Original article:

Abdominal lymphadenopathy – A clinical Enigma : Radiologic characterization and pathological correlation

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ABSTRACT:

Introduction: Abdominal lymphadenopathy is a diagnostic dilemma because of its diverse etiological causes. Inaccessibility of abdominal lymph nodes to clinical examination makes radiological imaging indispensable for their detection and characterization . Echotextural alteration on ultrasound & variable enhancement patterns on CT form the basis of differentiation of benign from malignant lymph nodes. FNAC under real time ultrasound guidance is a safe procedure for confirmation of the final etiological diagnosis. The present study was aimed at defining the morphological features of abdominal lymphadenopathy by ultrasonography & computed tomography , compare them for differentiation as benign or malignant & correlate the radiological features with histopathology (FNAC/ Biopsy).

Materials & methods: The study was conducted in the Department of Radiology & Pathology, Patna Medical college Hospital & Rohilkhand Medical College Hospital, Bareilly over a period of 6 years from august 2011 to august 2017. A total of 100 patients with suspected abdominal lymphadenopathy diagnosed on abdominal ultrasound were included. CECT abdomen was done for these patients followed by guided FNAC / histopathological examination of surgically excised lymph node.

Results & conclusions: High resolution gray scale sonography and contrast enhanced computed tomography can reliably define the morphological features of abdominal lymphadenopathy and characterize them as benign or malignant. In malignant cases, further classification as lymphomatous or metastatic was also possible as per our study.

Keywords: Abdominal lymphadenopathy, ultrasound , computed tomography , FNAC.

INTRODUCTION:

Abdominal lymphadenopathy is a clinical enigma both for the clinicians and the radiologists because of its various causes. Radiological imaging is prime modality for detection, localisation, delineation and characterization of enlarged abdominal lymph nodes. The various radiological modalities available for assessment of abdominal lymphadenopathy are Lymphangiography, Ultrasonography (USG), Computed Tomography (CT) and Magnetic Resonance Imaging (MRI). Lymphangiography is now obsolete while MRI is still not being widely used because of technical constraints. Ultrasonography is widely used as an initial sensitive screening imaging modality for evaluating abdominal lymphadenopathy. The criteria utilized to differentiate benign from malignant lymph nodes

include shape i.e. short to long axis ratio (S/L ratio), location and distribution of enlarged abdominal lymph nodes, their echotexture, echogenicity and changes in the surrounding tissues..

Computed tomography has a well defined place in the protocol of imaging of abdominal lymphadenopathy. Differences in location and contrast enhancement patterns of the enlarged lymph nodes are used as criteria to determine etiological cause of lymphadenopathy. Fine needle aspiring cytology (FNAC) of abdominal lymph nodes under sonographic / computed tomographic guidance is a safe and reliable technique for the etiological diagnosis of lymphadenopathy. In view of the paucity of work on this subject and initial encouraging results, present study was undertaken to correlate and assess the role of gray scale ultrasonography and computed tomography so as to improve the diagnostic confidence in evaluating the nature of abdominal lymphadenopathy.

MATERIALS & METHODS:

The study was prospective conducted in the Department of Radiology, Patna Medical college Hospital & Rohilkhand Medical College Hospital, Bareilly, comprising of a total of 100 patients. All these patients were included in the study irrespective of their age and sex.

All patients were worked up in following sequence :

- 1. Clinical assessment & Laboratory Investigations :
- 2. Radiological Investigations : After a detailed clinical workup and laboratory investigations, all patients were subjected to detailed radiological examination which included :
 - a) High resolution 2D gray scale ultrasonography
 - b) Contrast enhanced computed tomography of abdomen and/or pelvis.
 - c) Guided FNAC/ histopathological examination of surgically excised lymph node.

a) Ultrasonography of the abdomen

High resolution gray scale ultrasonography was performed on either a Toshiba Nemio XG machine or an E-Saote My Lab 50 (X vision) machine . Children less than 5 years were examined in non-fasting state but were sedated with syrup pedicloryl, wherever required.

