

Diagnosis of lymphoma by endoscopic ultrasound-assisted transendoscopic direct retroperitoneal lymph node biopsy: A case report (with video)

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ABSTRACT

Since its introduction in the early 1990s, endoscopic ultrasound-assisted fine-needle aspiration (EUS-FNA) has been used for sampling of extraintestinal mass lesions and peri-intestinal lymphadenopathy. Although EUS-FNA is highly accurate, lymphomas can be challenging to diagnose using EUS-FNA. We present the case of a 60-year-old male who had experienced upper abdominal discomfort for 1 month. Computerized tomography (CT) examination revealed multiple soft-tissue shadows located above the pancreatic body. The biggest shadow had a cross-sectional area of 7.7 cm × 7.2 cm. Positron emission tomography-CT (PET-CT) imaging showed increased uptake of ¹⁸F-FDG by these soft-tissue shadows. To investigate further, EUS was performed and it revealed the presence of multiple hypoechoic round lymph nodes. During the procedure, EUS-FNA was performed, but only a few dyskaryotic cells were observed by cytological evaluation. EUS-assisted retroperitoneoscopy and lymph node biopsy were performed to obtain more tissue for immunohistochemical analysis and subclassification of lymphoma. Finally, the patient was diagnosed with non-Hodgkin lymphoma, germinal center B-cell-like diffuse large B-cell lymphoma by this technique. EUS-assisted transendoscopic retroperitoneal lymph node biopsy is an alternative procedure for the diagnosis of lymphomas.

Key words: Diagnosis, endoscopic ultrasound, lymph nodes biopsy, lymphoma

INTRODUCTION

In spite of the relatively high accuracy of endoscopic ultrasound-assisted fine-needle aspiration (EUS-FNA) in diagnosing lymphomas, inadequate sampling by EUS-FNA often makes it difficult to perform immunohistochemical analysis, thus limiting its application in the classification of

lymphoma. Natural orifice transluminal endoscopic surgery (NOTES) is a surgical technique by which procedures such as exploration, biopsy, organ resection, and anastomosis can be performed using an endoscope passed through a natural orifice [such as the mouth, stomach, colon (or rectum), vagina, bladder, or esophagus] and then entered into the abdominal cavity, mediastinum, or thoracic cavity through an internal incision. The advantages of NOTES include reduced trauma, faster recovery, absence of scarring, and painlessness, and such procedures have been regarded as third-generation surgery. Here we report an EUS-assisted retroperitoneal lymph node biopsy performed in a patient who had developed enlarged retroperitoneal lymph nodes with an unknown cause. This procedure was carried out on November 10, 2014, after obtaining the approval of the Ethics Committee and informed consent documents signed by the patient.

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CASE REPORT

A 60-year-old male patient was admitted to our hospital complaining of epigastric discomfort, which had persisted for 1 month. A computerized tomography (CT) scan suggested the presence of multiple soft-tissue density masses in the patient's abdominal cavity, the largest of which was 7.7 cm × 7.2 cm [Figure 1a and b]. Positron emission tomography-CT (PET-CT) showed that these masses had abnormal ¹⁸F-FDG uptake [Figure 2a and b]. The patient then underwent EUS examination; multiple enlarged retroperitoneal lymph nodes were found between the body of the pancreas and the gastric wall. We then performed EUS-FNA [Figure 3] to obtain a tissue sample for biopsy. Pathological examination revealed only a few heterotypic cells [Figure 4]. Because of the lack of definite pathological evidence, diagnosis of the patient's condition was extremely difficult.

To obtain adequate tissue samples of the enlarged lymph nodes for immunohistochemical analysis, we performed EUS-assisted retroperitoneal lymph node biopsy. A standard single-channel gastroscope

(EPK-i, Pentax, Tokyo, Japan) was used throughout the endoscopic procedure; a linear array ultrasonic endoscope (EG3830UR; Pentax Precision Instrument Corporation, Orangeburg, NY, USA) was used to evaluate the size of the lymph nodes, their echo characteristics, and localization. A triangle-tip knife and an insulated-tip (IT) knife (both from Olympus Corporation, Tokyo, Japan) were used for resection of the gastric wall and enucleation of the lymph node. A pair of hot forceps (FD-410LR, Olympus Corporation, Tokyo, Japan) was used for gastric wall hemostasis. Metal clips were used for defect closure of the gastric wall.

