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***ULTRASOUND PATTERNS OF ABDOMINAL LYMPHOMA
AT TIKUR ANBESA HOSPITAL***

***A Dissertation as part of the qualifying paper for a
speciality in Clinical Radiology***

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List of abbreviations

AAU –Addis Ababa University

AIDS – Acquired immune deficiency Syndrome

CT – Computed Tomography

CXR – Chest X ray

HIV – Human Immunodeficiency Virus

MRI – Magnetic Resonance Imaging

TASH – Tikur Anbesa Specialized Hospital

US - Ultrasound

1. Abstract

Lymphoma is a general term for a group of cancers that originate in the lymphatic system and it is the most common hematopoietic malignancy.

Overall incidence of lymphoma is increasing globally, with age-adjusted incidence rates for NHL being highest in more developed countries. The incidence is also rising in sub-Saharan Africa where the prevalence of HIV is the highest in this part of the world (1). The lymphomas are divided into two major categories: Hodgkin lymphoma (HL) and non-Hodgkin lymphoma(NHL).

Appropriate management of lymphoma begins with an accurate and precise diagnosis. Traditionally, this has necessitated a surgical (either excisional or incisional) biopsy specimen to obtain adequate tissue.

Lymphomas have been historically staged by Ann Arbor staging system introduced in 1970. This system, however, was modified in 1989 because of the introduction of CT (Costwald staging classification).

Cross-sectional imaging (CT scan, MR imaging, US) is primarily used to detect lymph adenopathy and the pattern of nodal involvement. However, anatomic imagings are limited in accurate lymphoma evaluation as small lymph nodes may harbor malignant cells, whereas large lymph nodes may be benign. Functional imaging, such as positron emission tomography (PET) with fluorodeoxyglucose (FDG), has shown promising results in the diagnosis of lymphoma and complete assessment of the extent of disease. It is also very useful in the follow-up of PET-avid lymphoma (13, 39).

This study reviewed articles on imaging patterns of abdominal lymphoma and using qualitative and quantitative data collecting techniques we give the practicing physicians a good knowledge on ultrasound patterns of abdominal lymphoma.

And our study results showed lymph nodes in the abdomen and other sites are most common to be involved by lymphoma. According to the result liver involvement outnumbered from other abdominal organs. And pathology result showed NHL type is most common in our study .

2. Literature Review

2.1 Lymphoma, epidemiology, pathologic classification, diagnosis and staging

Lymphoma is a general term for a group of cancers that originate in the lymphatic system.

They are divided into two major categories: Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL).

Malignant lymphoma is the most common primary hematopoietic malignancy. The overall incidence of NHL is increasing globally, with age-adjusted incidence rates for NHL being highest in more developed countries. Recent figures from the USA give an incidence of 15.5 per 100 000 persons per year, representing a 73% increase since the early 1970s (1). This is due in part to secondary lymphoma arising in the setting of AIDS, but a steady increase had been noted before the AIDS epidemic (3.7 to 15.5 per 100000). Old African studies showed that anemia's accounted as the commonest hematological disorder while malignancy only accounted for only 3.5% hospital admissions (2). However shamebo in 1987 analyzed the pattern of hospital admissions in Tikur Anbessa hospital and found out that out of 450 hematologic pathologies hematologic malignancies i.e. leukemia and lymphoma accounted for 56% hospital admissions (3). Recent unpublished review of fourteen years data on 13,800 patients with malignancy in oncology department, hematologic malignancy account 1.5% of which lymphoma is the dominant tumor (Dr. Wondimagegn Department of Oncology, AAU).

In 2001, the World Health Organization published a comprehensive classification system for lymphoid neoplasms incorporating entities like morphology, immunology, genetic features, and clinical features. The three large groups are (1) the B-cell tumors, (2) the T-cell and natural killer cell tumors, and (3) HL(4,5).

The lymphomas are next classified as derived from either precursor or mature lymphocytes. More than 30 types of lymphoma are recognized, with clinical behavior spanning from remarkably indolent to profoundly aggressive (6).