The following gray scale features of the lymph nodes were noted : Location, Number, Size and short to long axis ratio (S/L) of representative lymph node, Echogenicity, Echotexture, Margins, Presence of calcification. Liver & spleen size and echo texture & associated findings such as ascites, pleural effusions and imaging findings in other organs were also noted..

b).Contrast Enhanced Computed Tomography :

CECT of abdomen and/or pelvis was done on **GE BRIGHTSPEED** 16 Slice MDCT scanner. 3% Gastrograffin (Trazogastro) was used as an oral contrast agent. Images were then obtained using helical data acquisition with 10 mm section thickness and pitch of 1.75:1 after giving IV contrast agent (60-80 ml of omnipaque or as required). Thin slices 3 mm or 5mm were also obtained wherever needed.

The size, number, location and enhancement patterns of abdominal lymph nodes were noted. Any associated findings were also recorded.

c).Ultrasound Guided Fine Needle Aspiration :

All the patients were finally subjected to guided fine needle aspiration cytology (FNAC) or histopathological examination of surgically excised lymph node specimen. FNAC was done under local anaesthesia & real time ultrasound guidance.

After preparation of slides, appropriate staining was done in pathology department.

RESULTS:

A total of 100 cases of abdominal lymphadenopathy were evaluated.

Tubercular lymphadenopathy(n=45) and metastatic lymphadenopathy(n=35)) comprised of the majority of cases of abdominal lymphadenopathy. These together accounted for 80% of the cases while Lymphomatous adenopathy was least common (n=20).

Table 1 : Comparison	of Sonographic Features	in Cases of Abdominal Lymphadenopathy.
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				n = 100				
Sonographic features		Tubercul	Tuberculosis		Lymphoma		Metastasis	
		n = 45		n = 20		n = 35		
		No. of	%	No. of	%	No. of	%	
		Cases		Cases		Cases		
Size	a) < 1 cm	-	-	-	-	-	-	
	b) 1-3 cm	36	80	7	35	24	68.5	
	c) > 3 cm	9	20	13	65	11	31.5	
Number	Single	-	-	-	-	2	5.8	
	Multiple	45	100	20	100	33	94.2	
Morphology	Discrete	32	71.1	14	70	23	65.7	
	Confluent	8	17.8	4	20	7	20	
	Both	5	11.1	2	10	5	14.3	
Echogenicity	Hypoechoic	45	100	18	90	31	88.6	
	Hyperechoic	-	-	-	-	4	11.4	
	Echofree	-	-	2	10	-	-	
Echotexture	Heterogenous	28	62.2	-	-	8	22.9	
	Homogenous	8	17.8	20	100	25	71.4	
	Mixed	9	20	-	-	2	5.7	
Margins	Well defined	45	100	14	70	29	82.8	
	Ill defined	-	-	6	30	6	17.2	

TABLE 2 : COMPUTED TOMOGRAPHIC FEATURES IN CASES OF ABDOMINALLYMPHOADENOPATHYn=100

Sonographic feature		Tuberculosis		Lymphoma		Metastasis	
		n = 45		n = 20		n = 35	
		No. of	%	No. of	%	No. of	%
		Cases		Cases		Cases	
Location	Portal	28	62.2	6	30	10	28.5
	Celiac	32	71.1	10	50	20	57.1
	Peripancreatic	29	64.4	10	50	19	54.2
	Para-aortic	6	13.3	15	75	20	57.1
	Interaortocaval	3	6.6	11	55	20	57.1
	Pre caval	3	6.6	13	65	6	17.1
	Pre aortic	3	6.6	15	75	14	40
	Mesenteric	11	24.4	3	15	-	-
	Iliac	-	-	3	15	3	8.5
	Splenic hilum	2	4.4	2	10	2	5.7
	Renal hilum	3	6.6	-	-	3	8.5
	Retrocaval	2	4.4	6	30	5	14.2
	Retroaortic	-	-	-	-	4	11.4
Calcification		4	8.8	-	-	1	2.8

