ORIGINAL ARTICLE

Pancreatobiliary Lymphadenopathy: Etiology, Location, and Factors Predicting Good Yield of Endoscopic Ultrasound-guided Biopsy

Abbas Ali Tasneem[1], Taha Yaseen[2], Syed Mudassir Laeeq[3], Zain Majid[4], Nasir Hassan Luck[5]

Received on: 12 April 2024; *Accepted on*: 14 May 2024; *Published on*: 12 June 2024

Abstract

Introduction: Pancreatobiliary lymphadenopathy (PBL) may be due to a number of benign or malignant causes. Tissue sampling of these lymph nodes (LN) can be possible with the help of endoscopic ultrasound (EUS). Aim of this study was to identify the etiology of the PBL, morphology, and factors predicting good yield of biopsy with EUS.

Materials and methods: All patients found to have pancreatobiliary lymph node (PBLN) enlargement (>10 mm) on abdominal imaging and referred for EUS-guided biopsy were included in this prospective observational study. The facility of rapid on-site evaluation (ROSE) was not available. Adequacy of the tissue specimen was assessed by the endoscopist with macroscopic on-site evaluation (MOSE) and then sent to histopathologist for final diagnosis. Factors predicting good yield of biopsy were then analyzed.

Results: Of the total 87 patients with PBL, 54 (62.1%) were males. Mean age of the patients was 52.0 (±13.4) and range 18–80 years. The commonest locations of PBL were porta hepatis 37 (42.5%), peripancreatic 24 (27.6%), celiac 16 (18.4%), and others 10 (11.5%). Histological reports showed: neoplastic tissue in 34 (39.1%), non-neoplastic in 20 (23%), normal lymphoid tissue (27.6%) and suboptimal in 9 (10.3%). Among the 34 neoplastic causes, 26 had metastatic adenocarcinoma, 5 had lymphoma, and 3 had metastatic neuroendocrine tumors. Among the 20 non-neoplastic causes, 10 had tuberculosis, 4 had anthracosis, and 6 had other findings. Factors predicting good yield of biopsy were a PBLN size ≥12 mm and satisfactory MOSE on both univariate [PBLN ($p = 0.005$); MOSE ($p < 0.0001$)] and multivariate [PBLN ($p = 0.011$); MOSE ($p < 0.0001$)] analysis.

Conclusion: The commonest etiology of PBLN enlargement was metastatic adenocarcinoma among the neoplastic causes and tuberculosis among the non-neoplastic causes. The most common PBLNs approached by EUS were in portahepatis and peripancreatic regions. A good biopsy yield can be predicted with PBLN size of ≥12 mm and a satisfactory MOSE.

Keywords: Endoscopic ultrasound, Etiology, Macroscopic on-site evaluation, Pancreatobiliary lymph nodes.

Euroasian Journal of Hepato-Gastroenterology (2024): 10.5005/jp-journals-10018-1433

Introduction

Pancreatobiliary lymphadenopathy (PBL) can be due to a number of causes including neoplastic as well as non-neoplastic causes. The neoplastic causes may in turn be primary, like lymphoproliferative disorder, or secondary like metastatic disease from various sources like liver, biliary tract, gallbladder, pancreas, or other organs of the body. The non-neoplastic causes can include various chronic infections like tuberculosis and brucellosis or inflammatory disorders like sarcoidosis or connective tissue disorders. Besides, certain etiologies manifest themselves more commonly in particular locations: lymphomas in retroperitoneal regions and metastatic disease in hepatic hilar regions.[1] Also, some morphological characteristics of enlarged lymph nodes (LN) are specific for some diseases: matted lymphadenopathy for tuberculosis and rounded shape for malignancies.[2]

In order to treat the underlying cause, it is essential to obtain a specimen of the tissue from the affected pancreatobiliary lymph node (PBLN). This is possible through various means including surgical, radiological, or endoscopical. Whereas surgery is rather more invasive, the radiological routes are more convenient because administration of general anesthesia is not required. However, the location of the lymph nodes may sometimes make the radiological approachability more difficult. In these circumstances, the endoscopic ultrasound (EUS) can be of particular advantage because abdominal locations like the portahepatis, perihepatic, peripancreatic, and celiac regions are far more easily accessible with EUS scope in stomach than with the conventional transabdominal ultrasound or computed axial tomography (CAT) scan.[3]

The neoplastic etiologies of the PBLN may be somewhat similar in the various geographic regions of the world but the non-neoplastic ones may be different because of the endemicity of certain infections in any particular region. Also, since the yield of biopsy should be maximum to make a proper histologic diagnosis, it is important to identify the factors that are associated with it.

