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ORIGINAL ARTICLE

Transjugular Liver Biopsy in Pediatric Patients with Uncorrectable Coagulopathies

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ABSTRACT

Objective: Transjugular liver biopsy is widely used in adult patients especially when percutaneous liver biopsy is contraindicated for various reasons. Our aim was to evaluate the safety and efficacy of transjugular liver biopsy in pediatric patients who had significant coagulopathy.

Materials and Methods: 19 children whose ages ranged from 2 months to 15 years and 5 months underwent procedure under general anesthesia or intravenous sedation. Despite platelet and fresh frozen plasma transfusions all patients were taken to the angiography suite with either increased international normalized ratio or thrombocytopenia, or both. Following the right hepatic vein cannulation, free and wedged hepatic venograms were routinely performed to evaluate the hepatic parenchyma and optimal biopsy position. The tissue samples obtained by using 18 or 19 Gauge semi-automatic core biopsy needles were sent for histopathological examination.

Results: The mean number of needle passes per procedure was 2.6 (range 1-5). Adequate biopsy samples for a definitive diagnosis were obtained in all patients at a single intervention session and the technical success rate was 100%. Neither major, nor minor complication was seen. The most common diagnosis was non-specific chronic fibrosis.

Conclusion: Despite the limited number of patients in our study; transjugular liver biopsy appears to be a safe and effective method in pediatric patients in whom percutaneous biopsy is contraindicated due to associated coagulopathies.

Key words: Image-guided biopsy, Liver diseases, Pediatrics.

Introduction

The most important complication of percutaneous liver biopsy is bleeding due to damaging of the liver capsule [1]. This risk is especially significant in the presence of coagulopathy and ascites. A transjugular approach to reach the liver was first described by Hanafee and Weiner in 1967 [2]. Transjugular liver biopsy makes the tissue sampling via to the hepatic veins by entering from the internal jugular veins. For this reason transjugular liver biopsy is a known alternative method when percutaneous liver biopsy is contraindicated for serious and/or uncorrectable coagulopathies [3].

The role of transjugular liver biopsy in diagnostic spectrum of adult patients is known and its safety and efficacy was shown in recent literature [4, 5]. On the other hand, the experience of transjugular liver biopsy in pediatric patients is quite limited [6, 7, 8]. Low body weight as well as the uncorrectable coagulopathy also increases the risk of technique and increases procedural difficulties when compared to adult patients [6, 7].

Our aim was to retrospectively evaluate the safety and efficacy of transjugular liver biopsy in pediatric patients who had high risk due to uncorrectable

coagulopathy, despite multiple units of platelet and fresh frozen plasma replacement.

Material and methods

2.1 Patients

A total of 19 pediatric patients (11 boys and 8 girls) with uncorrectable coagulopathies underwent transjugular liver biopsy in our Interventional Radiology Department.

Major indication for transjugular liver biopsy was uncorrectable coagulopathies in our patient series. The coagulopathy was defined as abnormal international normalized ratio (INR) or thrombocytopenia or both. Abnormal laboratory values that define coagulopathy have been reported as platelet count less than 150.000/mm^3 or INR more than 1.2 in our hospital laboratory system. Also severe coagulopathy values were determined as < 80.000/mm^3 for platelet count or >1.5 for INR measurement for this procedure.

Platelet and INR counts were obtained within 12 hours of the procedure for 19 patients after adequate multiple blood products replacement treatment. Despite multiple units of platelet and fresh frozen plasma transfusions; 19 of 19 children were taken to the angio suite with either increased international normalized ratio (>1.2) or thrombocytopenia (<150.000/mm^3), or both. In 17 out of 19 patients, these two bleeding parameters were both abnormal. Increased INR (> 1.2) were found in 19 of 19 cases (100%) after correction with fresh frozen plasma transfusions. Despite platelet transfusions, 17 of 19 cases (89%) had thrombocytopenia (<150.000/mm^3).

8 of 19 patients (42%) had severe thrombocytopenia (<80.000/mm^3), 8 of 19 patients (42%) had severe coagulopathy (INR > 1.5) and 3 of 19 patients had both severe abnormal values. 13 of 19 patients (68%) had at least one severe coagulopathy parameter.

All 19 patients had significant findings of chronic parenchymal liver disease or liver functional test's abnormalities. Complete blood counts and coagulation profiles were obtained in all our patients prior to the procedures. Selected data of these 19 patients was shown in Table 1.