Features		Tuberculosis		Lymphon	na	Metastasis		
		n = 45		n = 20		n = 35		
		Nos.	%	Nos.	%	Nos.	%	
Size	a) < 1 cm	-	-	-	-	-	-	
	b) 1-3 cm	36	81	7	35	24	68.4	
	c) > 3 cm	9	19	13	65	11	31.6	
Number	Single	-	-	-	-	2	5.3	
	Multiple	45	100	20	100	33	94.7	
Location	Portal	28	62.2	10	50	10	28.5	
	Celiac	32	71.1	6	30	20	57.1	
	Peripancreatic	29	64.4	10	50	19	54.2	
	Para-aortic	6	13.3	17	85	22	62.8	
	Interaortocaval	3	6.6	13	65	21	60	
	Pre Caval	2	4.4	13	65	6	17.1	
	Pre Aortic	3	6.6	15	75	14	40	
	Mesenteric	11	24.4	3	15	-	-	
	Iliac	3	6.6	7	35	4	11.4	
	Splenic hilum	2	4.4	3	15	-	-	
	Renal hilum	3	6.6	-	-	3	8.5	
	Retrocaval	3	6.6	8	40	5	14.2	
	Retroaortic	-	-	-	-	4	11.4	
Pattern	Peripheral/Rim	37	82.2	-	-	6	17.1	
of	Homogenous	6	13.3	17	85	22	54.2	
Enhance ment	Inhomogenous	2	4.4	3	15	7	20	
Calcification		4	8.8	-	-	1	2.8	

DISCUSSION

The study group included 45% cases of tubercular lymphadenopathy, 35% cases of metastatic abdominal lymphdenopathy and 20% cases of lymphomatous lymphadenopathy (Hodgkin's and Non- Hodgkin's lymphoma). Tubercular and metastatic abdominal lymphadenopathy accounted for 80% of all the cases with relative predominance of tubercular abdominal lymphadenopathy. Deutch et al reported lymphomatous and metastatic lymphadenopathy as the most common cause of abdominal lymphadenopathy accounting for 94% of the cases in their study (15). This is in variance to findings in our study. A higher incidence of tubercular lymphadenopathy observed in our study could be explained on the basis of a higher prevalence of tuberculosis in our country.

TUBERCULAR ABDOMINAL LYMPHADENOPATHY:

- Portal, celiac and peripancreatic lymph node group were predominantly involved accounting for 62.2%, 71.1% and 64.4% of cases respectively. The lower retroperitoneal lymph nodes were relatively spared. This distribution of involvement of abdominal lymph nodes reflects the lymphatic drainage of involved small bowel. Similar findings were made by Ganesan et al, Kedar et al and Batra et al (4,5,7).
- 71.1% of the cases were observed to have discrete lymph nodes while confluent lymph nodes were seen in 17.8% cases and both discrete and confluent nodes were seen in 11.1% of cases. Such variability in sonomorphology has been reported in various studies(Fig. 1).
- All the cases of tubercular abdominal lymphadenopathy had hypoechoic lymph nodes with well defined margins. Majority of the lymph nodes were heterogenous in echopattern accounting for 62.2% of the cases. Homogenous echopattern was seen in 16.7% while mixed echopattern was seen in 17.8% of the cases. Calcification was seen in 8.8% of the cases. Ganesan et al (4) also reported similar findings.
- On CECT ,peripheral pattern of enhancement of lymph nodes was the most common pattern seen in 82.2% of our cases (Fig.4). Homogenous enhancement was seen in 13.3% of the cases and inhomogenous enhancement was seen in 4.4% of the cases. Similar findings were observed by Hulnick et al, Srivastava et al, Pombo et al, Suri et al and Leder et al (14,17,20,18,21).
- FNAC smear (AFB stain) from tubercular nodes reveal a well-formed epitheloid granuloma in a background of caseous necrosis and lymphocytes. H&E section of the lymph nodes show caseous granuloma comprising of epitheloid cells, langhans giant cells, caseous necrosis & numerous lymphocytes. LYMPHOMATOUS ABDOMINAL LYMPHADENOPATHY
- In the present study 20 cases (20%) had lymphomatous abdominal lymphadenopathy. 70 percent of cases had discrete lymph nodes while 20% cases had conglomerate lymph nodes and 10% had both discrete and conglomerate lymph nodes.
- All the cases had homogenous echopattern with 90% nodes being hypoechoic while 10% were echofree. None of the cases showed heteroechoic echopattern, hyperechogenicity of lymph nodes or lymph node calcification. Hillman et al and Scholmerich et al reported sonolucent echopattern in 83% of lymphoma cased while 23% of their cases showed echofree appearance.(1,2) These findings were consistent with our observation.

