Chapter 2

Types of Liver Biopsy

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1. Introduction

Liver biopsy (LB) is an important procedure in the diagnosis and treatment of liver diseases. However, procedures for performing LB vary amongst institutions, and no universal guidelines exist. LB is performed for two main reasons: diagnosis of a liver condition itself, and as an adjunct to an existing surgical procedure. Recently, it has become possible to employ both approaches with minimal invasiveness using the transjugular route or under the guidance of ultrasound, computed tomography, or laparoscopic and endoscopic ultrasound. Techniques for liver tissue sampling include percutaneous liver biopsy [1-6], transjugular liver biopsy [7-14], laparoscopic liver biopsy [15], and transgastric liver biopsy [16-20]. This chapter introduces these techniques and evaluates their outcomes.

2. Percutaneous Liver Biopsy (PLB)

PLB is performed either blind or under imaging guidance. In the latter context, ultrasound (US) or computed tomographic (CT) guidance is used. Although these results of US-guided PLB depend greatly on the skills of the gastroenterologist, hepatologist or radiologist and the technical capabilities and quality of the US instrument, the available data indicate that it has a lower complication rate, requires a lower number of passes, is associated with less pain and pain-related morbidity, has a lower likelihood of the need for a repeat procedure, affords better-quality tissue specimens, and has only a marginally increased cost in comparison with blind PLB [21].

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PLB under image guidance essentially eliminates the risk of pneumothorax, or injury to the gallbladder or other viscera because the needle track is directly visualize of organ. Pain is the commonest complication, and up to 75% of patients suffer some discomfort after LB [21]. However, complications after PLB require careful observation. Piccinino et al. [22] reported that 61% of such complications appeared in the first 2 hours after the biopsy, 82% in the first 10 hours, and 96% in the first 24 hours. Strict observation is therefore required for the first 24 hours after PLB. Several large studies have shown rates of major complication after PLB ranging from 0.09% to 2.3%, severe complications in 0.57%, and mortality ranging from 0.03% to 0.11% [23-25]. Hardman et al. [4] reported one patient with graft vs. host disease and hypertension who died after PLB. This patient had multi-organ system failure at the time of biopsy and died within 24 hours of the biopsy. Furthermore, the complications of PLB seem to be related to the type of technique employed. In fact, the complications associated with US-guided PLB are significantly lower than those associated with blind PLB: 0.5% vs. 2.2% for severe complications [26], 2% vs. 4% [27] and 1.8% vs. 7.7% [28] for total complications. PLB under US guidance is recommended as a reasonable and cost-efficient procedure [1, 26, 28]. However, EI-Shabrawi et al. [5] have reported that blind PLB performed by the Menghini aspiration technique is safe even in infants and small children without mortality or major complications such as bile leakage, pneumothorax, and bleeding requiring blood transfusion. Szymczak et al. [6] also reported the safety and effectiveness of blind PLB based on an analysis of 1412 procedures, and showed that the rates of complications and failure were dependent on the experience of the operator. Moreover, the needle used was the Menghini-type suction needle, which carries a smaller risk of bleeding than cutting needles such as the widely employed Tru-cut needle. They concluded that the risk of complications and failure rate are low if the indications and contraindications are considered carefully and the biopsy is performed by a skilled and experienced operator.

Furthermore, with regard to bleeding after PLB, Alotaibi et al. [3] have reported that a positive color Doppler sign in US indicates bleeding along the biopsy tract, and that US-guided compression is effective for achieving appropriate hemostasis. Also, tract-plugging of the biopsy tract with Gelfoam or other thrombotic agents, is an important procedure for reducing the risk of bleeding and subcapsular hematoma in PLB [2]. Nevertheless, in patients with ascites or abnormal coagulation profiles, another procedure should be considered because of the high risk of possible bleeding complications.

3. Transjugular Liver Biopsy (TJLB)

TJLB was initially introduced in dogs as an experimental application by Dotter [29]. Rosch [7, 8] then reported its clinical application for transjugular cholangiography in 1973 and 1975. TJLB eliminates the need to traverse the peritoneal cavity and puncture the liver capsule. Furthermore, this technique is a safer biopsy option for patients with massive ascites, coagulopathy (prothrombin time greater than 3 seconds over the control value), thrombocytopenia (less then 60,000/cm^3), or those undergoing ancillary procedures such as measurement of pressures or opacification of the hepatic vein and inferior vena cava. It can also be

applied for patients in whom PLB has failed, or those with morbid obesity, a small cirrhotic liver, suspected vascular tumor or peliosis hepatitis, or medical conditions associated with bleeding disorders such as hemophilia for whom PLB is contraindicated [11, 30, 31], as any bleeding is returned to the venous system rather than leaking into the abdomen.