Epidemiologic associations for many of the common types of lymphoma remain incompletely understood. Risk factors for certain types of lymphoma can include chronic infection, immunosuppression, and hereditary traits. It is clear that chronic infection can lead to lymphomagenesis, either through direct viral effects (eg, Epstein- Barr virus [EBV] in HL, post-transplantation lymphoproliferative disorder [LPD], and endemic Burkitt lymphoma [BL];

human T lymphotropic virus type 1 [HTLV-1] in adult T-cell leukemia/lymphoma; human herpesvirus 8 [HHV8] and primary effusion lymphoma), or due to chronic stimulation of the immune system (eg, *Helicobacter pylori* gastritis in gastric mucosa-associated lymphoid tissue [MALT] lymphoma; hepatitis C virus in splenic and extranodal marginal zone lymphomas). (7, 8)

Autoimmune diseases may similarly increase the risk of lymphoma through chronic stimulation of the immune system, potentially giving rise to a dysregulated clone of B cells. Specific associations include rheumatoid arthritis and Sjögren's syndrome with both DLBCL and marginal zone lymphomas, and celiac sprue with enteropathy-associated T-cell lymphoma. Immunosuppression clearly confers an increased risk of both HL and NHL, as can be seen in the increased incidence of lymphomas in patients infected by human immunodeficiency virus (HIV) as well as patients on immunosuppressive treatment following solid-organ transplantation(9). Additional risk is associated with environmental stressors such as ionizing radiation (including sunlight), agricultural pesticides, and dark hair dyes before 1980.

Clearly, stressors, be they infectious, inflammatory, or toxic, interact with the host genetic makeup in a complex fashion to lead to lymphomagenesis. It has been established that hereditary risk of lymphoma, while apparently a lesser element epidemiologically, does exist. Odds of developing Hodgkin lymphoma are increased for first-degree relatives of probands, and further increased for siblings of probands. Risks of all types of NHL are increased in first-degree family members of probands, although patterns of apparent heritability vary by subtype(10). At this time, however, no specific genetic testing is available, and screening for family members is not routine.

Distribution of the subtypes of non-Hodgkin lymphoma (NHL) varies worldwide by geographic region. In the United States, more than half of newly diagnosed NHL consists of either diffuse large B-cell lymphoma (DLBCL), an aggressive B-cell lymphoma, or follicular lymphoma (FL), an indolent B cell lymphoma, comprising 31% and 22%, respectively. The 12 most common subtypes of lymphoma (treating Burkitt and Burkitt-like lymphoma as a single disease entity as in the WHO classification) accounts for 88% of new diagnoses of NHL in the United States. (11, 12)

According to the study by Shamebo(3) non hodgkins lymphoma accounts for more than 75% of his series and hodgkins less than 17 % unlike other African studies where the latter account for higher percentage(2).

Further classification based on more advanced lab techniques was not performed to analyze the different sub types in the shamebo series. NHL is also the common type of lymphoma in wondimagegehu's unpublished data.

Appropriate management of lymphoma begins with an accurate and precise diagnosis. Traditionally, this has necessitated a surgical (either excisional or incisional) biopsy specimen to obtain adequate tissue. However, as discussed earlier, the WHO classification is built not only on morphologic criteria but also incorporates immunophenotypic and, in some instances, genetic data in establishing a diagnosis.(13)

Staging is characterized as either clinical stage if it is based on physical examination, routine radiographic evaluation, including cross-sectional imaging of relevant anatomic regions and in select cases functional imaging such as 18F fluoro-2-deoxyglucose positron emission tomography (18- FDG PET) and bone marrow biopsy, or pathologic stage if confirmed by one or more additional surgical staging procedures, such as staging laparoscopy or gastrointestinal endoscopy.(14)

2.2 Abdominal lymphoma: spectrum of finding & organ involvement

All body organ systems can be involved at some stage of lymphoma, including the central nervous system, head and neck, thorax, abdomen, gonads, and bone. However, at onset, nodal and splenic involvements are more common in Hodgkin disease, whereas extranodal involvement is more frequent in non-Hodgkin lymphomas.

The NHL represents a diverse group of cancers, with the distinctions between types based on the characteristics of the cancerous cells. It is the fifth most common cancer in men and women. In NHL, involved lymph nodes tend to be larger as compared with HL. Involvement of nodal groups is common but extra nodal sites are also frequently involved. This includes extra nodal lymphatic tissue (e.g. Peyer's patches in the small bowel, spleen) and non lymphatic organs, such as /the liver, bone marrow, bone, and central nervous system.

Most patients with NHL compared with less than half of the patients with HL have abdominal involvement. Para-aortic lymphadenopathy is the most common finding HL and NHL may present with involvement of one or more lymph nodal groups, of an isolated organ, or as widely disseminated disease. In general, there is a displacement of structures by enlarged lymph nodes without invasion (15, 16)

Hodgkin's lymphoma (HL) is characterized by the presence of an abnormal cell called the Reed-Sternberg cell (a large, malignant cell found in HL tissues). HL is comprised of two disease entities: nodular lymphocyte predominant HL and classical HL, which in turn consists of nodular sclerosis, mixed cellularity, lymphocyte-depleted, and lymphocyte-rich subtypes. It is more common in adults in higher socioeconomic groups and peaks in both the third and the fifth decades of life. In HL, the most common sites of involvement are the cervical lymph nodes and intrathoracic lymphadenopathy (approximately 60%–80% of all patients with HL). Isolated infradiaphragmatic lymphadenopathy occurs in less than 10% of patients at diagnosis. HL spreads in a contiguous fashion from one lymph node group to the adjacent lymph nodes adjacent structures (16).

