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NOVEL TRANSOESOPHAGEAL APPLICATION OF EBUS-GUIDED CRYOBIOPSY FOR DIAGNOSIS OF A GASTRIC SUBEPITHELIAL LESION

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ABSTRACT

Background: Gastrointestinal subepithelial lesions (SELs) arising from the muscularis propria pose diagnostic challenges, particularly paucicellular tumours such as leiomyomas, which frequently yield insufficient tissue on endoscopic ultrasound -guided fine-needle biopsy (EUS-FNB). Endobronchial ultrasound-guided transbronchial mediastinal cryobiopsy (EBUS-TBMC) achieves superior diagnostic yield over conventional needle aspiration by obtaining intact tissue cores that preserve histologic architecture. Transoesophageal cryobiopsy has been reported for mediastinal lymph node sampling but has not been applied to gastrointestinal wall lesions.

Case report: A 50-year-old man presented with a progressively enlarging gastroesophageal junction mass originating from the muscularis propria (70 × 52 mm). Two EUS-FNB sessions (eight total passes with 19-, 22-, and 25-gauge needles) yielded only scant paucicellular smooth muscle fragments insufficient for definitive diagnosis. Positron emission tomography/computed tomography scan demonstrated fluorodeoxyglucose avidity (SUV_{max} 6.6), raising concern for malignancy. After the patient declined surgical excision and mucosal incision-assisted biopsy referral, transoesophageal cryobiopsy was performed using an EBUS bronchoscope with a 1.1 mm CO_2 cryoprobe advanced through the oesophageal wall under ultrasound and fluoroscopic guidance. Cryobiopsy yielded tissue fragments up to 0.4 cm with preserved architecture. Immunohistochemistry confirmed leiomyoma (SMM+, desmin+, DOG1–, c-kit–, S100–, CD34–), excluding gastrointestinal stromal tumour. The patient developed a post-procedural sterile inflammatory response (C-reactive protein 188.2 mg/l) requiring 3-day hospitalization; imaging excluded perforation. He remains asymptomatic at 3-month follow-up.

Conclusion: Transoesophageal EBUS-guided cryobiopsy can provide diagnostic tissue from gastric subepithelial lesions refractory to standard EUS-FNB. However, the significant inflammatory response underscores the need for systematic safety evaluation, beginning with animal model studies, before broader clinical application.

KEYWORDS

Endobronchial ultrasound, cryobiopsy, transoesophageal, subepithelial lesion, leiomyoma

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LEARNING POINTS

- Transoesophageal endobronchial ultrasound-guided cryobiopsy can yield architecturally preserved tissue sufficient for comprehensive immunohistochemical characterization of paucicellular gastric subepithelial lesions when standard endoscopic ultrasound-guided fine-needle biopsy fails.
- The significant post-procedural inflammatory response observed in this case highlights that the safety profile of transmural cryobiopsy at the gastrointestinal wall remains uncharacterized and requires systematic evaluation before broader application.
- Multidisciplinary collaboration between interventional pulmonology and gastroenterology is essential when adapting bronchoscopic techniques to gastrointestinal indications.

INTRODUCTION

Endobronchial ultrasound-guided transbronchial mediastinal cryobiopsy (EBUS-TBMC) achieves superior diagnostic yield compared to conventional transbronchial needle aspiration (91.8 vs. 79.9%), particularly for benign disorders and lymphomas, by obtaining intact tissue cores that preserve histologic architecture[1,2]. The transbronchial complication profile is favourable (pneumothorax 0.74%, pneumomediastinum 0.37%), though these rates cannot be extrapolated to a transoesophageal route[2].

Gastrointestinal subepithelial lesions (SELs) present analogous diagnostic challenges, making this technique potentially relevant beyond the mediastinum. Pooled diagnostic yields are 84.2% for endoscopic ultrasound-guided fine-needle biopsy (EUS-FNB) and 88.2% for mucosal incision-assisted biopsy (MIAB), but population-based data reveal substantially lower real-world yields for EUS-FNB (63.6% for lesions >20 mm, 22.5% for ≤20 mm)[3,4]. Paucicellular lesions such as leiomyomas are particularly resistant to needle-based diagnosis, as their bland, hypocellular nature often yields insufficient tissue for definitive immunohistochemical (IHC) characterization[4,5].

To our knowledge, this is the first application of transoesophageal cryobiopsy for gastric SEL diagnosis. Although Huang et al. demonstrated the feasibility of transoesophageal cryobiopsy for mediastinal lymph node sampling[6], its application to gastrointestinal wall lesions has not been described.