[1–5]Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation, Karachi, Sindh, Pakistan

Corresponding Author: Taha Yaseen, Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation, Karachi, Sindh, Pakistan, Phone: +92 3312812391, e-mail: raja_taha101488@hotmail.com

How to cite this article: Tasneem AA, Yaseen T, Laeeq SM, *et al*. Pancreatobiliary Lymphadenopathy: Etiology, Location, and Factors Predicting Good Yield of Endoscopic Ultrasound-guided Biopsy. Euroasian J Hepato-Gastroenterol 2024;14(1):40–43.

Source of support: Nil

Conflict of interest: None

© The Author(s). 2024 Open Access. This article is distributed under the terms of the Creative Commons Attribution 4.0 International License (https://creativecommons.org/licenses/by-nc/4.0/), which permits unrestricted use, distribution, and non-commercial reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The Creative Commons Public Domain Dedication waiver (http://creativecommons.org/publicdomain/zero/1.0/) applies to the data made available in this article, unless otherwise stated.

The aim of this study was to identify the etiology of the PBLN and recognize the factors that predict a good yield of biopsy.

Materials and Methods

This was a prospective observational study that was performed in the Department of Hepatogastroenterology, Sindh Institute of Urology and Transplantation, from October 2020 to December 2023. All patients of either gender or any age, with PBLN and referred for endoscopic ultrasound were included in the study. Informed consent was obtained from all patients participating in this study. The study was done in accordance with the Helsinki declaration of 1975, as revised in 2000.

Bio-data of all the patients was recorded in the prestructured proforma. History, clinical examination and relevant laboratory investigations were documented. The EUS procedure was performed as a daycare procedure and patients were asked to come in the fasting condition to our endoscopy unit on the day of the procedure. Majority of the procedures was done under conscious sedation, while general anesthesia was administered only if necessary, for instance, to children below age 16 years or those adults who could not tolerate the procedure under mild sedation.

The equipment used was Pentax (linear) echoendoscopes. Morphological characteristics of the PBLN including their size and location were noted. Type and size of the needle used and the number of passes performed were documented. A lymph node size (largest diameter) measuring greater than 10 mm was considered as enlarged lymph node. Needles used for biopsy were fine needle aspiration (FNA) and fine needle biopsy (FNB) (Boston scientific and Cook). The bore of the needles used was 22G and 19G. The facility of rapid on-site examination (ROSE) was not available. Therefore, macroscopic on-site evaluation (MOSE) was performed by the endoscopist. Macroscopically, the procurement of at least one worm-like, continuous tissue core fragment at least 1 inch long was considered as satisfactory MOSE. The secured tissue specimen was sent to the expert histopathologist for diagnosing the disease. The tissue was placed in formalin for histopathologic analysis. Various specialized tumor markers were used by histopathologist to identify the origin of the metastatic neoplasm. The diagnosis described on the final histopathological report was recorded. Histopathologically, a biopsy specimen was considered good yield if it was enough for establishing diagnosis.

The data were entered and analyzed on Statistical Package for Social Sciences (SPSS) version 26. Clinical characteristics were described in terms of mean and standard deviation for quantitative variables like age, and as frequencies and percentages for qualitative/categorical variables like gender. Predictors of good yield were identified using Chi-square and Fisher exact test. Variables found to be significant on univariate analysis were used to perform multivariate analysis. A p-value of <0.05 was considered as significant.

Results

Of the total 87 patients with PBL, 54 (62.1%) were males. Mean age of the patients was 52.0 (±13.4) and range 18–80 years. About three-fourths of the patients with enlarged PBLN had ages above 45, i.e., 63 (72.4%); while about one-fourth of the patients had ages 45 or less, i.e., 24 (27.6%). The commonest locations of PBL were porta hepatis 37 (42.5%), peripancreatic 24 (27.6%), celiac 16 (18.4%), and others 10 (11.5%) (Table 1). Among the other locations were the para-aortic, perihepatic, and perigastric. The mean largest dimension of the PBLN was 19.7 (±13.4) mm with range 6–88 mm; while the mean smallest dimension was 13.3 (±12.2) mm with range 4–87 mm.