2.2.1 Nodal Lymphoma

In HD, lymph node involvement is usually the only manifestation of disease, whereas in NHL nodal disease is frequently associated with extranodal sites of tumor. At presentation, differences exist between the patterns of lymph node involvement in HD and NHL. Lymph nodes tend to be larger in NHL than HD; indeed in nodular sclerosing and lymphocyte-depleted HD, nodal enlargement may be minimal. Typically, involved nodes tend to displace adjacent structures rather than invade them, except in the case of diffuse large B-cell lymphoma, which is often locally aggressive. (15)

At present, size is the only criterion by which lymph nodes demonstrated on US or CT or MRI are considered to be involved, though clustering of multiple small nodes, for example within the anterior mediastinum or the mesentery, is suggestive. A maximum short-axis diameter of 10 mm is taken to be the upper limit of normal, depending upon the exact site within the neck,

thorax, abdomen, or pelvis. Thus within the neck, the jugulodigastric node can measure up to 13 mm short axis diameter, whereas those in the gastro hepatic ligament and porta hepatis are considered abnormal if they measure more than 8 mm in diameter. Retrocrural nodes greater than 6 mm are taken as enlarged (17) and in the pelvis the upper limit of normal is regarded as 8 mm (18). Lymph nodes at some sites, such as the splenic hilum, presacral and perirectal areas are not usually visualized on cross-sectional imaging and, when demonstrated, are likely to be abnormal whatever the size.

Enlarged lymph nodes in both HD and in NHL are usually homogeneous and of soft-tissue density on CT. They may show mild or moderate uniform enhancement after intravenous injection of contrast medium. Calcification is uncommon but may be seen on post-treatment scans. Necrosis is rarely seen in large nodal masses in both HD (particularly nodular sclerosing HD) and aggressive NHL, more frequently after treatment. On MRI, lymph nodes are easily identified as relatively low to intermediate signal intensity masses on T1-weighted images, of intermediate to high signal on T2-weighted images and which may have very high signal intensity on short-tau inversion recovery (STIR) sequences. Though the signal intensity of involved nodes and the presence of necrosis do not appear to have much prognostic significance, there is some evidence that within large lymphomatous masses, heterogeneous T2 signal at MRI or heterogeneous enhancement at CT is associated with a worse outcome. (15, 18, 19)

The pattern of the disease in the abdomen and pelvis (below the diaphragm) is markedly different in HD and NHL. At presentation the retroperitoneal nodes are involved in 25–35% of patients with HD and 45–55% of patients with NHL (20). Mesenteric lymph nodes are involved in more than half the patients with NHL and less than 5% of patients with HD (20, 21). Other sites, as in the porta hepatis and around the splenic hilum, are also less frequently involved in HD than NHL.

In HD, nodal spread is predictably from one lymph node group to another through directly connected lymphatic pathways. Nodes are frequently of normal size or only minimally enlarged.

Spread from the mediastinum occurs through the lymphatic vessels to the retrocrural nodes, coeliac axis and so on. Around the coeliac axis, multiple normal-sized nodes may be seen, which can be difficult to evaluate because involved, normal-sized nodes are frequent in HD. The coeliac axis, splenic hilar and porta hepatis nodes are involved in about 30% of patients and splenic hilar nodal involvement is almost always associated with diffuse splenic infiltration. In the porta hepatis, the node of the foramen of Winslow (porta caval node), lying between the portal vein and the inferior vena cava, is important, as it is often overlooked and may be the only site of disease relapse. This node has a triangular or lozenge shape; its normal transverse diameter is up to 3 cm and in the anteroposterior plane is approximately 1 cm.

In NHL, nodal involvement is frequently noncontiguous and bulky and is more frequently associated with extranodal disease. Discrete mesenteric nodal enlargement or masses may be seen with or without retroperitoneal nodal enlargement. Large volume nodal disease in both mesentery and retroperitoneum may give rise to the so-called 'hamburger' sign, in which a loop of bowel is compressed between two large nodal masses. In NHL, regional nodal involvement is frequently seen in patients with primary extranodal lymphoma involving an abdominal viscus. Involved nodes tend to enhance uniformly and the presence of central necrosis or multilocular enhancement should suggest an alternative diagnosis such as tuberculosis or atypical infection.