However, there are several particular complications associated with TJLB, including hemorrhage, subcapsular or neck hematoma and ventricular arrhythmia. The rate of such complications ranges from 0% to 20% [11]. Hardman et al. [4] reported a large subcapsular hematoma caused by TJLB requiring embolization and prolonged admission. Lebrec et al. [9] also reported a fatal case of intraperitoneal hemorrhage due to perforation of the liver capsule caused by excessive of the needle. Therefore, such forward rotation must be avoided or carefully limited. Furthermore, there have been several direct instances of perforation of the liver capsule that resulted in aspiration of ascitic fluid, bile from the gallbladder, or renal tissue in patients with a small cirrhotic liver. In such patients, TJLB should be avoided or employed only with caution by advancing the needle into the liver parenchyma by only 1 cm instead of the usual 2 cm, or contrast medium should be injected after the biopsy to evaluate the integrity of liver capsule. The major drawback of TJLB is the size of the biopsy specimens obtained; they are generally smaller ($p < 0.001$) and more fragmented ($p < 0.01$) than those obtained by PLB [12]. Pathologically, in terms of the number of portal tracts ($p < 0.0001$) and the utility of specimens for histological evaluation ($p < 0.05$), the quality of TJLB samples appears to be significantly lower compared than those of PLB and LLB specimens [14]. With regard to technical success rate, that of TJLB (82%: 84/102) is significantly lower ($P=0.005$) than PLB (100%: 100/100) or LLB (99%: 111/112) [14]. However, Bull et al. [10] reported a success rate of 97% (188/197) in 1983, and a recent meta-analysis including more than 7500 cases revealed a technical success rate of 96.8% [13]. These reports suggest that there is no significant difference between TJLB and others techniques in terms of success rate. The most common reason for failure was inability to catheterize the right hepatic vein. In actual practice, TJLB requires a longer procedure time (40 min) than PLB. A few deaths after TJLB have been reported, with a mortality rate of 0-0.5% [10, 32, 33]; mortality was due to hemorrhage from the liver or ventricular arrhythmia.

Therefore, TJLB should be attempted only by a skilled interventional radiologist or physician experienced in catheterization and cannulation of the internal jugular vein due to its more time-consuming nature, use of intravenous contrast, and the need for a dedicated fluoroscopy suite. In fact, TJLB can be valuable in cases for which PLB is hazardous, or when pressure measurement or venography is also required [34]. Despite the smaller biopsy samples obtained, the impact of TJLB on clinical decision-making appears to be comparable to that of PLB and LLB. In particular, it may help to determine the need for liver transplantation in patients with acute liver failure.

4. Laparoscopic Liver Biopsy (LLB)

There are several approaches for LLB, including PLB under laparoscopic observation, LB through an additional port under laparoscopic observation, or LB combined with another

laparoscopic procedure. LLB allows direct observation of the biopsy site and yields with macroscopic information about the liver surface. This facilitates an adequate sample volume to be obtained, including wedge resection, without sampling error, and also allows laparoscopic confirmation of hemostasis. These are the advantages of LLB in comparison with PLB. If bleeding from the biopsy site persists, compression or coagulation can easily be applied using several types of special forceps.

However, LLB requires general anesthesia and specialized equipment, including insufflation devices and laparoscopic instruments. On the other hand, PLB under laparoscopic observation can be done under local anesthesia using pneumoperitoneum under sedation using midazolam and disoprivan, or under general anesthesia using an abdominal wall lift method [15]. For laparoscopy, pneumoperitoneum is created by N_2O insufflation via a Veress needle, generally inserted to the left of the umbilicus. A second port is added on the right side by inserting a trocar. A 16-gauge True-cut needle is inserted and biopsy samples of the liver can be taken from the left and right lobes under laparoscopic guidance. The biopsy sites can be prophylactically coagulated. Beckmann et al. [14] reported that the complications observed after LLB were bleeding and bile leakage, and that the complication rate (2.7%) was roughly equal to that of PLB (3%) and TJLB (2.9%).

In general, LLB requires a long set-up time for starting the procedure, gas insufflation to create an adequate operative field, preparation of several laparoscopic instruments, and an operating theater. LLB is the most appropriate method for patients who need both a pathological diagnosis of liver dysfunction or tumor and laparoscopic procedures for intra-abdominal diseases.

5. Transgastric Liver Biopsy (TGLB)

For TGLB, Hollerbach et al. [17] have reported an endoscopic ultrasound-guided fine-needle aspiration biopsy procedure for liver lesions. This method is one of several transgastric approaches and can be an alternative to PLB, particularly for patients with a risk of bleeding or small lesions in the liver, although targeting may be limited according to tumor location.

Recently, natural orifice translumenal endoscopic surgery (NOTES) has been introduced, creating no skin scars and involving only minimal invasiveness. NOTES has created a new access route (via the stomach) to the peritoneal cavity. TGLB using NOTES creates no damage to the outside of the body and allows direct observation of the biopsy site inside the body, unlike PLB or TJLB. In an experimental study, Mintz et al. [35, 36] reported successful LB using a hybrid technique that included standard laparoscope vision and surgical endoscopy. As outlined in a white paper from the American Society for Gastrointestinal Endoscopy and Society of American Gastrointestinal and Endoscopic Surgeons [37, 38], for clinical application of NOTES, it is necessary to establish safe access to the peritoneal cavity, complete closure of the access route, prevention of infection, correct intra-abdominal orientation, development of a multitasking platform, methods for management of accidental complications, awareness of unanticipated physiologic events, and training in the technique. In par-

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ticular, infection or bacterial contamination in the abdomen due to opening of the digestive tract is a great concern in NOTES. However, no studies have quantified the bacteriological load to which the peritoneum is exposed during transgastric procedures [19]. Steele et al. [20] reported a pilot feasibility study of transgastric peritoneoscopy and liver biopsy during laparoscopic Roux-en-Y gastric bypass. LB was performed from segment II, III or IVb of the liver to obtain tissue samples adequate for histologic examination. None of patients exhibited any signs or symptoms of intra-abdominal or trocar wound infection after the procedure.