Patients' clinic and demographic data, indications for transjugular liver biopsy, coagulation parameters after adequate replacements, number of needle passes performed, initial diagnoses and biopsy results were noted. Written informed consents were obtained from the parents for all patients. The study was reviewed and approved by the local ethics committee. General anesthesia was utilized in 15 patients and intravenous sedation was applied in 4 patients.

2.2 Technique

The sonographic guidance was used to visualize internal jugular vein as venous access and to evaluate hepatic parenchyma, presence of hepatic veins, position of gall bladder and presence of intra-abdominal free fluid. The right internal jugular vein was accessed under sonographic guidance in 18 patients. The left internal jugular vein was used in the remaining one patient because of the thrombosis of the right side due to previous venous catheterization.

The tissue samples were obtained through the middle portion of the right hepatic vein in all patients using 18 or 19 Gauge semi-automated core biopsy needles. We used transjugular liver access and biopsy set (LABS 100, 200, Wiliam Cook Europe, Bjaeverskov, Denmark) consist of a transjugular stiffening cannula with sheath, a straight catheter, a multipurpose catheter and a semi-automated core biopsy needle (18 or 19G). After puncture of the internal jugular vein under sonographic guidance, the 9-French introducer sheath was first advanced into the right atrium and then to the inferior vena cava over a stiff guide wire. Using the multipurpose catheter and a soft steerable wire, right hepatic vein was selected and the free and wedged hepatic venograms were routinely obtained with the multipurpose catheter to evaluate the hepatic parenchyma, hepatic venous anatomy and optimal position for biopsy (Fig. 1a). Following this, the outer sheath was advanced into this hepatic vein over a stiff wire under fluoroscopic guidance (Fig. 1b). Right hepatic vein was preferred for biopsy because of its smooth angle with inferior vena cava and larger size of right hepatic lobe. The core biopsy cannula and then the semi-automatic needle were advanced beyond the sheath into the hepatic parenchyma (Figs. 2a and 2b). Following optimal positioning of the inner core of the needle 1-2 centimeters within the hepatic tissue, the outer cutting portion was triggered with the manual pressure to spring over the inner core for obtaining the sample.

Technical success was determined by obtaining the appropriate tissue material for histopathological diagnosis. Currently, a liver biopsy specimen of >15 mm long and/or containing >6 complete portal tracts suffices for the histological diagnosis of diffuse liver disease (9). The biopsy samples were sent

Table 1. Selected data of our 19 transjugular liver biopsy patients.

Number	Age (months) and Gender	Initial diagnosis	Biopsy results	ALT (U/L)	Total bilirubin (mg/dl)	Platelets /mm^3	INR	Body Weight (kg)	Needle pass number per procedure
1	45-M	CLD	Cirrhosis	47	1.7	82000	1.27	16	3
2	108-M	CLD	Cirrhosis	28	0.6	85000	1.40	30	2
3	22-F	CLD	Micronodular cirrhosis	143	0.7	65000	1.27	9	2
4	4-M	NCH, Biliary atresia	Biliary atresia	134	23.4	84000	1.76	5	1
5	17-F	Mitochondrial disease	Non-specific	770	0.4	237000	1.36	10	2
6	2-M	Hemochromatosis	Non-specific	68	3.9	96000	1.40	5	4
7	42-M	Storage disease	Non-specific	13	0.3	194000	1.22	9	3
8	68-M	Hiper IgM SC	SC	123	3.5	46000	1.32	13	3
9	168-F	Wilson's disease	Wilson cirrhosis	39	0.96	52000	1.40	30	2
10	144-M	CLD	Fibrosis, steatosis	88	0.75	41000	1.76	40	2
11	121-M	Wilson's disease	Wilson cirrhosis	123	2.8	106000	1.58	30	2
12	11-F	NCH, mitochondrial disease, PFIC	Fibrosis, macro/ micro vesicular steatosis	102	3.4	105000	1.79	8	2
13	156-F	CLD, Myelodysplastic syndrome	Non-specific	22	0.4	80000	1.40	35	2
14	128-F	SLE, AIH	AIH	244	2.5	112000	1.62	33	4
15	8-M	NCH, Mitochondrial disease	Cholestasis, fibrosis	584	2.3	106000	1.47	5	2
16	86-M	Infantile refsum disease	Fibrosis, storage cell	50	8.3	50000	1.90	14	2
17	117-M	Wilson's disease	Wilson cirrhosis	68	1.0	130000	1.70	35	4
18	180-F	CLD	SC	30	2.2	56000	1.29	40	2
19	123-F	CLD AIH	AIH	44	2.7	38000	1.80	30	5

CLD: Chronic liver disease, NCH: Neonatal cholestatic hepatitis, AIH: Autoimmune hepatitis, SC: Sclerosing cholangitis, PFIC: Progressive familial intrahepatic cholestasis.

for histopathological examinations in an appropriate manner. Post-procedural abdominal ultrasonography was also performed on the procedure table in all patients in order to evaluate the liver parenchyma and the presence/development of intra-abdominal free fluid related to the procedure. Post-procedural follow up included 24 hours of hospitalization with bed-rest and hemoglobin control.

