Case Report

Endoscopic ultrasound-guided liver biopsy in pediatric patients

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ABSTRACT

Endoscopic ultrasound (EUS) is routinely used for diagnostic and therapeutic purposes in adults, and there is emerging literature on its feasibility and safety in children. A recent novel application is EUS-guided liver biopsy (EUS-LB), which has shown to be technically simple, safe, and provides adequate diagnostic yield in adults for evaluation of liver disease; but the use of EUS-LB has never been evaluated in the pediatric population. We report the first case series of EUS-LB in the pediatric population, performed on 3 children, 1 girl and 2 boys-ages 9, 14 and 17 respectively, using a 19-gauge EUS-fine needle aspiration needle. All three cases were performed for the evaluation of unexplained elevated liver enzymes, with above-average diagnostic yield and without any immediate or delayed complications in all children. The use of EUS-LB was pivotal in the management of all the cases. Our case series illustrates the diagnostic utility and safety of EUS-LB in pediatric patients.

Key words: Abnormal liver enzymes, endoscopic ultrasound, liver biopsy, liver disease, pediatric patients

INTRODUCTION

Endoscopic ultrasound (EUS) is a well-established technique for diagnostic and therapeutic evaluation of gastrointestinal and pancreaticobiliary disorders in adults, and there is emerging literature on feasibility and safety in pediatric patients.[1-3] A recent novel application in adults is EUS-guided liver biopsy (EUS-LB) which has proven to be technically safe, and provides adequate tissue yields for evaluation of liver disease;[4-7] but the use of EUS-LB has never been reported in the pediatric population. We report the first case series of EUS-LB performed in the pediatric population.

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Endoscopic ultrasound-guided liver biopsy technique

Preoperative evaluation was done to rule out thrombocytopenia (platelets <50,000), coagulopathy (international normalized ratio [INR] >1.5), or use of antiplatelet agents within 5 days of the procedure. Informed consent for EUS and EUS-LB was obtained from the patient's parents. All patients underwent deep sedation with propofol administered by staff anesthesiologist and/or nurse anesthetist. Preprocedure antibiotics were not given. Using a linear-array echoendoscope (GF-UC140P, Olympus America, Center Valley, PA, USA), EUS-LB was performed as per our institutional protocol.[4] Color Doppler imaging prior to needle puncture confirmed lack of significant vascular structures within the needle path. Using a 19-gauge EUS-fine needle aspiration needle, LB was performed with 1-2 passes from the left hepatic lobe using a transgastric approach and 1-2 passes from the right hepatic lobe using a transduodenal bulb approach [Figure 1]. After initial liver puncture, 7-10 to-and-fro motions were made with a "fanning" technique using

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full suction. The tissue was then expressed directly into formalin using the stylet, and visible cores of tissue were identified. The patient was observed in the recovery unit for 2 h after the EUS-LB, and discharged if no pain or signs of complication.

CASE REPORTS

Case 1

A 9-year-old girl presented with 5 months of crampy abdominal pain and 1-week of rectal bleeding and diarrhea. Colonoscopy showed confluent friable and ulcerated mucosa from cecum to the rectum. Colonic biopsies were consistent with active ulcerative colitis. Laboratory studies showed elevated liver tests (liver function tests [LFTs]) alanine aminotransferase (ALT) 327 (normal 10-35 U/L), aspartate aminotransaminase (AST) 320 (normal 10-35 U/L), alkaline phosphatase 273 (normal 0-153 U/L), gamma glutamyltransferase (GGTP) 187 (normal 0-20 U/L), INR 1.18 (normal 0.85-1.16), and total bilirubin 0.3 (normal 0.3-1.3 mg/dL). Serologic workup was negative for viral, autoimmune, or metabolic liver diseases. Abdominal ultrasound showed heterogeneous hepatic echotexture; and magnetic resonance cholangiopancreatography did not show ductal obstruction.

