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The Utility of Diagnostic Laparoscopic Biopsy for Mesenteric and Retroperitoneal Lymph Nodes

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Case series

Patient: —
Final Diagnosis: **Lymphoma**
Symptoms: **Fever**
Medication: —
Clinical Procedure: —
Specialty: **Hematology**

Objective: **Challenging differential diagnosis**

Background: Ultrasound (US) or computed tomography (CT)-guided biopsy of intra-abdominal lymph nodes is minimally invasive; however, percutaneous procedures are often difficult to perform because of the location and size of the lymph nodes. In many cases, this approach may result in insufficient specimens necessary to evaluate histopathology. In such cases, laparoscopic biopsy is useful to obtain adequate specimens, regardless of the location and size of the lymph nodes. Additionally, laparoscopic biopsy is an approach that can avoid the possible complications associated with a laparotomy.

Case Report: Between 2013 and 2016, a series of 11 patients underwent laparoscopic biopsy of mesenteric and retroperitoneal lymph nodes. All patients received a definitive histopathological diagnosis via laparoscopic biopsy. The median postoperative hospital stay was four days (range 3–13 days), and all patients were able to resume oral intake on postoperative day 1. No case was converted to laparotomy, and no major perioperative complication occurred, except for wound infection in one patient.

Conclusions: Diagnostic laparoscopic biopsy for mesenteric and retroperitoneal lymph nodes is safe and reliable.

MeSH Keywords: **Biopsy • Laparoscopy • Lymph Nodes • Lymphoma**

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Background

A patient presenting with intra-abdominal lymphadenopathy is a common scenario, and malignant lymphoma or metastasis from malignancy in other organs is an important clinical consideration. When a biopsy for diagnosis is necessary, using ultrasound (US) or computed tomography (CT)-guided biopsy methods, such as fine needle aspiration (FNA) and core needle biopsy (CNB), are considered minimally invasive. However, it is often difficult and even dangerous to perform a percutaneous biopsy due to the location and size of the lymph nodes. Mesenteric and retroperitoneal lymph nodes are often adjacent to the intestines, major blood vessels, and other important organs. Moreover, in regard to lymphomas, the diagnosis of an accurate subclassification based on the World Health Organization (WHO) classification of tumors of hematopoietic and lymphoid tissues (which influences treatment and prognosis) requires adequate tissue specimens for specialized studies such as immunohistochemical analysis or flow cytometry, fluorescence *in situ* hybridization, and genetic rearrangement testing. However, an image-guided biopsy frequently provides insufficient specimens to diagnose the subclassification. Previous studies reported that the rate of completely subclassified lymphomas from FNA or CNB specimens was 75–87% [1–3]. In such cases, laparotomy has been the gold standard until recent years; however, this approach can result in postoperative pain and a prolonged recovery time. Recent improvements in laparoscopic techniques and instruments help ensure safety, certainty of providing adequate biopsy specimens, and decreased recovery time. In this study, we reviewed our experience with diagnostic laparoscopic biopsy for mesenteric and retroperitoneal lymph nodes.

Case Report

From January 2013 to December 2016, a total of 11 patients underwent laparoscopic lymph node biopsy for suspected intra-abdominal lymphomas in our hospital. Preoperatively, we examined a whole-body CT scan for all patients to evaluate any palpable lymphadenopathy that could be approached more easily, such as via the inguinal or cervical regions. Furthermore, we decided which lymph nodes to target and planned trocar placement by viewing CT scans and magnetic resonance diffusion-weighted whole-body imaging with background signal suppression (MR-DWIBS) scans (Figure 1A, 1B). When multiple lesions were present, MR-DWIBS was a useful modality that showed which lesion was more likely to be problematic by measuring the value of the apparent diffusion coefficient. Preoperatively, we were able to identify the lesion from the difference of the color contrast such as seen with fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸F-FDG PET/CT) scans. When there were several lesions with

the same level of intensity on MR-DWIBS, we chose the target in the area where we were accustomed to handling such procedures or in the area we could perform easily and safely.

Under general anesthesia, we placed the first 12-mm trocar for the laparoscope in the umbilical area using standard open technique. After a preliminary exploration was performed, two working trocars (5-mm each) were inserted in positions depending on the location of the identified lymph node. In addition, to expose the site of the lymph node, the bowel was retracted cephalad or laterally by tilting the operating table. If necessary, further additional 5-mm trocars were inserted to visualize the lymph node. We obtained an entire lymph node, if possible, or a wedge-resected node sized at least 1 cm³. Especially in the latter case, we attached a suture thread to the excised specimen for the purpose of traction because lymph nodes are often fragile and difficult to grasp with forceps. The specimens were isolated from the surrounding tissue using an ultrasonic scalpel (Figure 1C) and placed in a plastic bag for removal. A suction drain was not placed in all patients. All the specimens were sent directly to the Hematopathology Service Department and reviewed using histologic and cytologic studies, flow cytometry, immunohistochemical analysis, and gene rearrangement studies as needed. Immediately after the histopathology and subclassification diagnosis was determined, the appropriate treatment was started in the Department of Hematology.