Results

The mean age for 19 patients was 6 years and 8 months ranging from 2 months to 15 years and 5 months. The mean weight was 20.9 kilograms (5-40 kilograms).

The mean platelet count for 19 patients was 95.000/mm^3, and the mean 'international normalized ratio' value for prothrombin time was 1.51 on the day of procedure.

The mean number of needle passes per procedure was 2.6 (range, 1-5 passes). Adequate biopsy samples for a definitive diagnosis were obtained in all patients at a single intervention session and the technical success rate was 100%.

Neither major, nor minor complications were observed at the jugular puncture site or related to the liver passes.

The initial and final histopathological diagnoses of patients were shown in Table 1. Cirrhosis in 6 patients was the main pathological finding in biopsies. Etiology of cirrhosis was Wilson's disease in two patients. Two patients had autoimmune hepatitis, and

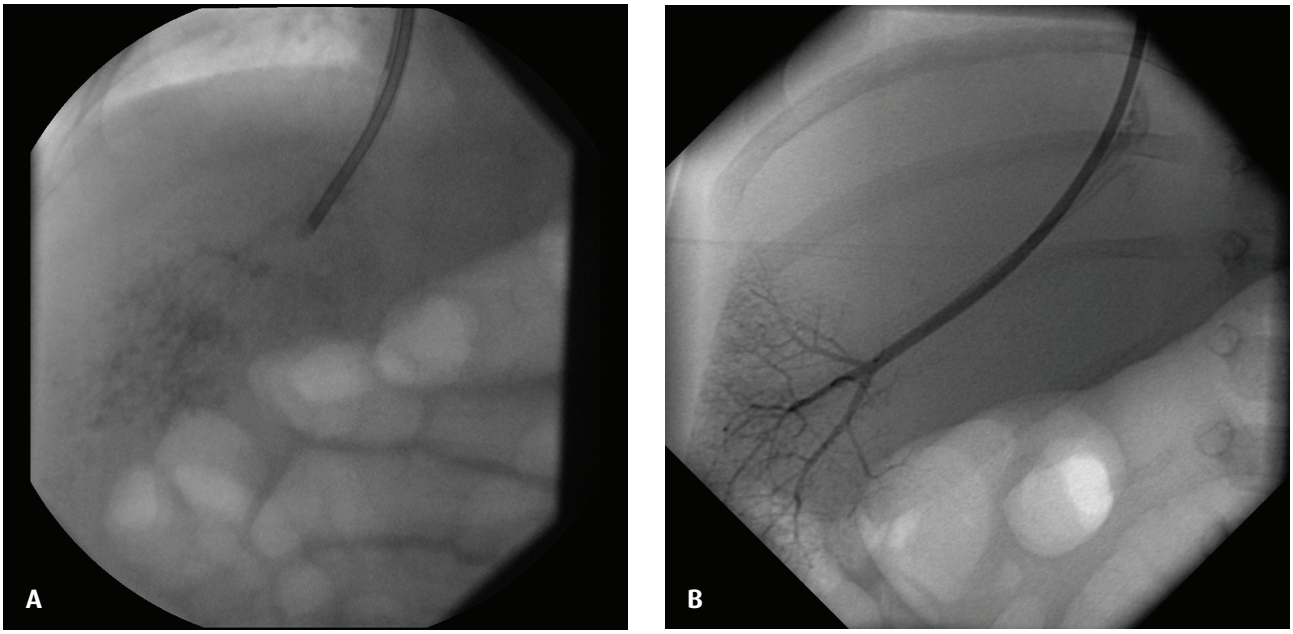

Figure 1. a, b. Free and wedge hepatic venograms were performed before the biopsy. The wedge venogram image (a) shows thinly granularly pattern which support chronic parenchymal disease. After injections, the sheath and the coaxial biopsy cannula was replaced over a stiff wire which were all positioned at the proximal-middle portion of the target vein. Sheath was retracted to the level of right atrium to be able to steer the biopsy cannula towards the vein wall and liver parenchyma (b).