Adequate preoperative communication with the patient and his family was performed and associated issues including the necessity, feasibility, safety, and probable complications of the operation were explained thoroughly. Any questions raised by the patient were also answered in detail. The informed consent documents were signed by the patient and his family. The preoperative fasting period started

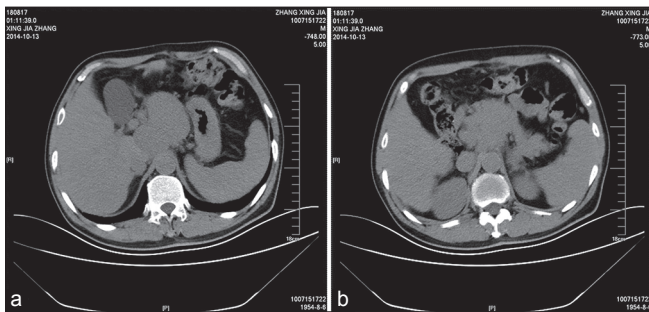


Figure 1. CT scan showing multiple, enlarged soft tissue-density images in the abdominal cavity

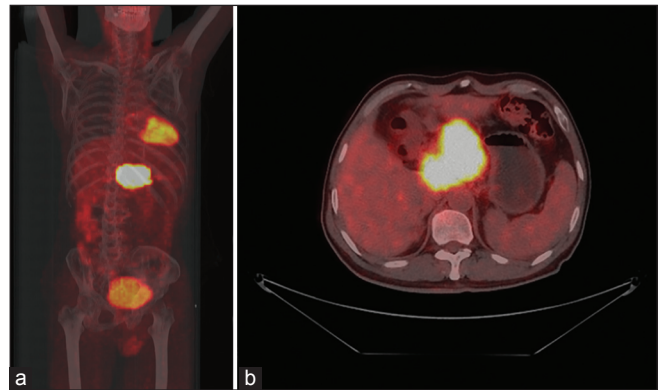


Figure 2. PET-CT showing the accumulation of abnormal radioactivity in soft tissue-density images in the abdominal cavity