Table 1: Location of the various pancreatobiliary lymph nodes approached for endoscopic ultrasound-guided biopsy (n = 87)

S. No.	*Location*	*No. of patients*	*Percentage (%)*
1.	Porta hepatis	37	42.5%
2.	Peripancreatic	24	27.6%
3.	Celiac	16	18.4%
4.	Others	10	11.5%
	Para-aortic	5	5.7%
	Perihepatic	4	4.6%
	Perigastric	1	1.1%

Table 2: Etiological findings of pancreatobiliary lymphadenopathy biopsied through endoscopic ultrasound (n = 87)

		Number	*Percentage*
A.	Neoplastic PBLN	34	39.1%
	1. Metastatic adenocarcinoma	26	76.5%
	• Biliary tract (bile duct/gallbladder)	12	
	• Pancreas	9	
	• Unknown origin	3	
	• Hepatocellular carcinoma	2	
	2. Lymhoma	5	14.7%
	• **Non-Hodgkin's lymphoma**	4	
	• B-cell lymphoproliferative disorder	2	
	• Diffuse large B-cell lymphoma	1	
	• Follicular B-cell lymphoma	1	
	• **Hodgkin's disease (recurrent)**	1	
	3. Neuroendocrine tumor	3	8.8%
	• Small cell neuroendocrine cancer	2	
	• Poorly differentiated NE cancer	1	
B.	Non-neoplastic PBLN	20	23%
	1. Tuberculosis	9	
	2. Anthracosis	4	
	3. Other findings	7	
C.	Normal lymphoid tissue	24	27.6%
D.	Suboptimal tissue	9	10.3%

The etiologies of the various PBLN are shown in Table 2. Notably, neoplastic etiology was found to be present in 34 (39.1%), non-neoplastic in 20 (23%), normal lymphoid tissue (27.6%), and suboptimal in 9 (10.3%). Among the 34 neoplastic causes, 26 had metastatic adenocarcinoma, 5 had lymphoma, and 3 had metastatic neuroendocrine tumors. Among the 20 non-neoplastic causes, 10 had tuberculosis, 4 had anthracosis, and 6 had other findings. The frequency of the various perigastric locations (approachable with endoscopic ultrasound scope) of PBLN affected by various diagnoses is shown in Table 3. The age-group affected by the various common causes of PBLN is shown in Table 4.

A statistical analysis of the factors associated with good yield of biopsy is shown in Table 5. Factors predicting good yield of biopsy were found to be a PBLN size ≥12 mm and satisfactory

Table 3: Frequency of perigastric locations affected by the common causes of pancreatobiliary lymphadenopathy

	Location of the pancreatobiliary lymph nodes				
Diagnosis	*Portahepatis*	*Peripancreatic*	*Celiac*	*Para-aortic*	*Others*
Metastatic cancers (29)	13	8	6	0	2
Lymphoma (5)	1	2	0	2	0
Tuberculosis (10)	3	4	2	1	0
Anthracosis (4)	0	1	1	1	1

Table 4: Age-groups affected by the various etiologies of pancreatobiliary lymphadenopathy

	Age-groups	
Diagnosis	*>45 years*	*≤45 years*
Metastatic cancers ($n = 29$)	24	5
Lymphoma ($n = 5$)	3	2
Tuberculosis ($n = 10$)	5	5
Anthracosis ($n = 4$)	4	0

MOSE on both univariate [PBLN ($p = 0.005$); MOSE ($p < 0.0001$)] and multivariate [PBLN ($p = 0.011$); MOSE ($p < 0.0001$)] analysis. The performance of MOSE in predicting good yield of biopsy is shown in Table 6. With the criteria, we used for satisfactory MOSE, the sensitivity, specificity, positive predictive value, negative predictive value, and diagnostic accuracy of MOSE in predicting good yield of biopsy were 88.4, 88.9, 98.6, 47.1, and 88.5%, respectively.