CASE DESCRIPTION

A 50-year-old man presented with a progressively enlarging gastroesophageal (GE) junction mass. He reported tobacco and alcohol use. Initial EUS (October 2025) identified a lobulated, hypoechoic intramural lesion in the gastric cardia originating from the muscularis propria, measuring 70 × 52 mm. Three transgastric passes with a 22-gauge Acquire FNB needle yielded scant smooth muscle bundles. IHC showed smooth muscle myosin (SMM)-positive, SOX10-negative, and DOG1-negative staining, consistent with smooth muscle tissue but insufficient for definitive diagnosis.

Positron emission tomography/computed tomography (PET/CT) scan (November 2025) demonstrated abnormal circumferential wall thickening at the GE junction (SUV_{max} 6.6), an enlarged perigastric lymph node (2.3 × 1.7 cm, SUV_{max} 2.8), and mildly prominent periceliac nodes (SUV_{max} 1.9), raising concern for malignancy. No distant metastatic disease was identified *(Fig. 1)*.

A second EUS (December 2025) showed the lesion measuring 76 × 46 mm, likely reflecting measurement interobserver variability. Five transgastric passes with 19-gauge and 25-gauge core biopsy needles again obtained only scant bland paucicellular smooth muscle fragments. The 19-gauge needle was selected based on evidence of higher diagnostic yield for muscularis propria lesions (92 vs. 71% for 22-gauge); the 25-gauge was used for supplementary passes given GE junction angulation that limited larger-calibre needle manoeuvrability[5]. IHC showed SMM-positive, S100-negative, and DOG1-negative staining. The pathologist commented that the tissue "might represent muscularis mucosa, or a paucicellular leiomyoma."

The patient declined surgical excision and referral for MIAB at a tertiary centre. After thorough informed consent, including discussion of unquantified risks, absence of prior safety data, and alternatives, the interventional pulmonology team performed transoesophageal cryobiopsy using an EBUS bronchoscope (February 2026). The gastroenterology service was consulted during procedural planning and post-procedure management.

Under general anaesthesia with endotracheal intubation, an EBUS bronchoscope was advanced into the oesophagus under fluoroscopic and real-time ultrasound guidance. The mass was visualized sonographically, and a 21-gauge fine needle aspiration (FNA) needle was used to create an access tract through the oesophageal wall into the lesion. Two FNA passes were performed. A 1.1-mm CO_2 cryoprobe was advanced through the tract under ultrasound visualization with fluoroscopic confirmation. Five transoesophageal cryobiopsies were obtained using 4–6 second freeze cycles, based on the 3–6 second activation times standard for EBUS-TBMC. However, the oesophageal cryoablation literature demonstrates that even 4–10 second surface-applied freeze cycles produce oedema extending to the serosa, with necrosis reaching a median depth of 3.2–4.5 mm[7,8]. The oesophageal puncture

site was left to heal by secondary intention, analogous to standard EUS-FNA practice. Estimated blood loss was minimal around 5 ml; no immediate complications occurred *(Table 1)*.

Same-procedure FNA specimens again showed only bland spindle cell bundles insufficient for definitive diagnosis. Cryobiopsy yielded multiple tissue fragments up to 0.4 cm with preserved histologic architecture. Histology demonstrated bland spindle cell bundles without atypia, mitoses, or necrosis. Comprehensive IHC: SMM positive, desmin positive, DOG1 negative, c-kit (CD117) negative, S100 negative, CD34 negative; confirming leiomyoma and excluding gastrointestinal stromal tumour (GIST)[5] *(Fig. 2)*. This immunophenotype (c-kit–/CD34–/desmin+/S-100–) is characteristic of leiomyoma and distinct from GIST (c-kit+/CD34+/desmin–/S-100–) and schwannoma (c-kit–/CD34–/desmin–/S-100+)[9] *(Table 2)*.

The patient developed substernal chest pain beginning within 24 hours of the procedure and presented to the emergency department on post-procedure day 6. He was hemodynamically stable. Laboratory evaluation revealed leucocytosis (white blood cell count 15.4 $\times 10^3$/µl; baseline 10.1 $\times 10^3$/µl), markedly elevated C-reactive protein (CRP; 118.8 mg/l on admission, peaking at 188.2 mg/l on hospital day 3), elevated erythrocyte sedimentation rate (erythrocyte sedimentation rate; 28 mm/hr, rising to 48 mm/hr), and normal troponin and lactate levels. Blood cultures remained negative.