Due to persistently elevated LFTs, EUS and EUS-LB were done. The LB specimen showed a yield of 30 mm of tissue length and 20 complete portal tracts (CPTs) [Figure 2]. Histopathology was consistent with active pericholangitis, suggestive of primary sclerosing cholangitis (PSC) [Figure 3]. Oral steroids and mesalamine were started with significant clinical improvement and subsequent normalization of LFTs.

Case 2

A 14-year-old boy presented with predominantly unconjugated hyperbilirubinemia (total bilirubin 1.2, alkaline phosphatase 322, INR 1.45, with normal AST/ALT), with a positive direct Coombs test and thrombocytopenia. Serologic workup was negative for viral, autoimmune, or metabolic liver diseases. Ultrasound showed increased hepatic echotexture without biliary abnormalities. Treatment with steroids for auto-immune hemolytic anemia resulted in significant improvement of LFTs. Another flare of LFTs during a viral respiratory illness prompted a transjugular-LB showing histology consistent with sero-negative autoimmune hepatitis, which was treated with 6-mercaptopurine (MP) and steroid therapy.

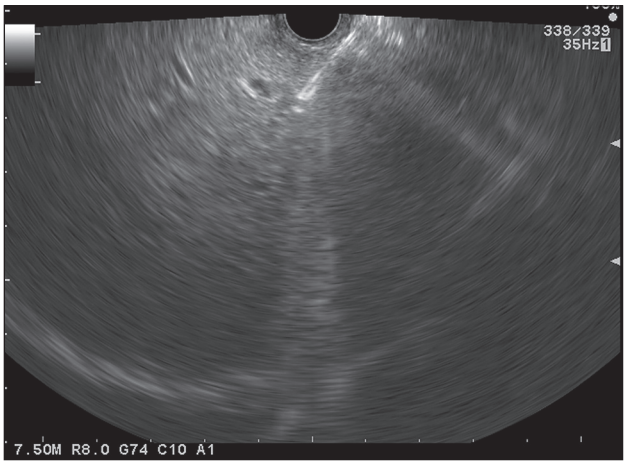

Figure 1. Endoscopic ultrasound-guided liver biopsy using 19-gauge fine needle aspiration needle, tissue acquisition from the right lobe of the liver

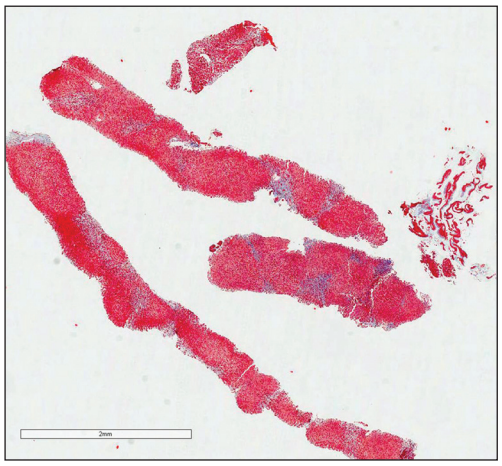

Figure 2. Low-power view of the aggregate core tissue length of the right lobe of the liver

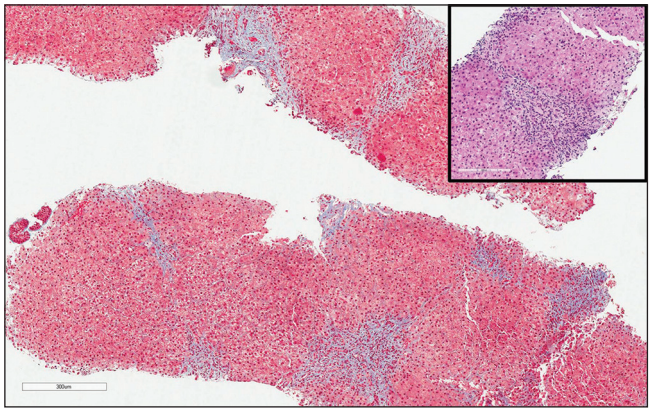

Figure 3. Trichrome stain of the liver tissue showing portal and focal periportal fibrosis; with (inset) hematoxylin and eosin stain high-power view showing portal triad with pericholangitis, seen in patient 1

He initially did well but started having elevation of GGTP. EUS-LB was done to assess disease activity. There was a total yield of 62 mm of liver tissue and

16 CPTs. Histopathology review showed mild steatosis, without significant inflammation, suggestive of well controlled disease activity. The 6-MP was continued with gradual improvement of GGTP.