Tables 1 and 2 show each patient's clinical characteristics, surgical outcomes, and histopathological diagnosis. A total of nine men and two women with a median age of 64 years (range, 29–85 years) participated in this study. The presenting chief complaints included four complaints of persistent high fever, three complaints of chronic abdominal pain, three incidental findings on the CT scan, and one case of petechiae. Soluble interleukin 2 receptor (sIL2-R) levels were elevated in eight patients (range, 770–5,650 U/mL). None of these patients had palpable superficial lymphadenopathy. Biopsy specimens were obtained from the following sites: three specimens from the small bowel mesentery, two specimens from the lesser curvature of the stomach, one specimen each from the small bowel and transverse colon mesentery, one specimen from the right colon mesentery, one specimen from the left colon mesentery, one specimen from the left iliac artery, one specimen from the right external iliac artery, and one specimen from the pancreas. An entire lymph node biopsy was performed in nine patients, and wedged resection was performed in two patients. In eight patients, three trocars were required. The other patients required placement of four or five trocars to visualize the lymph nodes.

No cases requiring conversion to laparotomy occurred. The mean operative time was 60 minutes (range, 26–85 minutes), and the mean blood loss was 5 mL (range, 1–10 mL). All patients were able to resume oral intake and were mobile on

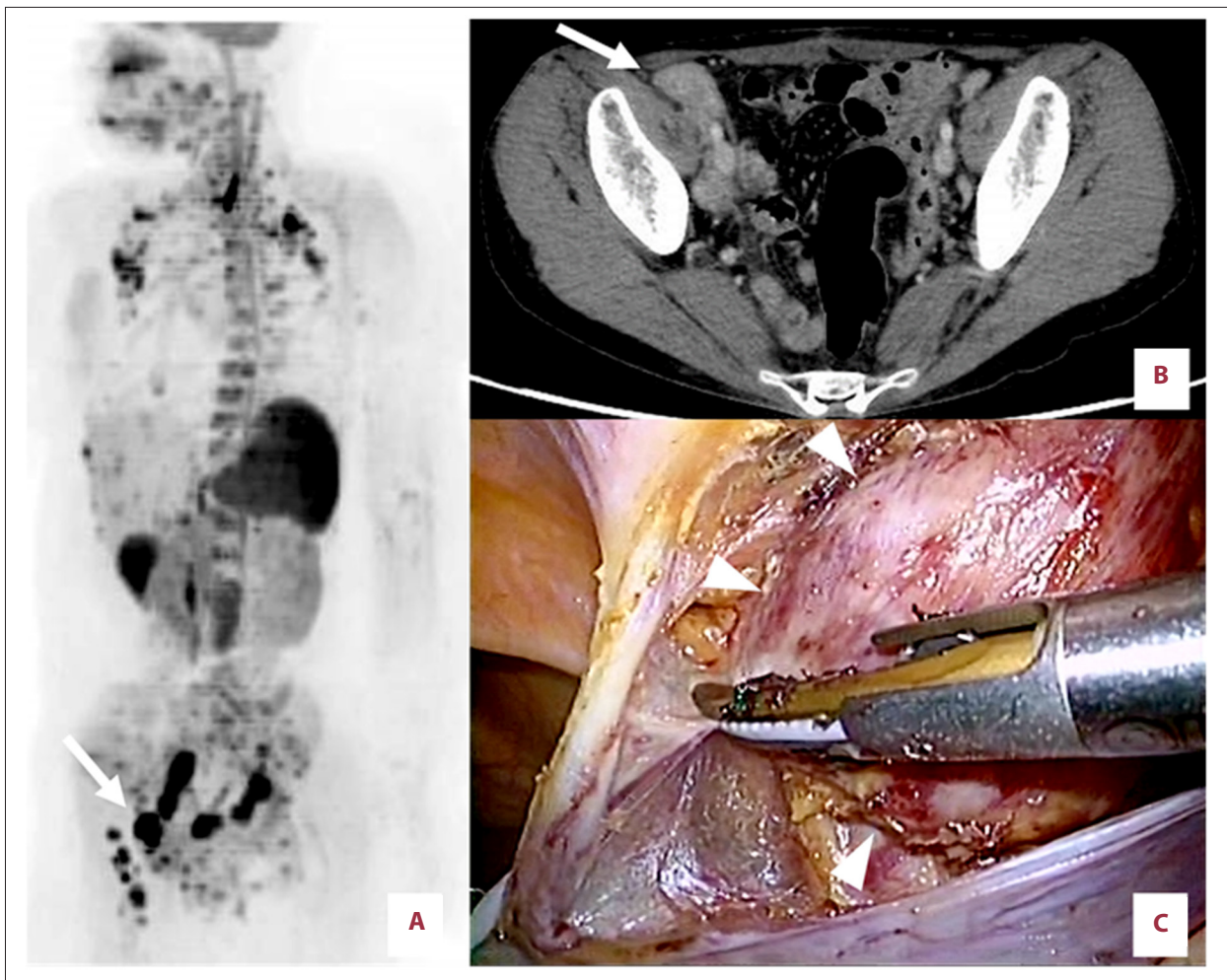


Figure 1. A 50-year-old female was found to have numerous lymphadenopathies during a checkup for the cause of chronic high fever. She had taken methotrexate for rheumatoid arthritis. **(A)** 3-D reconstruction image of magnetic resonance diffusion weighted imaging with body suppression (MR-DWIBS). The maximum signal intensity was identified at the right external iliac artery region (arrow). **(B)** Axial section on computed tomography (CT). CT scan shows the lymph node consistent with the finding of MR-DWIBS (arrow). **(C)** Laparoscopic image. The lymph node (arrow) was isolated circumferentially from the surrounding tissue by using a laparoscopic ultrasonic scalpel.

postoperative day 1. The mean postoperative hospital stay was four days (range, 3–13 days). Two patients had further examination postoperatively and continued hospitalization. No major perioperative complications occurred except for one case that had an umbilical wound infection that met the criteria for grade 1 of the Clavien-Dindo classification system. After reopening the wound, the patient recovered well within one week.