CT angiography of the chest excluded pulmonary embolism and pneumomediastinum. Gastrografin oesophagram demonstrated no perforation but showed moderate irregular narrowing of the distal oesophagus, consistent with extrinsic compression by the known GE junction mass. CT abdomen and pelvis confirmed the stable GE junction mass without free air. Transthoracic echocardiography showed left ventricular ejection fraction at the lower limit of normal (50–54%) without pericardial effusion.

The patient was admitted for 3 days and treated with intravenous pantoprazole, sucralfate, colchicine (for

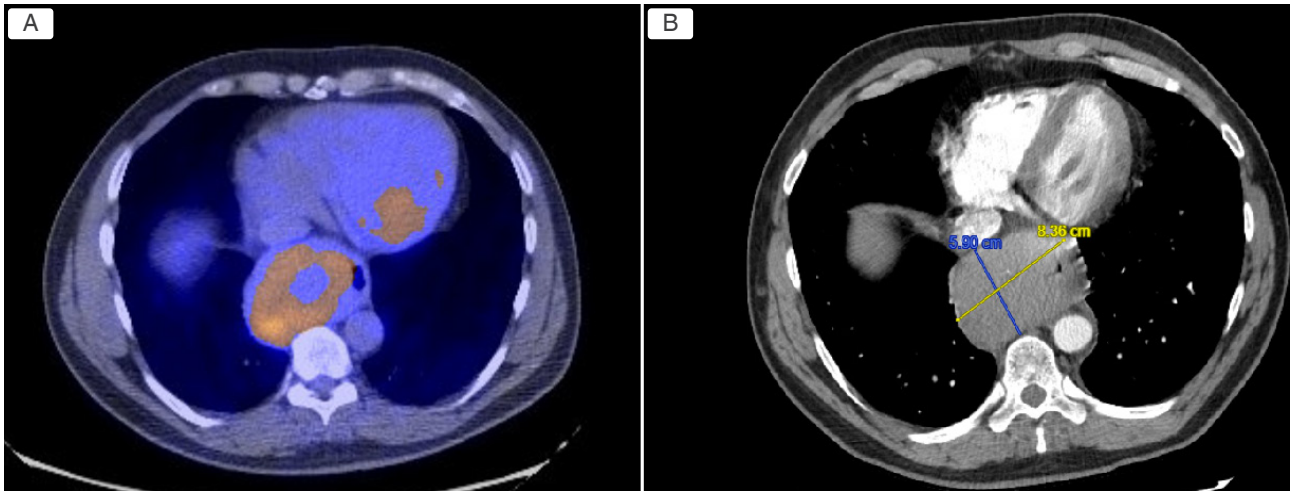


Figure 1. *A) Positron emission tomography/computed tomography scan demonstrating fluorodeoxyglucose-avid gastroesophageal junction mass (SUV_{max} 6.6). B) Computed tomography scan of the chest demonstrating a soft tissue mass at the distal oesophagus/gastroesophageal junction.*

Procedure	Date	Needle/device	Passes	Gross yield	IHC results	Diagnostic outcome
EUS-FNB #1	Oct 2025	22G Acquire FNB	3	Scant smooth muscle bundles	SMM+, SOX10–, DOG1–	Nondiagnostic - insufficient for definitive diagnosis
EUS-FNB #2	Dec 2025	19G + 25G core biopsy	5	Scant bland paucicellular fragments	SMM+, S100–, DOG1–	Nondiagnostic - "muscularis mucosa or paucicellular leiomyoma"
Transoesophageal FNA	Feb 2026	21G FNA (EBUS)	2	Bland spindle cell bundles	Not performed	Nondiagnostic
Transoesophageal cryobiopsy	Feb 2026	1.1 mm cryoprobe (CO_2)	5	Fragments up to 0.4 cm, preserved architecture	SMM+, desmin+, DOG1–, CD117–, S100–, CD34–	Leiomyoma

Table 1. *Summary of tissue acquisition procedures and outcomes.*

Abbreviations: IHC, immunohistochemistry; EUS-FNB, endoscopic ultrasound-guided fine-needle biopsy; FNA, fine needle aspiration; EBUS, endobronchial ultrasound.

pleuritic chest pain, given concern for post-procedural pleuritis/pericarditis), and multimodal analgesia. The clinical picture was most consistent with a post-procedural sterile inflammatory response with pleuritis, though subclinical microperforation with contained mediastinal inflammation cannot be definitively excluded despite negative imaging. The patient was discharged on post-procedure day 9 and remains asymptomatic at 3-month follow-up, with planned continued surveillance of the mass and the unsampled perigastric lymph node.