- Para-aortic group of lymph nodes was found to be most frequently involved by lymphoma, seen in 75% of cases. These cases were arranged either as a mass surrounding aorta or as a rosette of discrete lymph nodes around aorta (Fig. 2,4).
- On Computed tomography, majority of lymph nodes had homogenous pattern of enhancement (Fig.4)(85%) while inhomogenous pattern of enhancement was seen in 15% of the cases. Similar findings were reported by Srivastava et al and Pombo et al (17,20). Srivastava et al reported homogenous enhancement in 82% cases while Pombo et al reported homogenous enhancement in 92% inhomogenous enhancement in 4% and peripheral enhancement in 4% of their cases.
- Pap stain of FNAC smear and H&E section from lymphomatous nodes show lymphoid cells with coarse chromatin.

METASTATIC ABDOMINAL LYMPHADENOPATHY

- Metastatic abdominal lymphadenopathy accounted for 35% of the cases in our study. Similar findings were reported by Devita et al who found that most of the malignancies increase with age.(32)
- 65.7% had discrete lymph nodes, 20% had confluent lymph nodes(fig. 4) and 14.3% had both discrete and confluent lymph nodes(Fig. 11). These findings were not specific for either differentiating benign from malignant nodes or for type of primary malignancy. Similar nonspecific findings were observed by Deutch et al. (15)
- The distribution of abdominal lymph nodes was primarily in the area of drainage of the primary involved site(Fig 3). Para-aortic group of lymph nodes were found to be most commonly involved in 57.8% of the cases.
- In this study 88.6% of the metastatic abdominal lymph nodes were hypoechoic while 11.4% were hyperechoic in echogenicity. None of the metastatic lymph nodes were echofree. 71.4 percent of cases showed homogenous echopattern while 22.9% had heteroechoic echopattern and 5.7% had both types of echopattern. 81.6 percent of the cases had well defined margins. Calcification was seen in 1 case ,which was a known case of abdominal tuberculosis with carcinoma stomach.
- On computed tomography, metastatic lymph nodes showed homogenous enhancement (Fig. 4) in 54.2% cases, inhomogenous enhancement in 20% and peripheral enhancement in 17.1% cases. Similar findings were observed by Srivastava et al (17). They reported homogenous enhancement in 58%, rim enhancement in 25% and inhomogenous enhancement in 17% of the cases.
- Pap & Giemsa stained FNAC smear from metastatic nodes show malignant epithelial cells arranged in glandular pattern. Hematoxilin & Eosin (H&E) section reveals malignant epithelial cells infiltrating into stroma.

COMPARATIVE ANALYSIS

• On comparative analysis of sonomorphological features of the lymph nodes, lymph node morphology, echogenicity, echotexture, calcification and location were found to be the important criteria for characterization of lymphadenopathy. Number and size of abdominal lymph nodes were not found useful in differentiating benign from malignant lymph nodes. Echofree nodes were pathognomonic for lymphoma.

• Comparative analysis of contrast enhanced computed tomographic findings revealed that number and size of lymph nodes was not useful in characterizing them. Location and pattern of enhancement were found be useful.

CONCLUSION:

The present study concluded that non-invasive imaging modalities like High resolution gray scale Sonography and Contrast enhanced Computed Tomography do help in evaluation and characterization of abdominal lymphadenopathy in an appropriate clinical setting. However, they cannot obviate the need for FNAC /biopsy to reach final diagnosis in all cases.



Fig. 1.Tubercular lymphadenopathy (a) Ultrasound image showing enlarged necrotic mesenteric nodes. (b) Real time ultrasound guided FNAC image showing the needle tip in the node. (c) Thickened small bowel loops in the right iliac fossa. (d & e) Axial CECT image showing necrotic peripherally enhancing upper retroperitoneal nodes. (f). Microphotograph of MGG (May-Grunwald Giemsa) stain of FNAC smear from lymphnode showing ill defined epitheloid granuloma in the background of caseous necrosis.



Figure 2. Tubercular lymphadenopathy . (a). High resolution ultrasound image showing enlarged heterogeneously hypoechoic nodes along with thickening of small bowel loops. (b). Thickened mesentry with multiple enlarged nodes forming a mass-like structure with increased vascularity. (c). Microphotograph of tubercular lymphadenitis. H & E Section showing well formed epitheloid granuloma along with caseous necrosis.