(15)

2.2.2 Extranodal lymphoma

Extranodal lymphomas may arise anywhere outside the lymph node region: from sites with primary lymphoid organs (e.g., spleen, thymus, Waldeyer ring); from organs or tissues devoid of lymphoid tissue (eg, brain, soft tissue); or from organs with a significant lymphoid tissue component (e.g., gastrointestinal tract).

Involvement of extranodal sites by lymphoma usually occurs in the presence of widespread advanced disease elsewhere. Such secondary involvement occurs in both HD and NHL and it is a recognized adverse prognostic feature. However, in approximately 30–40% of cases, primary involvement of an extranodal site occurs, with lymph node involvement limited to the regional

group of nodes—stages I–II E. Both primary and secondary extranodal involvement is more common in NHL than HD. As primary extranodal HD is extremely rare, rigorous exclusion of disease elsewhere is essential before this diagnosis can be made. The incidence of extranodal involvement in NHL depends on a number of factors, including the age of the patient, the presence of pre-existing immunodeficiency and the pathological subtype of lymphoma. There is an increased incidence of extranodal disease in children, especially in the gastrointestinal tract, the major abdominal viscera and extranodal locations in the head and neck, (22) and in the immunocompromised host. In both these patient groups, the high incidence of extranodal involvement is a reflection of the fact that such lymphomas are usually of the more aggressive histological subtypes. As the frequency of NHL is increasing (both in the general population and in the immunocompromised), the incidence of extranodal disease is rising faster than that of nodal disease (23). Of the various pathological forms of NHL, mantle cell (a diffuse low-grade B-cell lymphoma), lymphoblastic lymphomas (80% of which are T-cell), Burkitt (small cell noncleaved) and MALT lymphomas demonstrate a propensity to arise in extranodal sites (11, 15)

The gastrointestinal tract: GI tract is the commonest site of primary extranodal NHL, accounting for 30–45% of all extranodal presentations. It is the initial site of lymphomatous involvement in up to 10% of all adult patients and up to 30% of children (16, 22). In the gastrointestinal tract, lymphoid elements occur in the lamina propria and submucosa. The quantity of lymphoid tissue varies among segments, but either primary or secondary lymphomatous neoplasms may occur in any portion of the gastrointestinal tract. Secondary gastrointestinal involvement is common because of the frequent origination of lymphomas in the mesenteric or retroperitoneal nodes and the abundance of lymphoid tissue in the gastrointestinal tract. Multiple sites are typically involved. On the other hand, primary lymphomas of the gastrointestinal tract usually involve only one site.

Dawson et al (24) cited five criteria that must be met for the diagnosis of a primary gastrointestinal lymphoma to be made:

- No palpable superficial lymph nodes are seen.
- Chest radiographic findings are normal (i.e. no adenopathy).
- The white blood cell count (both total and differential) is normal.
- At laparotomy, the alimentary lesion is predominantly involved, with lymph node involvement (if any) confined to the drainage area of the involved segment of gut.
- There is no involvement of the liver and Spleen

However, advanced lymphomas arising in the gastrointestinal tract may eventually disseminate widely and be clinically, radiologically, and pathologically indistinguishable from secondary gastrointestinal lymphomas (25). Primary gastrointestinal lymphoma is the most common extranodal manifestation of non-Hodgkin lymphoma, accounting for up to 20% of all cases (26). Primary involvement of the gastrointestinal tract is exceedingly rare in Hodgkin disease, with only isolated case reports in the literature (27). Malignant lymphoma of the gastrointestinal tract has diverse radiologic manifestations and may mimic a variety of diseases, particularly other malignancies (28).

Mesentery: In general lymphoma of the mesentery can range in size from small to bulky and in shape from round or oval to irregular masses and can appear as multiple round, mildly enhancing, homogenous masses that often surround mesenteric arteries and veins. Lymphoma can grow so large that it encases the mesenteric vasculature without causing ischemia. The sandwich sign is a hallmark of lymphoma characterized by lobulated, confluent mesenteric soft tissue masses that resemble two halves of a sandwich and the mesenteric vessels in between represent the filling -like heterogeneous mass with areas of low attenuation representing necrosis that displaces bowel loops (15).

Mesenteric or peritoneal infiltration by lymphoma is seen almost exclusively in NHL. Lymphoma typically spreads in sheets along the peritoneal surface causing a rigid pleating of thickened

mesenteric leaves. This stellate appearance may also be seen in ovarian, colonic, and pancreatic carcinoma. Ascites is more common than in carcinomatosis.