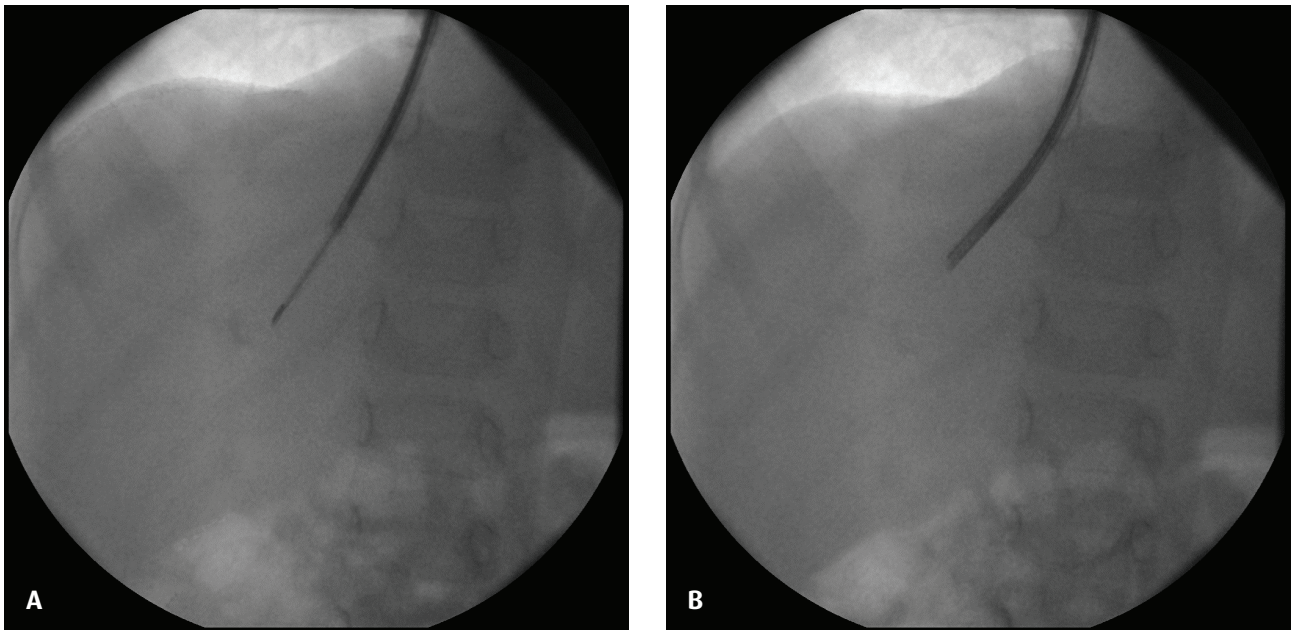

Figure 2. a, b. The scopic image (a) demonstrates the optimal position of the introducer sheath in the right hepatic vein with the needle is almost at the tip of the biopsy cannula (compare with figure 2b). Image (b) shows semi-automated core biopsy needle's inner portion in the parenchyma just before the outer cutting portion was fired to obtain tissue sample. 1-4 passes were required for adequate sampling in our patients.

two other had sclerosing cholangitis according to biopsy findings.

Discussion

Transjugular liver biopsy has become an accepted alternative method for histopathological diagnosis in adult patients with an established contraindication to percutaneous liver biopsy [5, 10]. Major indications of transjugular liver biopsy are severe or uncorrectable coagulopathy, thrombocytopenia or ascites. Less common indications include small cirrhotic liver, obesity, peliosis hepatis and unsuccessful

percutaneous biopsy [8, 11]. Liver transplantation is another use of transjugular liver biopsy due to impaired hemostasis and ascites in early periods [12]. It is also a safe alternative method in renal failure and for bone marrow recipients [10,12]. There are many great experiences about the safety and efficacy of transjugular liver biopsy in patients who are suffered from congenital bleeding disorders; many of these patients are also infected with hepatitis C virus [13]. In these groups when transjugular liver biopsy was used, the rates of complications were reported to be lower than percutaneous liver biopsy [6, 7]. Shin at al. reported 1 major complication (1.4%) in 65 congenital bleeding disorder patients [14]. Also in patients with acute liver failure associated with coagulation abnormalities and massive ascites, transjugular liver biopsy is a safe alternative method when compared to the percutaneous liver biopsy [15].