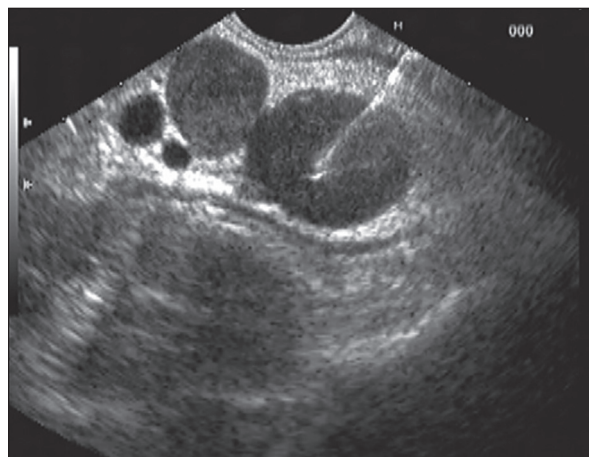


Figure 3. EUS-FNA of a lymph node

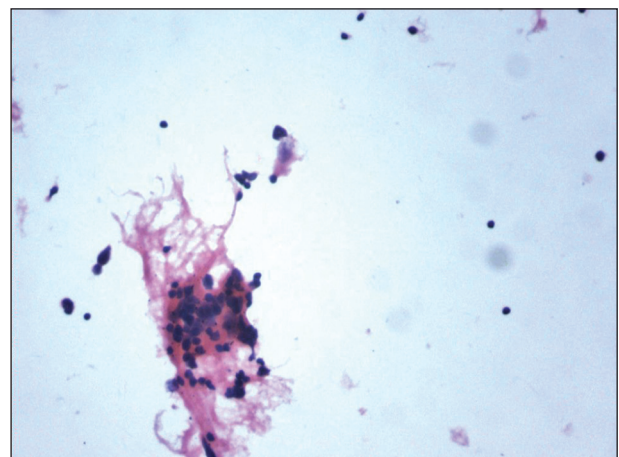


Figure 4. EUS-FNA showing a few heterotypic cells

12 h before the procedure. For the procedure, the patient was placed in a supine position and he received standard intravenous anesthesia with propofol. A linear array ultrasound scanner was passed into the stomach through the mouth. The site nearest to the retroperitoneal lymph nodes in the posterior wall of the gastric body was chosen for puncture. A 22G needle was then used to puncture the lymph node. After the puncture was performed, the stylet was pulled out. A methylthioninium chloride and saline compound solution was injected into the puncture channel for labeling when the needle was retrieved. The lymph node was also marked by a triangle tip knife with the cautery under EUS-guidance. Then, the ultrasound transducer was pulled out; therapeutic gastroscopy with a transparent cap was then performed. A triangle-tip knife was used to incise the full thickness of the gastric wall along the labeled site. The endoscope entered the abdominal cavity through the incision. The triangle-tip knife was used to separate the tissues surrounding the stomach wall sufficiently until the targeted lymph node capsule was exposed. Then, enucleation of the targeted lymph node was performed using an IT knife [Figure 5]. After tissue samples were obtained, the hot forceps were used to stop the bleeding. The endoscope was retrieved from the stomach and the procedure was completed by closing the incision in the stomach wall using metal clips [Video 1]. The lymph node tissue samples were then sent for pathological and immunohistochemical testing. The results showed: CD3(large cell-); vimentin(+); PAX-5(-); CD15(-); CD20(large cell+); CD21(+); Ki-67(large cell8%+); CD30(-); CD68(partly+); CK(-); MUM-1(-); CD10(-); Bcl-6(+); Bcl-2(+). The diagnosis was: Non-Hodgkin lymphoma, germinal center B-cell-like diffuse large B-cell lymphoma [Figure 6].

The patient was given standard postoperative treatments and nursing care including ECG monitoring, ceftazidime

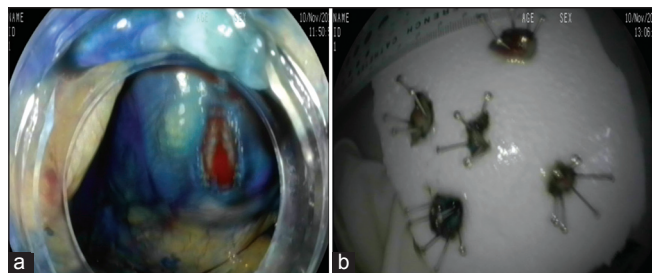


Figure 5. (a) The gastroscopy entered into the abdominal cavity after incision of the full thickness of the gastric wall. The prelabeled lymph node was found, (b) The removed lymph node tissues

as prophylaxis against infection, proton pump inhibitors, and nutritional support. The patient's highest temperature after the procedure was 37.2°C and he only felt mild epigastralgia. The blood test results after the procedure were: White blood cell (WBC) count $12.8 \times 10^9/L$ and percentage of neutrophils 80.3%. The WBC count decreased to $6.5 \times 10^9/L$ and the percentage of neutrophils decreased to 61.8%, 4 days after the procedure. The patient gradually returned to a normal diet and normal physical activities by 3 days after the procedure.

The patient was then transferred to the Department of Hematology to undergo further therapy. The R-CHOP regimen (Rituximab, Cyclophosphamide, Vincristine, epirubicin and Dexamethasone) was used. The patient's pain was reduced significantly and the tumor shrank after chemotherapy.

DISCUSSION

Pathological evidence is an indispensable part of the diagnosis and differential diagnosis of lymphoma and is significant for the classification of lymphomas. Precise pathological classification is critical for the choice of chemotherapeutic regimen in cases of lymphoma.

