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Endoscopic ultrasound-guided tissue acquisition of lymph nodes

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ABSTRACT

One of the most common indications for endoscopic ultrasound (EUS)-guided tissue sampling is to diagnose the etiology of suspicious lymphadenopathy. Although most cases of lymphadenopathy are benign and self-limiting, patients with deep-seated lymph nodes living in tuberculosis endemic areas or with suspected malignancy require tissue diagnosis to guide treatment. Fine-needle aspirate and fine-needle biopsy systems have excellent reliability for evaluating both benign and malignant lymph node diseases. The advent of new technologies and addition of ancillary molecular diagnostics have improved the diagnostic potential obtained by fine-needle sampling. In turn, the clinical applications of EUS tissue sampling have evolved and further expanded to include granulomatous diseases and lymphoma. Optimizing tissue acquisition to obtain high-quality specimens is of utmost importance and may be achieved with operative strategies unique to lymph node sampling. This chapter discusses the powerful clinical impact of EUS-guided lymph node sampling and technical considerations of optimizing diagnostic yield.

1. Introduction

Evaluating lymph node disease is a common and important reason for endoscopic ultrasound (EUS)-guided tissue sampling. Endoscopic technologies can reach lymph node regions throughout various anatomic regions and are limited only by proximity to the gastrointestinal tract. The clinical implications for sampling lymph nodes is extensive, as it includes many diseases that may be both malignant and benign. The endosonographer may consequently be presented with a variety of clinical scenarios in practice and each may require specific technical and clinical considerations to achieve the desired outcome. The primary goal of EUS-guided tissue sampling is making a diagnosis to ultimately guide therapeutic management for the patient. Successful tissue sampling therefore hinges on obtaining an adequate specimen and many technologic advances and new techniques have been described to promote sampling performance for this purpose. The available literature for lymph node sampling is limited, but reveals important technical considerations that should be incorporated in practice. Advances in technologies are also expanding clinical applications for EUS-guided tissue sampling to include essentially any type of malignancy that can metastasize to accessible lymph nodes. This chapter will discuss EUS-guided tissue sampling technique and clinical applications with emphasis on its evolving role for managing granulomatous disease, lymphoma, and non-small cell lung cancer (NSCLC).

2. Echoendoscope systems and equipment

The platform for EUS-guided tissue sampling consists of a suitable echoendoscopic system coupled with a tissue-acquiring accessory needle. There are several systems available including radial and linear scanners, the latter which includes both curvilinear and forward viewing systems [1]. Lymph node sampling is primarily performed using curvilinear echoendoscopes owing to superior needle control and needle visualization [1]. Curvilinear systems have an oblique camera view for direct needle visualization at the scope tip, as well as a distal elevator and balloon for additional control when advancing the needle into tissue [1]. The linear scanner generates a 100-180° ultrasound field that is parallel to the long axis of the scope and is essential for real-time sonographic needle visualization during sampling [1]. In comparison, the cross-sectional radial scanners lack real-time sonographic needle visualization and, while forward viewing echoendoscopes also have a linear scanner, the 90° ultrasound range, lack of elevator, and balloon limit its use for lymph node sampling [2].

Fine-needle aspiration (FNA) and fine-needle biopsy (FNB) are the two types of tissue-acquiring needle accessories used in EUS-guided lymph node sampling. FNA collects an aspirate of target

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cells for cytologic analysis with needles available in four sizes (19, 20, 22, and 25 gauge) [3]. The needle is hollowed to house a removable stylet and this unit is covered with a semi-rigid protective sheath. There is a proximal handle with a port to insert or remove the stylet and to place a syringe for suction during aspiration [3]. The procedure generally involves multiple to-and-fro movements of the needle within the target lymph node, with or without coordinated stylet manipulation and applied suction. The stylet is designed to improve specimen quality by remaining within the needle during passage into the target and reducing amount of normal tissue inadvertently collected during sampling [4,5].

FNB using a newer "core" needle system is being more frequently used and has been gaining traction with certain clinical applications that will be discussed later [3,6]. These systems are designed to collect a core sample with preserved tissue architecture for histologic analysis. There are 19, 22, and 25 gauge needles available and they are also contained within a protective sheath to protect the endoscopic channel [3]. The tissue biopsy is collected by tissue tray cutting mechanism that varies depending on the manufacturer [3].

3. Technical and clinical considerations for lymph node sampling

The primary goal of lymph node sampling is to make a diagnosis and this relies on obtaining an adequate specimen. Effective lymph node sampling is dependent on various technical factors to promote tissue acquisition and show high value in various clinical applications. The following sections will discuss these operative considerations in detail as well as their clinical implications in practice.