Discussion

In our study, we found that the neoplastic etiologies were more common than the non-neoplastic ones. Among the neoplastic etiologies, metastatic adenocarcinoma was the most common and most of these cancers originated from the biliary tract or from the pancreas. A study done by Pausawasdi from Thailand showed that the commonest etiologies of abdominal lymphadenopathy, as evaluated by EUS-guided biopsy, were metastatic disease, lymphoma, and tuberculosis.[4] These results are similar to ours, demonstrating that patients of Asian countries share somewhat similar demographic characteristics. Another study done by Korenblit from USA showed that metastatic cancers and lymphoma accounted for majority of the patients with abdominal lymphadenopathy biopsied through EUS.[5] They also demonstrated that the majority of the lymph nodes targeted were perigastric, periportal, and peripancreatic. In our study, the greatest number of lymph nodes targeted was in the porta hepatis region, possibly because most of the patients referred to us were those who had undergone endoscopic biliary stent for common bile duct structure and were strongly suspected to have cholangiocarcinoma. Similarly, a study done by Krishna from USA that evaluated periportal lymphadenopathy without identifiable pancreatic or liver malignancy, found that a significant number of patients harbor malignancy and other pathologic processes including granulomatous disease.[6] In our study, the commonest cause of benign pathology was tuberculosis. This was confirmed by the presence of caseating granulomas on histopathology. A study done by Rao from India, shows that EUS-FNA/B has a high diagnostic yield with a good sensitivity and specificity in the evaluation of intra-abdominal lymphadenopathy due to TB.[7] Moreover, it also indicates the prevalence of tuberculosis in Asian countries and the need to take appropriate measures to control its spread. In our study, we also found that a significant number of patients had normal mature lymphoid tissue that was devoid of any findings suggestive of malignancy or other benign pathology. A study by Wang from China showed that among the benign causes of intra-abdominal and mediastinal lymphadenopathy, non-specific inflammation was the commonest finding followed by tuberculosis.[8] These findings reflect the resemblance of results of PBLN biopsies among the different parts of the world. However, these normal biopsies may also represent misdiagnosing the disease because EUS-guided biopsies secure only a tiny part of the lymph node tissue that may not be carrying features of the disease present in other parts of the lymph node.

Among the various factors associated with good yield of biopsy, we found that large size of the PBLN and satisfactory MOSE showed statistical significance. A study by de Moura from USA showed that FNB is more preferable than FNA, and is equivalent to FNA plus ROSE in acquisition of abdominal lymph node biopsy.[9] In contrast, we found that size of the lymph node was more important in this regard. Although FNB has been shown to be superior to FNA in tissue acquisition, we did not observe any statistically significant difference, possibly because of our relatively smaller sample size. A study by Mohan from India showed that a MOSE definition of a visible core of tissue with opacity and "wormlike" features of adequate size and length (≥4 mm), showed excellent diagnostic accuracy.[10] We too demonstrated that MOSE was associated with good biopsy yield; however, the definition we employed was the presence of at least one core of continuous worm like tissue with length at least one inch. The diagnostic accuracy of MOSE in our study was 88.5% which is comparable to the work in other parts of the world. A study by So from South Korea, confirms these results and further states that MOSE after EUS FNB has the potential to replace ROSE.[11] Furthermore, another study from the same center by Oh showed that MOSE using filter paper provided adequate histologic samples by minimizing blood contamination.[12] It is quite likely that in the near future even better strategies will emerge that will help in predicting good yield of biopsy.

Conclusion

The commonest etiology of PBLN enlargement was metastatic adenocarcinoma among the neoplastic causes and tuberculosis among the non-neoplastic causes. The most common PBLNs approached by EUS were in portahepatis and peripancreatic regions. A good biopsy yield can be predicted with PBLN size of ≥12 mm and a satisfactory MOSE. In those centers where the facility of ROSE is not available, macroscopic on-site evaluation can prove to be a promising strategy to ensure good yield of biopsy.

Orcid

Taha Yaseen https://orcid.org/0000-0002-5504-5084

Table 5: Factors predicting good yield of biopsy of pancreatobiliary lymph nodes approached through endoscopic ultrasound

	Univariate analysis					
Clinical variable	*Good yield*	*Poor yield*	*Odds ratio*	*Confidence interval*	*p-value*	*Multivariate analysis*
Age						
≤45	19	5	0.258	0.063–1.058	0.107	
>45	59	4				
Gender						
Male	48	6	1.250	0.291–5.377	1.000	
Female	30	3				
Location of node						
PH	34	3	1.545	0.360–6.631	0.727	
Others	44	6				
Size of LN						
≥12 mm	69	4	9.583	2.166–42.395	**0.005***	**0.011****
<12 mm	9	5				
Bore of needle used						
22G	76	9	–	–	1.000	
19G	2	0				
Type of needle						
FNB	64	8	0.571	0.066–4.944	1.000	
FNA	14	1				
Number of passes						
≥2	56	4	3.182	0.781–12.958	0.129	
<2	22	5				
MOSE						
Satisfactory	69	1	61.333	6.852–549.00	**<0.0001**	**<0.0001****
Unsatisfactory	9	8				