Imaging findings may mimic peritoneal carcinomatosis, with peritoneal nodules, ascites, and mesenteric infiltration. Omental caking, hallmark of metastatic ovarian cancer, can also be seen. Alternatively, misty mesentery may be the presentation; however, this is more common after therapy (29, 30)

The genitourinary system: GUS usually secondarily affected by extranodal spread of lymphoma, and is the second most commonly affected anatomic entity next to the hematopoietic and reticuloendothelial organs. Renal lymphoma usually occurs in the setting of widespread non-Hodgkin lymphoma. In a series of 322 autopsies, lymphoma involved the kidneys in 37.6% of cases but the urinary bladder and testes in only 8.4% and 5.9% of cases, respectively (31). Despite the relatively high prevalence of renal involvement, imaging studies demonstrate renal abnormalities in only 3%–8% of patients undergoing routine evaluation for staging or during the course of therapy (2, 5).

This apparent discrepancy between the pathology literature and the radiology literature can be explained by several factors: Renal lymphoma is often poorly documented, since the disease is often clinically silent and renal biopsy is rarely indicated to confirm the diagnosis in the context of systemic disease.

There are five patterns of renal involvement in lymphoma described by different authors with slight differences in frequency (32). Most common pattern of renal involvement is the infiltration of kidney by multiple masses and the diffusely enlarged lobular kidneys. The renal arteries and veins remain patent despite tumor envelopment, a finding that is characteristic for lymphoma.

Diffuse renal infiltration: This pattern may present as enlarged kidneys. The renal parenchyma remains relatively hypodense in the early postcontrast study. Parenchymal enhancement is exhibited in the nephrographic phase and normal excretion is evident on the excretory phase

Multiple renal masses: These tend to be hyperdense on CT scans before contrast administration relating to the hypercellularity of the lymphomas. Otherwise, these are characterized by multiple, bilateral, focal intraparenchymal, and hypoattenuating masses.

Renal invasion from contiguous retroperitoneal disease: Renal involvement from retroperitoneal lymphoma commonly occurs either by invasion through the renal capsule or by extension through the renal sinus. Retroperitoneal adenopathy is invariably present, and many patients show obstructive hydronephrosis. Retroperitoneal tissue secondary to treated lymphoma can be difficult to differentiate from retroperitoneal fibrosis, which typically does not elevate the aorta from the spine

Solitary masses: Seen as a single, focal, intraparenchymal, hypoenhancing hypoattenuating mass.

Perirenal infiltrates: Perirenal or capsular involvement is often associated with retroperitoneal lymphomatous masses. (33)

Adrenal glands: are unusual sites for primary lymphoma. The adrenal gland is involved in 4% of patients with NHL. At autopsy, however, the adrenal gland has been found to be involved in 25% of the cases of disseminated NHL, may present as a solid mass or masses; however, the most /common presentation is of diffuse bilateral enlargement of the adrenal gland. In addition, there may be associated retroperitoneal lymphadenopathy and extranodal disease. (15)

Gynecological disease: can be involved by NHL, and the ovary is one of the more common anatomic sites to be involved. Ovarian involvement by NHL usually occurs as a part of systemic disease. Localized NHL of the ovary is rare (33). A common pattern of involvement is diffuse bilateral homogeneous enlargement, usually associated with retroperitoneal or extranodal manifestations of lymphoma elsewhere. Ovarian lymphoma demonstrates a propensity to be bilateral. Uterine involvement by lymphoma is rare and is usually observed in the cervix. US and CT evaluation demonstrates diffuse homogeneous enlargement of the uterus.

Primary pancreatic lymphoma: is a rare (<2%) extranodal manifestation of any histopathologic subtype of B-cell non-Hodgkin's lymphoma that predominantly involves the pancreas at a disease stage of either I_E or II_E according to the modified Ann Arbor staging system. Instead of being primary in the gland, pancreatic lymphoma can also represent direct extension from adjacent peripancreatic lymphadenopathy. (34)

Diagnostic criteria of primary pancreatic lymphoma include a pancreatic mass that predominates with gross involvement of only the peripancreatic lymph nodes, no hepatic or splenic involvement, no palpable superficial lymphadenopathy, no enlargement of the mediastinal lymph nodes on chest radiography, and a normal leukocyte count. Secondary involvement is more than primary 30% vs 2%) (35)

Two distinct morphologic patterns of pancreatic involvement are seen. One is a well-circumscribed focal mass. In patients with pancreatic lymphoma, pancreatic ductal dilation usually absent, even with ductal invasion. The combination of a bulky localized tumor in the pancreatic head without significant dilatation of the main pancreatic duct strengthens a diagnosis of pancreatic lymphoma over adenocarcinoma (34).