Figure 3. Lymphomatous lymphadenopathy (a). Ultrasound image showing discrete, round to oval enlarged nodes in patient of lymphoma. (b). Diffuse small bowel loop thickening in the same patient. (c) Doppler image showing encasement of the superior mesenteric artery by the enlarged nodes. (d). Microphotograph of Non-Hodgkin lymphoma. Pap stain of FNAC smear of lymphnode showing lymphoid cells with coarse chromatin.



Figure 4. Lymphomatous lymphadenopathy (a). Ultrasound image shows markedly hypoechoic round to oval iliac lymph nodes adjacent to the urinary bladder. (b) Enlarged spleen with multiple hypoechoic lesions. (c&d) Axial CECT image showing enlarged discrete para-aortic and mediastinal nodes with mild homogenous enhancement. (e)Microphotograph of H&E section of lymph node shows multiple lymphoid cells with coarse chromatin.



Figure 5. Metastatic lymphadenopathy (a,b,c) Ultrasound image shows irregular eccentric gall bladder wall thickening with loss of fat planes with liver and entrapped calculus. Enlarged homogenously hypoechoic portal, celiac and para-aortic nodes &liver metastases in the same patient. (d&e) Axial CECT image (in a different patient of carcinoma GB) showing enlarged homogenously enhancing portal and celiac nodes encasing the celiac trunk. Intrahepatic biliary radicles are dilated due to infiltration at the porta by the GB mass.(e) Microphotograph of FNAC smear(MGG stain) of metastatic adenocarcinoma showing epithelial cells arranged in glandular pattern.

REFERENCES:

- 1. Hillman BJ, Haber K : Echographic characteristics of malignant lymph nodes. . Clin. Ultrasound 1980 ;8 : 213-215.
- Scholmerich J, Volk BA : Differential diagnosis of anechoic/hypoechoic lesions in the abdomen detected by ultrasound. J Clin. Ultrasound 1986; 14: 339-353.
- Kriegshauser JS, Corrol BA : The adrenal gland and retroperitoneum in : Rumack CM, Wilson SR, Charbonneau JW eds. Diagnostic ultrasound, Missouri : Mosby year book, 1991 : 289-314.
- 4. Ganesan S, Indrajit IK : US in abdominal lymph node tuberculosis ; A review of 42 cases. Ind. J. Radiol. Imag. 1993; 3 : 231-236.
- 5. Kedar RP, Shah, PP, Shivde RS, Maide HM : Sonographic findings in gastrointestinal and peritoneal tuberculosis. Clinical Radiology 1994; 49 : 24 29.
- Jain R, Sawheny S, Bhargava DK, Manorama Berry : Diagnosis of abdominal tuberculosis : sonographic findings in patients with early diseases. AJR 1995 : 1391-1395.
- Batra A, Gulati MS, Sharma D, Paul SB : Sonographic appearance in abdominal tuberculosis. J. Clin Ultrasound 2000; 233-245.
- 8. Vayner N, Caret A, Pollack G, Weiss B, Hertz M : Mesenteric lymphadenopathy in children examined by US for chronic and/or recurrent abdominal pain : Pediatr Radiol. 2003 Dec; (12) : 864 7.
- 9. Ghazinoor S, Desser T, Jerery RB : Journal ultrasound Medicine 2004, 6 (23), : 837 41.
- Donal B Downey : The retroperitoneum and great vessels. In : Rumack CM, Wilson SR Charboneau JW eda : Diagnostic ultrasound. 3rd Ed.. 2005 : 454 – 459.
- 11. Krishna NB, Gardner L, Collins BT, Agarwal B : Peripheral lymphadenopathy in patients without identifiable pancreatobiliary or hepatic Malignancy : Clin gastronterol Hepatol 2006 Oct 21.
- Simanovsky N, Hiller N : Importance of sonographic detection of enlarged lymph nodes in children; JIUM May 1, 2007, Vol. 26 no. 5 581 – 584. (www.jultrasoundmed.org)
- 13. Parajuli S, Tuladhar A, Basnet RB : Ultrasound and computed tomography guided fine needle cytology in diagnosing intraabdominal and intrathoracic lesions –. Journal of pathology of Nepal (2011) Vol. 1, 17 21.
- 14. Hulnick DH, Megibow AJ, Naaidich DP, Hilton S, Cho KC, Balthazar EJ : Abdominal tuberculosis : CT Evaluation Radiology 1985; 157 : 199-204.
- Deutch SJ, Sandler MA, Alpern MB : Abdominal lymphadenopathy in benign diseases : CT detection Radiology 198; 163 : 335 - 338.
- 16. Pombo F, Rodriguez E, Mato J, Perez FJ, Riveria E, Valvuena L : Patterns of contrast enhancement of tuberculous lymph nodes demonstrated by computed tomography.. Clin Radiology 1992 ; 46: 13 17.
- 17. Srivastava DN. Gupta BS, Vashisnt S, Gupta R, Berry M : Image morphology of abdominal lymphadenopathy on CT. Ind J, Radio imag. 1993; 3 : 121 25.
- 18. Suri S, Kaur H, Wig JD, Singh K : CT in abdominal tuberculosis. Comparison with barium studies. Ind J. Radio. Imag. 1993; 3: 237-242.
- 19. Shah P, Gastrointestinal tuberculosis A review. Ind J. Radio. Imag. 1993; 3: 243 251.
- 20. Pombo F, Rodriguez E, Caruncho MV, Villava C, Crespo C : CT attenuation values and enhancement characteristics of thoracoabdominal lymphomatous adenopathies. J. computed Assist. Tomography. 1994 ; 18 : 59- 62.
- 21. Leder R.A. Low V.H.S. :Tuberculosis of abdomen: RSNA 1995 ; 33 : 691-705.
- 22. Miles K.A., Kelly B.B : CT measurement of capillary permeability within nodal masses : a potential technique for assessing the activity of lymphoma. BJR 1997; 70 : 74-79.