*Significant *p*-values in univariate analysis; **Significant *p*-values in multivariate analysis

Table 6: Performance of macroscopic on-site evaluation in predicting good yield of biopsy

	Good biopsy yield	*Poor biopsy yield*	*p-value*
Satisfactory MOSE	69	1	<0.0001
Unsatisfactory MOSE	9	8	
	78	9	

Sensitivity, 88.4%; Specificity, 88.9%; Positive predictive value, 98.6%; Negative predictive value, 47.1%; Diagnostic accuracy, 88.5%

References

1. Wang W, Han C, Ling X, et al. Diagnostic role of endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) in abdominal lymphadenopathy of unknown etiology. Front Med (Lausanne). 2023;10:1221085. DOI: 10.3389/fmed.2023.1221085.
2. de Melo SW Jr, Panjala C, Crespo S, et al. Interobserver agreement on the endosonographic features of lymph nodes in aerodigestive malignancies. Dig Dis Sci 2011;56(11):3204–3208. DOI: 10.1007/s10620-011-1725-8.
3. Tamanini G, Cominardi A, Brighi N, et al. Endoscopic ultrasound assessment and tissue acquisition of mediastinal and abdominal lymph nodes. World J Gastrointest Oncol 2021;13(10):1475–1491. DOI: 10.4251/wjgo.v13.i10.1475.
4. Pausawasdi N, Maipang K, Sriprayoon T, et al. Role of endoscopic ultrasound-guided fine-needle aspiration in the evaluation of abdominal lymphadenopathy of unknown etiology. Clin Endosc 2022;55(2):279–286. DOI: 10.5946/ce.2021.218-IDEN.
5. Korenblit J, Anantharaman A, Loren DE, et al. The role of endoscopic ultrasound-guided fine needle aspiration (eus-fna) for the diagnosis of intra-abdominal lymphadenopathy of unknown origin. J Interv Gastroenterol 2012;2(4):172–176. DOI: 10.4161/jig.23742.
6. Krishna NB, Gardner L, Collins BT, et al. Periportal lymphadenopathy in patients without identifiable pancreatobiliary or hepatic malignancy. Clin Gastroenterol Hepatol 2006;4(11):1373–1377. DOI: 10.1016/j.cgh.2006.09.002.
7. Rao BH, Nair P, Priya SK, et al. Role of endoscopic ultrasound guided fine needle aspiration/biopsy in the evaluation of intra-abdominal lymphadenopathy due to tuberculosis. World J Gastrointest Endosc 2021;13(12):649–658. DOI: 10.4253/wjge.v13.i12.649.
8. Wang J, Chen Q, Wu X, et al. Role of endoscopic ultrasound-guided fine-needle aspiration in evaluating mediastinal and intra-abdominal lymphadenopathies of unknown origin. Oncol Lett 2018;15(5):6991–6999. DOI: 10.3892/ol.2018.8253.
9. de Moura DTH, McCarty TR, Jirapinyo P, et al. Endoscopic ultrasound fine-needle aspiration versus fine-needle biopsy for lymph node diagnosis: A large multicenter comparative analysis. Clin Endosc 2020;53(5):600–610. DOI: 10.5946/ce.2019.170.
10. Mohan BP, Madhu D, Reddy N, et al. Diagnostic accuracy of EUS-guided fine-needle biopsy sampling by macroscopic on-site evaluation: A systematic review and meta-analysis. Gastrointest Endosc 2022;96(6):909–917.e11. DOI: 10.1016/j.gie.2022.07.026.
11. So H, Seo DW, Hwang JS, et al. Macroscopic on-site evaluation after EUS-guided fine needle biopsy may replace rapid on-site evaluation. Endosc Ultrasound 2021;10(2):111–115. DOI: 10.4103/EUS-D-20-00113.
12. Oh D, Seo DW, Hong SM, et al. The impact of macroscopic on-site evaluation using filter paper in EUS-guided fine-needle biopsy. Endosc Ultrasound 2019;8(5):342–347. DOI: 10.4103/eus.eus_34_19.