An accurate diagnosis including the subclassification of lymphomas was obtained in all patients. There were three patients with Hodgkin lymphomas, three patients with follicular lymphomas, two cases of diffuse large B-cell lymphomas, one case of methotrexate-associated lymphoproliferative disorder (MTX-LPD), one patient with follicular hyperplasia, and one case of inflammatory granulation tissue.

Discussion

Laparoscopic biopsy and percutaneous biopsy methods such as FNA or CNB are characterized by a low degree of invasiveness for collecting tissue specimens in the case of suspected intra-abdominal lymphomas and these methods offer an alternative to a laparotomy. There are no evidence-based guidelines recommending one technique over the other [4]. However, percutaneous biopsy of mesenteric or retroperitoneal lymph nodes is often difficult due to the location and size of the lymph nodes. In most of our cases, the intestines obstructed the puncture route to the targeted lymph nodes, and the size of the lymph nodes was less than 1.5 cm. Regardless of the location and size, we were able to identify the target lymph nodes, ranging in size from 8 mm to 80 mm, and were able to perform the biopsies laparoscopically.

Table 1. Clinical characteristics.

Case	Age	Sex	Chief complain	IL-2R	Location	Diameter (mm)
1	53	M	Finding by CT	470	Small bowel mesentery	10
2	63	M	Finding by CT	5650	Small bowel mesentery	80*
3	29	M	Finding by CT	277	Right colon mesentery	8
4	66	M	Fever	2240	Left colon mesentery	10
5	64	M	Abdominal pain	3590	Small bowel & transverse colon mesentery	5, 10
6	64	F	Fever	2200	Left iliac artery	20
7	45	M	Petechiae	770	Lesser curvature of the stomach	12
8	50	F	Fever	3480	Right external iliac artery	35
9	72	M	Abdominal pain	5204	Pancreas tail	100*
10	85	M	Fever	4323	Lesser curvature of the stomach	14
11	68	M	Abdominal pain	351	Small bowel mesentery	10

* Wedge resection; CT – computed tomography; sIL2-R – soluble interleukin 2 receptor.

Table 2. Surgical outcomes and histopathological diagnosis.

Case	Op time (min)	Blood loss (mL)	Postoperative stay (day)	Histopathological diagnosis
1	50	5	3	Follicular lymphoma
2	30	10	4	Follicular lymphoma
3	85	10	3	Follicular hyperplasia
4	50	5	8	Inflammatory granulation tissue
5	53	5	5	Malignant B cell lymphoma
6	60	8	5	Hodgkin lymphoma
7	74	3	4	Hodgkin lymphoma
8	69	3	3	MTX-LPD
9	65	1	3	Malignant B cell lymphoma
10	26	1	13	Hodgkin lymphoma
11	69	5	3	Follicular lymphoma

Op time – operation time; MTX-LPD – methotrexate-associated lymphoproliferative disorder.