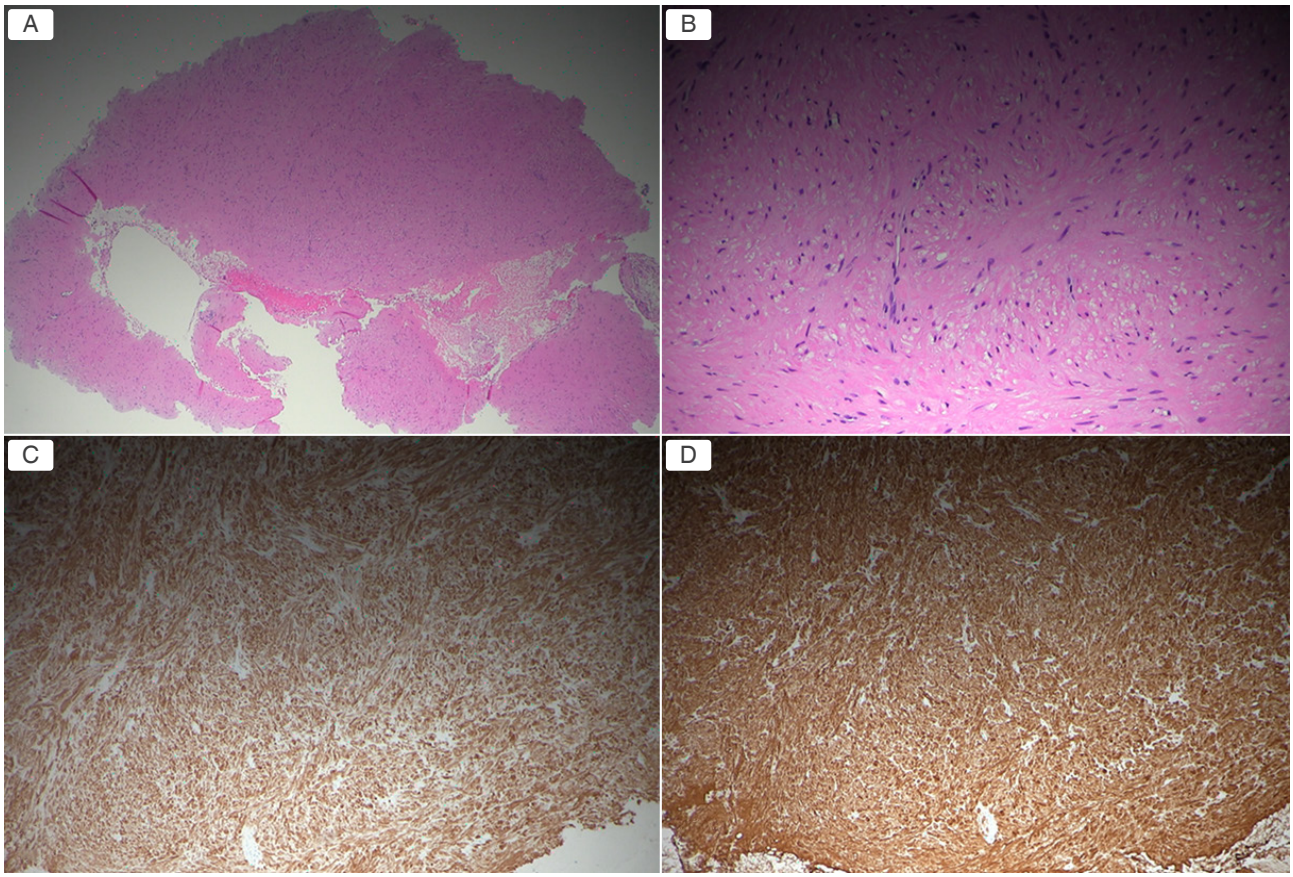


Figure 2. *Histopathology and Immunohistochemistry. A) Cryobiopsy of the gastroesophageal junction mass demonstrated fragments of spindle cell bundles (H&E ×40). B) Higher-power magnification revealed spindle cells with bland nuclei; no atypia, mitotic figures, or necrosis was identified (H&E ×200). C) Immunohistochemical staining demonstrated that the spindle cells were positive for desmin (×100) and D) smooth muscle myosin (×100), with cytoplasmic staining pattern. The spindle cells were negative for gastrointestinal stromal tumour markers, including DOG1 and c-kit (CD117) (not shown), as well as the neural differentiation marker S100 (not shown). The histologic and immunohistochemical findings are consistent with a diagnosis of leiomyoma.*

Marker	Leiomyoma	GIST	Schwannoma	This case
c-kit (CD117)	–	+ (95%)	–	–
CD34	–	+ (60–70%)	–	–
Desmin	+	– (rare +)	–	+
SMM/SMA	+	+/– (30–40%)	–	+
S100	–	– (rare +)	+	–
DOG1	–	+ (98%)	–	–

Table 2. *Immunohistochemical differentiation of gastric spindle cell tumours.*
Abbreviations: GIST, gastrointestinal stromal tumour.