- 23. Rodriguez H, Rehn S.N. Nyman R.S., Sundstrom J.C., Ahlstrom H, glimelius B.L.G : CT in malignancy grading and prognostic grading of Non-Hodgkin's Lymphoma. Acta Radiologica 1999 ; 40 : 191 197. CT.
- 24. Tariq sinan, Mehraj Sheikh, Salwa Ramondan ,Sukhpal Sehwney CT features in Abdominal Tuberculosis 20 years experience. 2002
- 25. Indian Journal of T.B. 2004; 51 : 43-46.
- Yuan Li et al : Session : Gastrointestinal (Abdominal multidetector CT : General) Differentiation between Tuberculosis and lymphoma in abdominal lymph nodes : Evaluation with contrast enhanced multi detector Row CT – RSNA 2005, CODE :SSE09-05.
- Ri-sheng Yu, Wei-Min Zhang, Yi-Qing Liu : CT diagnosis of 52 patients with lymphoma : World J Gastroenterol 2006 Dec. 28; 12 (48) : 7869 – 7873. (www.wjgnet.com)
- Dong P, Wang B, Sun QY, Cui H: Tuberculosis versus Non-Hodgkin's lymphoma involving small bowel mesentery : Evaluation with contrast enhanced tomography. World J Gastroenterol 2008 June; 14 (24) : 3914 – 3918. (www.wjgnet.com)
- 29. Lee M J et al : Para-aortic lymph nodes metastasis in patients with intraabdominal malignancies : CT Vs PET: World J Gastroenterol 2009 Sept. 21; 15 (35) : 4434 4438. (www.wjgnet.com).
- Shaukat A, Shaukat A : Multidetector CT findings in intraabdominal tuberculosis –. Professional Med. Jun. 2010; 17 (2) : 352 – 354.
- Zhang M, Li M, Xu G P, Liu HJ : Neoplasm-like abdominal non-hematogenous disseminated tuberculous lymphadenopathy : CT evaluation of 12 cases and literature review – World J Gastroenterol 2011 Sep. 21; 17 (35) : 4038 – 4043. (www.wjgnet.com)
- 32. Devita JR, VT, Hellman S, Rosengerg S.A., : Cancer principles and practice of Oncology. 1997 5th Ed. ; 232-233, 2243.