The second is diffuse enlargement infiltrating or replacing most of the pancreatic gland. This pattern involves organ enlargement and irregular peripancreatic fat infiltration, which may resemble acute pancreatitis on imaging. (16)

Liver: involvement is present in up to 15% frequently in middle-aged adult immune compromised individual, such as after organ transplant or in patients with AIDS with NHL at presentation, though this figure is higher in the pediatric population and with recurrent disease. In HD, liver involvement occurs in about 5% of patients at presentation, almost invariably in association with splenic HD. True primary hepatic lymphoma is rare but the incidence is rising, up to 25% of affected patients being hepatitis B or C positive and are NHL large cell type. In both HL and NHL, the portal area is typically involved initially because this is the region where lymphatic tissue is present. (11, 15, 19)

Pathologically, *diffuse microscopic infiltration* around the portal tracts is the most common form of involvement. US, CT and MRI are therefore insensitive in the detection of liver involvement. However, hepatomegaly strongly suggests the presence of diffuse infiltration (in contradistinction to the significance of splenomegaly).

Larger focal areas of infiltration are seen and only present in 5–10% of patients with hepatic lymphoma.

Miliary nodules or larger solitary or multiple masses, resembling metastases can occur. On ultrasound they are usually well defined and hypoechoic; on CT they are hypodense before and after intravenous injection of contrast medium; and on MRI they are of higher signal intensity than the surrounding parenchyma on T2-weighted sequences. Super paramagnetic iron oxide particles can increase the conspicuity of such focal deposits.

Occasionally, especially in children, periportal infiltration is manifest as may be seen extending from the porta hepatis along the margins of the portal veins resulting in periportal patchy, irregular areas.

Bile ducts and gallbladder: NHL is rare. It is seen most often with multisystem involvement; isolated involvement of the gallbladder may be difficult to differentiate from acute or chronic cholecystitis. Lymphoma may present as homogeneous thickening of the gallbladder wall without a hypoechoic edematous middle layer within the gallbladder wall (e.g. no halo sign (15, 16).

Spleen: is involved in 30–40% of patients with HD & NHL at the time of presentation, usually in the presence of nodal disease above and below the diaphragm (stage III), but in a small proportion it is the sole focus of intra-abdominal disease. In the majority of patients, the involvement is microscopic and diffuse and thus particularly difficult to identify on cross-sectional imaging, as splenomegaly does not necessarily indicate involvement; 33% of patients have splenomegaly without infiltration and, conversely, 33% of normal-sized spleens are found

to contain tumor following splenectomy. Measurements of splenic volume and splenic indices are not generally utilized.

Focal splenic deposits occur in only about 10–25% of cases which, when they are more than 1 cm in diameter, can be demonstrated on any form of cross-sectional imaging. Up to 40% of patients with NHL have splenic involvement at some stage. Imaging findings include solitary mass, military nodules, or multiple masses, all of which tend to have a nonspecific appearance.

Primary splenic NHL is rare, accounting for 1% of all patients with NHL. Patients present with splenomegaly, often marked and focal masses are usual. Splenic involvement is also a particular feature of certain other pathological subtypes of NHL, such as mantle cell lymphoma and splenic marginal zone lymphoma. Infarction is a well-recognized complication (15, 16)

3. Statements Of The Problem

Lack of local study assessing the spectrum of radiological findings in lymphoma

Lymphoma is known to involve all organs in the abdomen including the central nervous system, head and neck, thorax, abdomen, gonads, and bone. However, at onset, nodal and splenic involvement is more common in Hodgkin disease, whereas extranodal involvement is more frequent in non-Hodgkin lymphomas. The subtypes of lymphoma encountered differ in frequency between the adult and pediatric groups, with a strong bias towards precursor B- and T-lymphoblastic lymphoma and Burkitt lymphoma in childhood (15)

All subtypes of lymphoma are not uncommon in Ethiopia. Experience of physicians who care for these patients has shown the prevalence of the disease and involvement of diverse anatomic regions.

Abdominal organs are one of the common regions involved in lymphoma and they are involved in different frequency. The patterns of imaging findings have also been suggested. However no local study done to assess the condition in Ethiopia. Knowing the imaging patterns specially those associated with HIV/AIDS contributes much on diagnosis and follow up of patients with lymphoma. There is no a similar local study in the past and we believe this study gives a lot of information on abdominal pattern of lymphoma especially on the ultrasound findings.

4. Objectives

Based on the problem and challenges associated in diagnosis , management and follow up of patients with abdominal lymphoma in our set up, this study has the following primary objectives:

- Assess the frequency of different organs involved by lymphoma in the abdomen
- Study the patterns of ultrasound findings in patients with abdominal lymphoma.

5. Materials and Methods

Combinations of different methodological approaches were used in this study. Both qualitative and quantitative data collection methods.

The first method is reviewing literature on imaging patterns of abdominal lymphoma.