The transjugular liver biopsy method reduces the risk of hemorrhage because the biopsy samples are obtained through the hepatic vein and it avoids the potential risk of hepatic capsular damage. In theory, any bleeding occurs along the biopsy track into the venous system, thereby avoiding intraperitoneal blood loss [16]. Relative contraindications to the transjugular liver biopsy include lack of upper venous access, occluded superior or inferior vena cava, abnormal vascular anatomy due to congenital heart disease and small patient size [6, 7].

A technical failure rate of 3.2% has been reported in a review article that included more than 7500 cases. Inability to catheterize the hepatic veins (43.3%) and failed cannulation of the jugular vein were the most common two reasons (25.8%) [10]. Quality of the biopsy specimens is another factor that effects the technical success. Previously published comparative studies showed the superiority of the automated biopsy technique over the conventional aspiration biopsy technique for obtaining larger and less fragmented hepatic tissue samples required for a definite diagnosis [17]. Soyer et al. reported an overall success rate of 98% allowing definitive histological diagnosis in 200 transjugular liver biopsies with automated device [18]. Smith et al. also reported a success rate of 98% in 409 procedures in pediatric and adult patients with automated device [3].

The complication rate of transjugular liver biopsy is reported as 1-7% in the literature [10, 19]. Kalambokis et al. reviewed sixty-four series reporting 7649 transjugular liver biopsies. They reported 6.7% minor and 0.5% major complication rates in adult series and mortality rate was 0.09% due to intraperitoneal hemorrhage or ventricular arrhythmia. Pediatric compared to adult series showed higher minor (20%) and major (1.9%) complications while mortality was 0.6% [10]. Major complications of transjugular approach are intraperitoneal hemorrhage, hepatic hematoma, ventricular arrhythmia, pneumothorax and inferior vena cava perforation. Most common minor complications were neck hematoma, neck bleeding, carotid puncture, supraventricular arrhythmia, Horner syndrome, hypotension, haemobilia and hepatic-portal vein fistula [10].

Although there is great experience in adult patients, only a few papers have been reported on the experience of transjugular liver biopsy in pediatric patients [3, 6-8].

Furuya et al. reported the first pediatric series in 1992 which included 30 transjugular biopsies in 27 patients. Mean body weight was 42 kg. They reported that adequate tissue sampling was obtained in all patients for histopathological diagnosis and the histopathological results changed the diagnosis and provided additional information in 30% of all patients. In this study 23% complication rate was reported (five small subcapsular contrast extravasations, one small intrahepatic hematoma, and one inferior vena cava perforation) [6].

Bergey et al. showed the diagnostic quality of tissue material obtained by using 'Quick core' transjugular liver biopsy set regardless of age and body weight in children in 1998. They reported two complications in 24 biopsies (one capsular perforation and one intraperitoneal hemorrhage) [20].

In another series of 51 oncologic pediatric patients, percutaneous liver biopsy was performed in 22 patients and transjugular liver biopsy was preferred in 29 patients. The smallest body weight was 7 kg. Transjugular liver biopsy was preferred in patients with thrombocytopenia, ascites, or coagulopathy or patients that had undergone bone marrow transplantation. As a result adequate tissue material for histopathological diagnosis was obtained in all patients. Bleeding complications were seen in 3 of the 22 percutaneous liver biopsy patients although tract embolization was used during the procedure. However, no major or minor complications were reported in the transjugular liver biopsy group with high risk patients [7].

Habdank at al. reported 74 transjugular liver biopsies in 64 pediatric patients due to the presence of thrombocytopenia, coagulopathy or ascites. The

mean weight was 28.8 kg and the mean age was 8.3 years. Complication rate was noted 8.1% and the technical success was 98.6%. [8]. It was emphasized in this study that there was no relationship between the complication rate and the weight or the age of the patient.

Despite the limited number of patients in our study; transjugular liver biopsy does appeared to be a safe and effective method in very small pediatric patients in whom percutaneous biopsy is contraindicated due to associated coagulopathies. The key is to manipulate the wires, catheters and sheaths very gently and of course make the right choices of angiographic materials. We have a high technical success rate in obtaining adequate tissue samples for histopathological diagnosis.

Considering the fact of having limited number of publication in the related literature on the results of transjugular liver biopsy in pediatric population, prospective studies with larger series of patients are needed to establish the role of transjugular liver biopsy in the diagnostic tool spectrum in pediatric patients.

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