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How Can We Obtain Tissue from a Subepithelial Lesion for Pathologic Diagnosis?

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See "Mucosal Incision and Forceps Biopsy for Reliable Tissue Sampling of Gastric Subepithelial Tumors" by Sa Young Shin, Sang Jin Lee, Jae Hyuck Jun, et al., on page 64-68.

Currently, endoscopic ultrasonography (EUS) is the best available tool for evaluation of a subepithelial lesion (SEL). However, imaging study alone with EUS does not always provide an accurate diagnosis.¹ If the information provided by EUS on the echogenicity and originating layer of SEL is not typical for an "educated guess," patients may become anxious because of the uncertainty of the diagnosis. In that situation, the endoscopist should try to obtain tissue for definitive pathologic diagnosis of SEL. EUS-guided sampling is the traditional approach, but the diagnostic yield varies widely, depending on factors such as location, size, histological type of lesion, experience of the endosonographer, availability of an on-site cytopathologist, and needle and technique used.²

Various alternative methods for tissue sampling from SEL have been reported. Bite-on-bite biopsy using standard forceps (FB-25K-1: Olympus, Tokyo, Japan; jaw volume 5–6 mm³), with 2–8 bites per lesion, achieved a 38% diagnostic yield (14 of 38 lesions).³ Blood oozing occurred in 14% and was treated with diluted epinephrine injection or clipping.³ In a large cohort, when bite-on-bite biopsy samples were obtained with jumbo biopsy forceps (RJ-4 Boston Scientific, Inc., Natick,

MA, USA; jaw volume 12–13 mm³) in 129 patients with SEL, the median sample size was 12.5 mm (range 3–50 mm), and diagnostic yield was 58.9%.⁴ Significant bleeding requiring endoscopic hemostasis occurred in 35.7%, and admission was needed in 3.1%.⁴

More aggressive endoscopic techniques have been used to acquire tissue samples. Lee et al.⁵ described "endoscopic partial resection with unroofing" to get tissue from SEL. After EUS, they first removed mucosa overlying the SEL with a snare to expose the tumor. Then, they partially resected the exposed tumor with the snare. The median size of lesions was 16.3 mm (range 11.4–25.0 mm). Definitive diagnosis was made in 15 of 16 cases. Blood oozing was frequently noted from the cut surface during the procedure, but was easily controlled by argon plasma coagulation (APC). Dolak et al.⁶ recently reported a retrospective study of endoscopic unroofing for small gastric SELs. After EUS examination, they partially resected the SEL together with covering mucosa in one step, with a single-use polypectomy snare. The mean diameter of SELs was 26±13 mm (range 10–60 mm). Tissue acquisition was possible in 13 of 14 cases. The mean diameter of obtained tissues including covering mucosa was 23±10 mm (range 7–40 mm). This access yielded a histologic diagnosis in 12 of 13 cases. Bleeding occurred in 4 cases during the procedure, and all were managed with clipping and/or APC.

In this issue of *Clinical Endoscopy*, Shin et al.⁷ reported the results of "mucosal incision and forcep biopsy for SEL." After submucosal injection of glycerol solution mixed with indigo carmine, they made a 10-mm linear incision with a hook knife on the top of the mucosa covering the SEL. After

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exposing SEL through the incision site, forcep biopsy was performed. After biopsy (median 8 pieces), the incision site was closed with clips. Definitive pathologic diagnosis was possible in 11 of 12 cases without major complications. All procedures were done on an inpatient basis. A similar technique was previously proposed by de la Serna-Higuera et al.⁸ They described an “EUS-guided single-incision with needle knife (SINK) and deep forcep biopsy” procedure. They first performed EUS examination of SEL and made a 6–12-mm linear incision over the highest convexity zone of the lesion with a conventional needle-knife sphincterotome. The biopsy forcep was introduced deeply through the incision to obtain 3 to 5 samples. The incision site was also closed with endoclips. Pathologic diagnosis was possible in 13 of 14 patients. Among 8 gastrointestinal stromal tumors, immunohistochemical staining was possible in 7 cases. Analysis of malignant potential was feasible in 5 cases. Another method named “bloc biopsy by submucosal endoscopy with a mucosal flap” is slightly different from SINK.⁹ After creating a 10-mm incision near the margin of the SEL, they approached the mass through a tunnel from the incision site by submucosal dissection. Using submucosal endoscopy beneath the mucosal flap, they excised part of the visible SEL by harvesting a 5×5×2 mm block specimen with a needle-knife. The detached surface was closed with clips after the procedure. Pathological diagnosis was attainable in all 8 patients without serious complications. The procedure time was about 50 minutes.

Other researchers implemented more invasive endoscopic procedures to remove the entire SEL endoscopically for simultaneous diagnosis and therapy. Binmoeller et al.¹⁰ introduced “suck-ligate-unroof-biopsy (SLUB)” for small SELs less than 20 mm in diameter on EUS examination. They tightly ligated the base of a SEL with a 20-mm loop placed along the outer rim of an 18-mm oblique transparent cap mounted on the tip of a therapeutic endoscope. Then, they made two perpendicular incisions over the covering mucosa with a needle-knife to unroof the SEL. A tissue specimen was obtained from the exposed lesion using standard forceps. The mean diameter of the SELs was 10 mm (range 6–15 mm). Histologic diagnosis was possible in all 24 SELs without bleeding or perforation. On follow up endoscopy and EUS, no residual lesion was noted due to spontaneous sloughing elicited by ischemic necrosis after ligation. For SELs larger than 20 mm, they used “retract-ligate-unroof-biopsy” technique.¹¹ Using a double-channel endoscope, they simultaneously retracted and ligated the SEL with a 3-pronged anchoring device/rat-tooth forcep and endoloop. Incision and biopsy were performed as for SLUB. The procedure was successful in 13 of 16 cases. Two cases had delayed bleeding that required repeated looping. In addition, SEL enucleation by standard or modified submucosal dissec-

tion technique, submucosal tunnel dissection, and endoscopic full-thickness resection have also been successfully performed with little risk of complications.¹²

There is still no consensus regarding the method of tissue diagnosis for SEL. Although there are reports using various techniques, the numbers of included cases are relatively small and there are few results of long-term follow-up. When histologic diagnosis of SEL is urgent, an easy, safe, and cost-effective method that yields sufficient tissue for accurate diagnosis is necessary. Continuous data collection on various techniques and their analysis are mandatory for consensus. Further development of needles for EUS-guided sampling and accessories for an endoscope will improve the ability to obtain tissue from SEL.

Conflicts of Interest

The author has no financial conflicts of interest.

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