The second approach was examining patients who arrived to the US unit of radiology department starting from the month of July , 2013 to June, 2014 G.C and their record cards reviewed subsequently.

In reviewing literatures the English language evidence published on imaging lymphoma particularly abdominal lymphoma was searched through MEDLINE using the following words “lymphoma, imaging, and imaging treatment response”. The pertinent literatures’ identified are cross referenced to select further articles. No specific search strategy was adopted rather those literatures which recommend particular diagnostic approach for lymphoma patients are reviewed. Emphasis was given for those literatures which:

- Included patients with confirmed lymphoma,
- Evaluated CT, CXR , or Ultrasonography, and few MRI and nuclear medicine literatures
- Described an objective diagnostic standard,
- Review articles on imaging lymphoma particularly those involving the abdominal organs

Those articles with a definitive recommendation on the imaging approaches, articles which has evidence on value of various imaging modalities are reviewed to assess the significant role of each modality. Because a systematic review of the literature identified few randomized studies either due to unavailability of free literature to provide guidance on the use of cross-sectional imaging in the management of patients with cancer, cohort studies and case series reports were also included in the evidence review.

Patient selection for image analysis done from the radiology department of AAU. Candidate patients were those who came to US unit of TASH with the diagnosis of lymphoma . Requests screened daily and those patients whose clinical diagnosis states that they are suspected or proved to have lymphoma either on treatment or not, were selected and scanned by a senior resident(author) and/or a consultant (the advisor) based on agreed upon protocol

Scanning methods and sequences agreed based on routine standard scanning techniques. All examinations were performed by Toshiba US machine using 5 MHz sector probe and 7.5 MHz linear probe when ever superficial sites are scanned.

6. Results of the study

Patterns of ultrasound findings in patients with lymphoma

Ultrasound examination was performed on sixty nine consecutive patients who came to the US unit of radiology department of Tikur Anbessa hospital from July, 2013 to End of June, 2014. The population characteristics of the patients are depicted in Table 1. Eighty nine percent of our patients are below the age of 60 and the majorities are between the ages of 21 to 50. Significant percentages of our patients are young (below 30 years, 41%). Female's accounts for only twenty five percentage of the total study population.

Common imaging modalities done are CXR and US, where all patients undergone US examination and 81% (56/69) had CXR while only 9% (6/50) have CT scan. No MRI or any nuclear medicine exam performed on our patients.

Among these patients 45% did not start treatment and the rest have taken different cycles of anti lymphoma regimen. The reason for not starting treatment is either due to they are newly diagnosed patients or diagnosis is not yet confirmed

40 % of our patients are not biopsied so diagnosis is based on clinical and radiological basis (Table 5 & Fig 2).

Tables 2 show the regional involvement of lymphoma. Lymph node, be it in the abdomen and/or else where is the common organ involved and account for 62% of cases of which abdominal nodes in 35 % neck and other superficial nodal region 27 %.

These lymph node regions are involved individually or in combination. Isolated Abdominal node involvement noted in 13%, However abdominal organ and node involvement is commonest 30% (Table 2). Isolated Abdominal regional involvement is seen in 46% of cases (node + abdomen + combined)

The common lymph node region involved in the abdomen is mesenteric node followed by retroperitoneal and parasolid organs nodes (43 vs. 23% Table 3).

Most lymph node (52%) is homogenous and hypoechoic in echo appearance and 20% are heterogeneous with irregular and thickened lymph node hilum (table 4). Majority of nodal pattern of involvement, 54%, is multiple and discrete nodes and are hypovascular. Classical sandwich sign, conglomerate nodal involvement, seen in 25% of cases (Fig 3). One patient with this sign had CT scan.

Abdominal organs are involved in about 37 % and isolated solid abdominal organ involvement is seen in only 2 cases (3%). No patient with positive abdominal finding is pathologically proved to be lymphoma. Such practice of confirming every individual finding is not the routine practice in our set up and probably not also advised elsewhere. It is assumed positive finding in a patient with proved or clinically suspected to be lymphoma is assumed to be lymphomatous change in this study.

Positive US gastrointestinal and renal findings are seen in only 6 % of cases each (Fig 1 & Fig 6) No pancreas GB, and pelvic positive findings noted in this series. The most commonly involved abdominal organ is the liver and spleen which account for 35 and 29 percent respectively (Fig 1). For both organs among the positive findings the most common finding is non-specific Hepatomegally in 53% and splenomegally in 56% of patients. The other findings observed in the liver were few or multiple variable sized lesion (Fig 5) in 25 % of cases. Multiple small hypoechoic lesions observed in 30 % of patients with splenic involvement (Fig 4).