CNB and FNA typically yielded insufficient specimens necessary to assign the subclassification, and thus ancillary studies are needed. Amador-Ortiz et al. evaluated the accuracy of lymphoma diagnosis using CNB or FNA in a large series of 263 percutaneous biopsies [3]. In this series, a diagnosis was made in 237 cases (90.1%); however, of all the lymphoma cases diagnosed (n=175), a specific lymphoma classification was possible in only 75% (n=131) of the biopsies. Moreover, adequate tissue for immunohistochemical and/or flow cytometric studies was obtained only in 176 (66.9%) and 137 (52.1%) cases, respectively. In a study of 103 image-guided core biopsies by Vandervelde et al., 78% of the biopsies provided a fully graded and subtyped diagnosis of lymphoma with sufficient information to initiate therapy [1].

These results provide the evidence that supports our decision to perform laparoscopic biopsies for mesenteric and retroperitoneal lymph nodes as a first approach. When re-biopsy via a surgical procedure under general anesthesia is needed, a prolonged period of time is needed to confirm the diagnosis including the subclassification. Furthermore, getting a correct histopathological diagnosis is very important to ensure making the best decision about treatment options. As for lymphomas in particular, the selection of the chemo-radiotherapy regimen for the different lymphoma types can be very different. Performing a biopsy is a diagnostic step, and treatment should be started as soon as possible, especially when urgent chemotherapy is required for patients suspected of having a high-grade malignant lymphoma.

In our small case series, there were no conversions to laparotomy. The outcomes of operative time, blood loss, and complications were acceptable. All patients received an accurate diagnosis including subclassification of the lymphoma without any false-negative results. Asoglu et al. reported that conversion to laparotomy was necessary in 17% of 94 patients because of inadequate exposure and insufficient tissue, and the laparoscopic procedure resulted in false-negative results in 6% of patients [5]. Diulus et al. reported that 13% of 30 patients required conversion to laparotomy due to difficulty identifying the mass, an inadequate sample, and uncontrolled bleeding, and that 10% of their patients had false-negative results [6]. To avoid conversion to laparotomy or false-negative results, sufficient exposure of the targeted lymph node and an adequate quality/quantity of the specimen are very important. Unstinted additional trocars make a substantial contribution to visualization. However, especially in the cases of obese patients, we often have difficulties even identifying the target during surgery. In such cases, exposure of the anatomical landmarks, such as vascular bifurcation, is helpful for the target orientation. If the targeted lymph node is well visualized, isolating it from surrounding tissues becomes safe, and blood loss is minimized. When multiple small lesions are present, a blind single biopsy may lead to an inadequate specimen in terms of the quality and quantity needed for an accurate diagnosis. In such a case, preoperative MR-DWIBS helps to select a targeted biopsy site that is more likely to be a lesion, or several biopsy specimens should be obtained by utilizing the laparoscopic advantage of the biopsy of multiple sites from almost any intra-abdominal location. Although ^{18}F -FDG-PET/CT is currently regarded as the standard imaging modality in the staging of lymphoma, MR-DWIBS is of great interest as an emerging and promising functional whole-body imaging modality to evaluate oncologic and non-oncologic lesions, resulting in images that remarkably resemble ^{18}F -FDG PET/CT studies. Several

studies reported that MR-DWIBS was useful for initial staging of lymphoma or monitoring the response to treatment compared to ^{18}F -FDG PET/CT [7–10]. Furthermore, in contrast to previous reports, we do not routinely perform intra-operative frozen section consultation because we identify the most likely lesion by MR-DWIBS preoperatively. We have not seen a decrease in definite diagnostic rate without this frozen section diagnosis. The strategies presented in this study have the possibility of reducing the rates of conversion to laparotomy and false-negative results, and shortening the operative time.

Casaccia et al. reported that no major postoperative complications or mortality occurred in 36 patients who underwent laparoscopic lymph node biopsy [11]. Diulus et al. and Cavaliere et al. also reported that no postoperative complications occurred in any patients [6,12]. Asoglu et al. reported that the only intra-operative laparoscopic complication was a case with a previously undiagnosed neuroblastoma that required a laparotomy was hemorrhage [5]. Thus, although only a few studies have reported on laparoscopic biopsy for intra-abdominal lymphadenopathy, their results confirm that laparoscopy is a safe procedure and serves as an alternative to laparotomy.

Conclusions

Diagnostic laparoscopic biopsy for mesenteric/retroperitoneal lymph nodes is a safe and reliable procedure to obtain adequate specimens for diagnosing suspected lymphomas, regardless of the location and size of the lymph nodes.

Conflict of Interest

None.

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