DISCUSSION

This case demonstrates proof-of-concept for transoesophageal cryobiopsy of a gastrointestinal wall lesion when standard EUS-FNA/FNB has failed and established alternatives are unavailable. The same-procedure comparison; FNA yielding nondiagnostic spindle cell bundles while cryobiopsy obtained tissue fragments up to 0.4 cm with preserved architecture sufficient for comprehensive IHC, provides preliminary evidence of the potential superiority of cryobiopsy for paucicellular lesions[4,5].

Transoesophageal cryobiopsy was first reported by Huang et al. for diagnosis of mediastinal nodular lymphocyte-predominant Hodgkin lymphoma, in which the cryoprobe was advanced through the oesophageal wall to sample a mediastinal lymph node[6].

The present case differs in that the cryoprobe targeted the gastric wall itself (a muscularis propria lesion) rather than an extraluminal lymph node. This distinction carries important safety implications: cryothermal injury at a transmural gastric wall puncture site may carry different risks of perforation and inflammatory response compared to a mediastinal lymph node approach, where the oesophageal wall serves only as a transit route.

This technique leverages existing interventional pulmonology skills in EBUS bronchoscopy. Transoesophageal use of the EBUS bronchoscope is well-established for FNA of mediastinal lymph nodes, lung masses, and adrenal glands[10]. The novel element is advancement of a cryoprobe through the oesophageal wall for tissue acquisition from a gastric SEL.

The post-procedure complication; a significant sterile inflammatory response requiring 3-day hospitalization, warrants careful consideration. Although imaging excluded perforation and blood cultures were negative, the markedly elevated CRP (peaking at 188.2 mg/l) underscores that transoesophageal cryobiopsy carries a different risk profile than the transbronchial approach. The oesophageal cryoablation literature provides important context: Schölvinck et al. demonstrated that 4–10 second surface-applied cryoablation produced necrosis ranging from submucosa to serosa at a median depth of 3.2 mm at 48 hours, and Raju et al. showed dose-dependent injury with necrosis limited to mucosa after 15 seconds but extending to muscularis propria after 45 seconds[7,8]. Although the freeze durations used here (4–6 seconds) were shorter, the cryoprobe was advanced through the full thickness of the oesophageal wall rather than applied to the mucosal surface, potentially exposing deeper tissue layers to cryothermal injury at the puncture site.

The cryobiopsy provided definitive confirmation of leiomyoma through comprehensive IHC, which is clinically meaningful for excluding GIST; a distinction that directly affects management, as GISTs may require imatinib therapy and carry malignant potential[5]. However, the enlarged perigastric lymph node was not sampled during any of the three endoscopic procedures, which represents a limitation of this case. While the lymphadenopathy may represent reactive changes related to the large mass, a coexistent process cannot be excluded, and continued surveillance is warranted.

This case raises scope-of-practice considerations. Although transoesophageal EBUS is established for mediastinal staging by interventional pulmonologists, cryobiopsy of a gastric lesion extends beyond the typical scope of practice[10]. Multidisciplinary collaboration with gastroenterology, as performed here, is essential for any future applications.

The American College of Gastroenterology Clinical Guideline recommends EUS-FNB or MIAB as first-line tissue acquisition for SELs[5]. Transoesophageal cryobiopsy should not be considered an alternative to these established approaches but rather a potential salvage option in the narrow clinical scenario where standard approaches have failed, and alternatives are unavailable or declined.

CONCLUSIONS

This proof-of-concept case demonstrates that transoesophageal cryobiopsy (previously reported only for mediastinal lymph node sampling) can be applied to gastrointestinal subepithelial lesions, yielding architecturally preserved tissue sufficient for comprehensive immunohistochemical characterization when standard EUS-guided tissue acquisition fails. However, the significant post-procedural inflammatory response highlights that the safety profile of transmural cryobiopsy at the gastrointestinal wall remains uncharacterized. Systematic evaluation: beginning with animal model studies assessing cryothermal injury depth at transoesophageal puncture sites, followed by a prospective registry is essential before broader clinical application can be considered.

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