3.1. Identifying lymph node targets

Suspicious lymphadenopathy is oftentimes first identified by non-invasive cross-sectional imaging and then followed-up with endoscopic evaluation. Careful EUS examination can further identify lymph nodes to target and promote diagnostic accuracy. Curvilinear scanners offer various scanning modes including B-Mode, color Doppler, pulse wave Doppler, H-Flow, tissue harmonic echo, and elastography to facilitate safe and successful sampling [1]. Lymph nodes larger than 10 mm, with hypoechoic appearance, sharp boarders and/or rounded shape are associated with malignancy and should prompt tissue sampling [7]. Measuring tissue stiffness with elastography is a more recent technology that can add to B-mode evaluation [8]. Reports indicate that elastography can detect areas of high tissue stiffness suggestive of early metastasis in a node that may otherwise appear normal [8]. Once targets are identified with these methods, lymph node sampling is recommended as imaging alone is inadequate to rule out or diagnose malignancy [7].

3.2. Performing EUS-FNA

Successful EUS-FNA is facilitated by technical considerations that optimize performance and circumvent technical failures. Wallace et al [9] demonstrated the primary factors influencing FNA performance in a randomized control trial. They showed sensitivity incrementally increased from 78% to 89%, and then 100% on consecutive passes with the FNA needle and thereafter [9]. They also reported that applied suction during FNA improves sample cellularity, but produces a bloody sample 4.7 times more often and thereby reducing overall specimen quality [9]. Other techniques studied such as sampling lymph node edge versus center and stylet use, demonstrate no significant gains to tissue-acquiring performance [4,5,9]. Interestingly, needle size has also failed to demonstrate superior performance with larger gauge by several groups. Songür et al [10] showed in a prospective study that both 19 and 22 gauge needles achieved similar diagnostic yield for lymph node sampling, 96.3% and 92%, respectively. Similarly, 22 and 25 gauge needles show no difference in FNA performance and diagnostic yield for lymph node sampling [11–13]. Despite no head-to-head differences in needle size, other properties correlating to needle size must be considered for certain cases. The 19-guage needle is more rigid than smaller needles and seems more ideal for sampling hard or calcified lymph nodes, while the more flexible 25-gauge needle may be better for passing through an angulated endoscope tip when targeting lesions through the duodenum.

3.3. FNA and malignant lymph node disease

Evaluating malignant lymph node disease is the most important indication for minimally invasive tissue sampling. EUS-FNA has a sensitivity and specificity between 89.7%-92% and 93%-98%, respectively, with high diagnostic accuracy (up to 98%) for diagnosing malignant lymph node involvement [14–16]. Lymph node EUS-FNA is performed to evaluate for either primary lymphoid cancers or metastasis from gastrointestinal or extra-gastrointestinal origin. Given the extensive reach of EUS-FNA, this includes a role for staging esophageal, gastric, pancreatic, intestinal, liver, rectal, adrenal, ovarian, lung, and other cancers that have metastasized to lymph nodes. Lymphoma and lung cancer represent unique and challenging diagnostic conditions that have evolved with advent of new technologies and will be the focus of this section.

3.3.1. Lymphoma

Lymphoma is characterized as a heterogeneous group of lymphoid cancers with many subtypes, each with their own prognosis and treatment. Surgical excision biopsy to preserve tissue architecture for lymphoma subtyping is ideal to guide medical management. However, deep-seated lymphomas are not readily accessible by surgical methods and EUS-guided sampling offers a minimally invasive diagnostic alternative [17]. EUS-FNA has demonstrated a sensitivity (57%-100%) and specificity (97%-100%) when combined with flow cytometry for diagnosing lymphomas [17]. Unfortunately, the rate of sub-classification with these samples may range from 66% to 100%, meaning that up to 34% of cases may not provide enough information to initiate treatment and this is an ongoing challenge [17]. FNB may theoretically yield more suitable samples for subtyping lymphomas which will be discussed further in the section below [17].

3.3.2. Lung cancer

EUS-FNA plays an important and evolving role in managing lung cancer, a leading cause of death worldwide [18]. Eighty percent of lung cancers are NSCLCs, which unlike small cell lung cancer, may be treated surgically when tumor burden is confined local-regionally [19]. Accurate pre-operative staging is of utmost importance in NSCLC and this represents the majority of cases where EUS-FNA is performed for this disease. Routine mediastinal sampling is indicated for intermediate or high-risk NSCLC (stages IB-IIIA) to evaluated for loco-regional spread despite lack of lymphadenopathy on cross-sectional imaging [19,20]. These recommendations stem from reports showing up to 40% of lymph node metastasis that may not present with lymphadenopathy and even with the addition of PET scans, a tissue diagnosis is need for appropriate pre-operative staging [21,22].