low-risk and well-tolerated procedure for diagnosing neoplastic etiology of PVT as reported by others [3,14-17].

In our study, FNAC was positive for malignancy in 14/20 cases (70%). Similar to our results, other authors [7,10,18] reported positive rates of malignancy in 64.7%, 76% & 71.4% respectively.

But our results were not in agreement with the study done by Lin et al., (2001) that included 112 patients, FNAC was positive (malignant) in 106 patients (94.6%) and Yang et al., (2005) who reported positive FNAC (malignant) in 19 patients (86.4%) out of 22 patients with HCC & PVT. Such discrepancy could be attributed to the pattern of the studied patients in different studies and the small number of the patients in our study in comparison to other studies.

In conclusion: Ultrasound-guided fine-needle aspiration of portal vein thrombosis is a feasible, safe, low-risk, well-tolerated procedure and has high positive rate and a diagnostic value and Color coded duplex sonography is a valuable technique in assessment of PVT with HCC.

References

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