Case 3

A 17-year-old boy presented with jaundice and elevated LFTs (ALT 1248, AST 961, alkaline phosphatase 157, total bilirubin 3.2, mostly conjugated, and INR of 1.2). He had a long history of drug abuse with heroin and marijuana. He had just completed a course of INH therapy for positive tuberculin skin test. Diagnostic workup was negative for viral, autoimmune, and metabolic liver diseases. Abdominal US was unremarkable. EUS did not show biliary obstruction. EUS-LB yielded 53 mm of liver tissue with 31 CPTs. Histology showed marked periportal inflammation with focal necrosis suggestive of acute hepatitis. Repeat serologies now showed positive viral hepatitis C (HCV) antibodies, and a high-HCV viral load (genotype 1a).

Anti-HCV therapy was started with sofosbuvir and simeprevir with significant improvement of LFTs within 2 weeks.

DISCUSSION

This is the first case series of the use of EUS-LB for assessment of liver disease in pediatric patients. Due to higher risk of potential complications with the "blind" liver biopsy technique, liver biopsies are increasingly done under image guidance with percutaneous, transjugular or laparoscopic approaches.[8] As fewer pediatric and adult gastroenterologists are performing liver biopsy, accrediting bodies no longer require technical expertise in actually performing this procedure for both pediatric and adult gastroenterology fellowship training programs.

Endoscopic ultrasound was indicated in all the patients for evaluation of abnormal LFTs. EUS-LB was added on to these cases as histologic evaluation was also needed; thereby avoiding an extra procedure. These patients were already undergoing sedation and procedure related risks from the EUS, thus, minimal additional risks were conferred with EUS-LB other than the needle puncture; which would be the same if they underwent a percutaneous liver biopsy. EUS-LB is an image-guided approach which allows visualization and avoidance of blood vessels even 1 mm in size. EUS-LB provides an access area to a much wider segment of liver parenchyma as the entire left lobe, and the majority of the right lobe can be evaluated for possible needle puncture sites from the stomach and duodenal bulb, respectively. There were no technical difficulties encountered during any of the cases.

Endoscopic ultrasound-LB can be done in an outpatient setting and offers the comfort of sedation and analgesia, reducing pain and anxiety. This is particularly important in pediatric patients. It eliminates the need for breath hold and is less frightening than the percutaneous or transjugular approaches. In addition to obtaining tissue, EUS-LB also offers the benefit of evaluating the biliary tree, gallbladder, pancreas, lymph nodes, and vascular anatomy for a more comprehensive evaluation in the same setting. There have been no reports of complications of EUS-LB, which uses ultrasound visualization and Doppler.[5-7] Recent papers evaluating the technique of EUS-LB have suggested that the yield of at least 15 mm of aggregate tissue length containing 6 or more CPTs is needed for an accurate histopathologic diagnosis.[5-7] All three of our patients yielded more than twice as much, with an aggregate tissue length of 30-62 mm and 16-31 CPTs. During the histopathological analysis, these tissue pieces were separated from the blood clot and arranged in linear cords [Figure 2]. The diagnostic yield from this tissue handling was, in fact, comparable to core samples, and our larger multi-center study has shown a diagnostic yield of 97.4% with these samples.[4] No immediate or delayed complications were seen in our patients.

The role of EUS-LB was pivotal in the management of our patients. In the first patient, it helped make the elusive diagnosis of small duct PSC for better prognostic evaluation; in the second patient it helped avoid unnecessary treatment escalation by assessing disease activity, and in the third patient it unearthed the diagnosis of acute HCV despite negative serological markers. Our case series illustrates the diagnostic utility and safety of EUS-LB in pediatric patients.

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