For TGLB [39], under general anesthesia a forward-viewing, double-channel endoscope is advanced into the stomach. Puncture of the gastric wall is performed with a 3-mm cutting-wire needle knife. The puncture site is enlarged to 8mm with a balloon dilator and then the endoscope is advanced into the peritoneal cavity. The peritoneal cavity is then inflated with air through the endoscope. The liver is easily visualized by retroflexion of the endoscope. LB is performed using routine biopsy forceps from the edge of the liver (segment III) (Fig. 1), and hemostasis of the biopsy site is achieved by electrocautery with biopsy forceps (Fig. 2). The gastric artificial orifice is then closed using endoscopic clips.

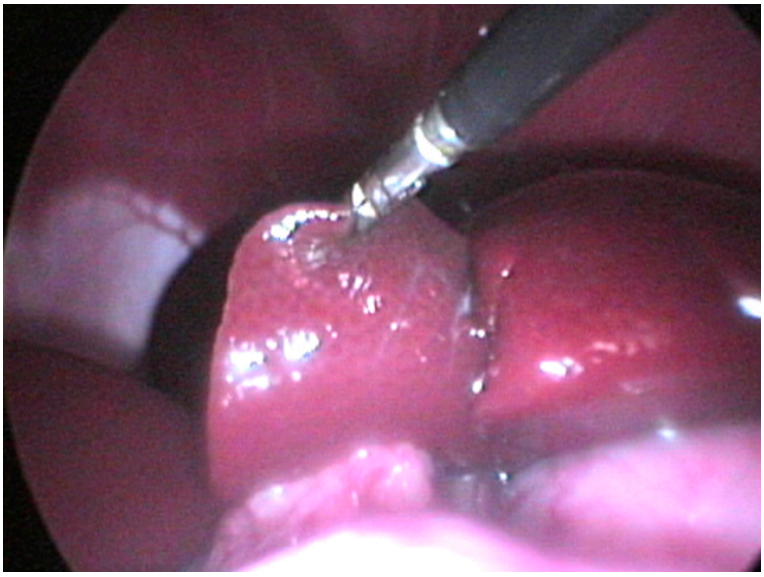

Figure 1. Liver biopsy was performed using routine biopsy forceps from the edge of the liver.

Transgastric peritoneoscopy developed by Kalloo et al. [16, 18] showed no association with serious infection or other complications in the peritoneal cavity during long- term observation. Furthermore, Hazey et al. [40] reported that although contamination of the peritoneal cavity was observed during laparoscopic Roux-en-Y gastric bypass, no clinically significant episode, such as abscess formation or infectious complications, occurred. From these find-

ings, although peroral TGLB requires the creation of an artificial injury in a normal organ, it will likely become a widely used alternative to other LB methods.

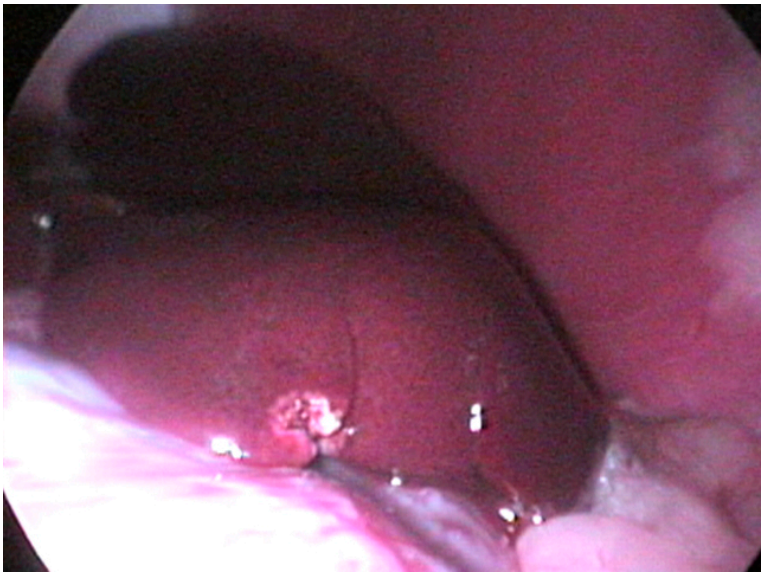

Figure 2. Hemostasis was confirmed at the site of liver biopsy.

6. Conclusion

In conclusion, TGLB is technically feasible and has the potential to become an alternative to routine liver biopsy. The transgastric endoscopic approach has a wide range of diagnostic and therapeutic applications.

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