In the early 1990s, EUS-FNA was first used for tissue biopsy of tumors around the gastrointestinal tract. In spite of its high accuracy, the lack of sufficient tissue material obtained using this technique often renders immunohistochemical staining inconclusive and limits its application in the classification of lymphomas.^[1-4] How to obtain an adequate sample that can be used

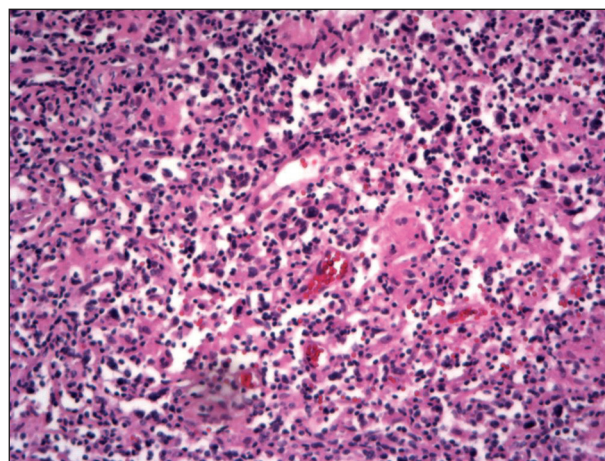


Figure 6. Immunohistochemical staining: CD3(large cell-); Vimentin(+); PAX-5(-); CD15(-); CD20(large cell+); CD21(+); Ki-67(large cell8%+); CD30(-); CD68(partly+); CK(-); MUM-1(-); CD10(-); Bcl-6(+); Bcl-2(+). The diagnosis was non-Hodgkin lymphoma, germinal center B-cell-like diffuse large B-cell lymphoma

for immunohistochemical testing is a primary problem in need of a solution. In a study by Mohamad *et al.*,^[5] the results of EUS-FNA of two patients who had suspected lymphoma were negative. However, positive results were obtained by use of EUS-guided trucut biopsy (EUS-TCB). The authors suggested that the use of EUS-TCB with 19G needle could permit more tissue materials to be obtained in those who had a negative EUS-FNA result. This minimally invasive procedure can be used for the preoperative diagnoses of some difficult cases. Ribeiro *et al.*^[6] analyzed and compared the efficacies of EUS-FNA and EUS-TCB in the diagnosis and classification of lymphoma. Among the 24 included patients, 23 patients underwent EUS-FNA. Only one patient received EUS-TCB alone, while the other 22 patients received both EUS-FNA and EUS-TCB. The results showed that the accurate diagnostic rate of EUS-guided biopsy was 79% (19/24) and the accurate rate of EUS-guided biopsy for classification was just 66.6% (16/24). This indicated that EUS-guided biopsy was of limited value in the classification of lymphoma.

There have been more than 300 reports of NOTES clinical applications from around the world. Over 50 cases of cholecystostomy and endectomy by transvaginal NOTES have been performed in Germany, and 116 NOTES surgeries (including 77 transgastric cholecystotomy cases) have been reported in Brazil. However, there are few case reports regarding the clinical application of NOTES in China. Wang *et al.*^[7] presented a case of laparoscopy-assisted transgastric endoscopic biopsy of a retroperitoneal lymph node. In this case, an endoscopic full-thickness resection (EFTR) with the aid of laparoscopy was used to extirpate an enlarged retroperitoneal lymph node. Pathological and immunohistochemical tests confirmed the diagnosis of retroperitoneal B-cell lymphoma (diffuse large B-cell lymphoma). In recent years, several animal studies using EUS-based NOTES have been promising. These studies showed that EUS was very useful for creating transgastric access and locating the targets.^[8-13]

In this study, we successfully used EUS-assisted NOTES to perform enucleation of a retroperitoneal enlarged lymph node without laparoscopic assistance. Lymphoma was diagnosed and classified using pathology and immunohistochemistry. The use of a minimally invasive

procedure not only enables more tissue materials to be obtained but also causes less trauma than a laparoscopy-assisted approach. In this patient, blood test results recovered to normal levels by 4 days after the procedure and the highest postoperative body temperature was just 37.2°C. He was also able to return to a normal diet 3 days after the procedure. Our experience suggests that this is an alternative and minimally invasive approach for the biopsy of retroperitoneal lymph nodes.

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