The findings seen in the kidney were two cases as multiple well defined hypoechoic lesions (Fig. 6) and one case was an infiltrative perirenal mass which is the usual finding in renal lymphoma involvement .

One patient had bilateral hypoechoic , lobulated adrenal lesions

Positive bowel finding is seen in 4 cases(6 %)of cases and the findings seen was a polypoid thickening of the bowel wall with associated dilatation of its lumen and lymphadenopathy . One of this patient has CT scan and the finding is comparable with US .

Review of the pathology report either from the card or from the patient personal record showed the majority of patients are reported to have high grade NHL . Only 19% of patients who have pathology result have Hodgkin's lymphoma while the rest about 81% have NHL (Table 5, Fig 2).

Table 1. Population Profile of 69 Lymphoma Patients

Characteristics	Age range	Frequency	Percentage	Cumulative percentage
Age	0 – 10	7	10.5	10.5
	11 -20	7	10.5	21
	21 – 30	14	20	41
	31 – 40	13	19	60
	41 - 50	11	16	76
	51 – 60	9	13	89
	61 – 70	5	7	96
	70 +	3	4	100
Sex	M	44	64	64
	F	25	36	100
Examination Performed	US	69	100	
	CXR	56	81	
	CT	6	9	
	MRI	0		

Table 2. Pattern of Regional Involvement of Lymphoma

<i>Regions Involved</i>	<i>Frequency</i>	<i>Percentage</i>
Neck or other Superficial Nodes	32	46
Abdominal Nodes	42	61
Abdominal Organs	37	54
<i>Mode of Regional involvement</i>		
Neck and other nodes only	9	13
Abdominal Nodes Only	9	13
Abdominal Organ Only	2	3
Abdominal Organ and Node	21	30
Combined involvement	18	26

Table 3. Pattern of Lymph Node Involvement in Lymphoma

<i>Nodal Region Involved</i>	<i>Regions</i>	<i>Frequency</i>	<i>Percentage</i>
Nodal Regions	Retroperitoneal	16	23
	Mesenteric	30	43
	Para solid organ	16	23
	Para aortic	14	20
	Neck and Other	25	36
<i>Mode of Regional Node involvement</i>			
Mode of involvement	Retroperitoneal Only	1	1
	Mesenteric Only	11	16
	Para aortic Only	1	1
	Neck and Other only	13	19
	Combined Regions	27	39

Table 4:- US Appearance of Involved Lymph Nodes

<i>Pattern of node involvement</i>		<i>Frequency</i>	<i>Percentage</i>
Nodal pattern	Discrete Multiple Node	37	54
	Conglomerate and Matted Node	17	25
	Discrete few Node	4	6
Echo Appearance	Homogenously hypoechoic	36	52
	Heterogeneous	14	20
Nodal Vascularity	Hypo vascular	28	41
	Hyper vascular	19	28

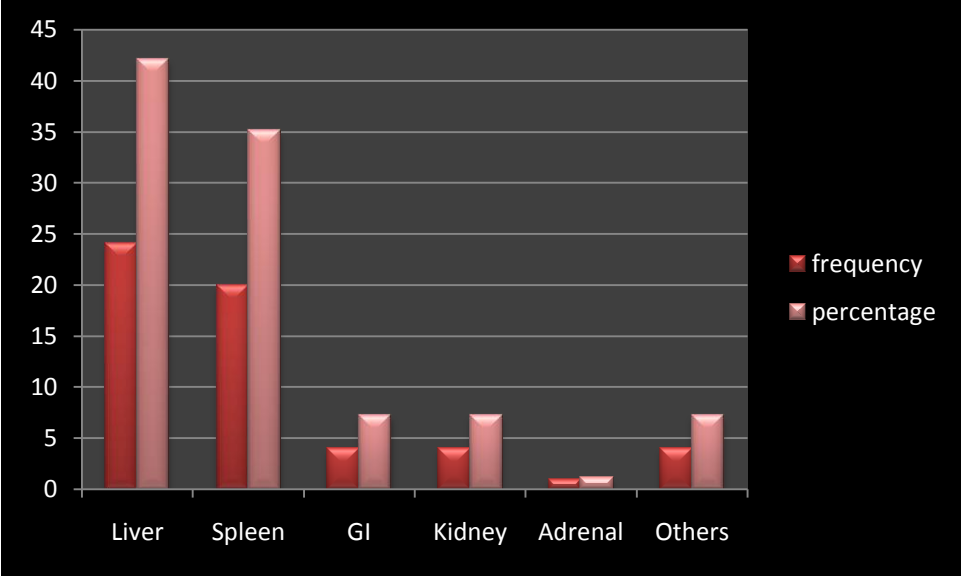


Fig 1: Frequency of abdominal organs involved

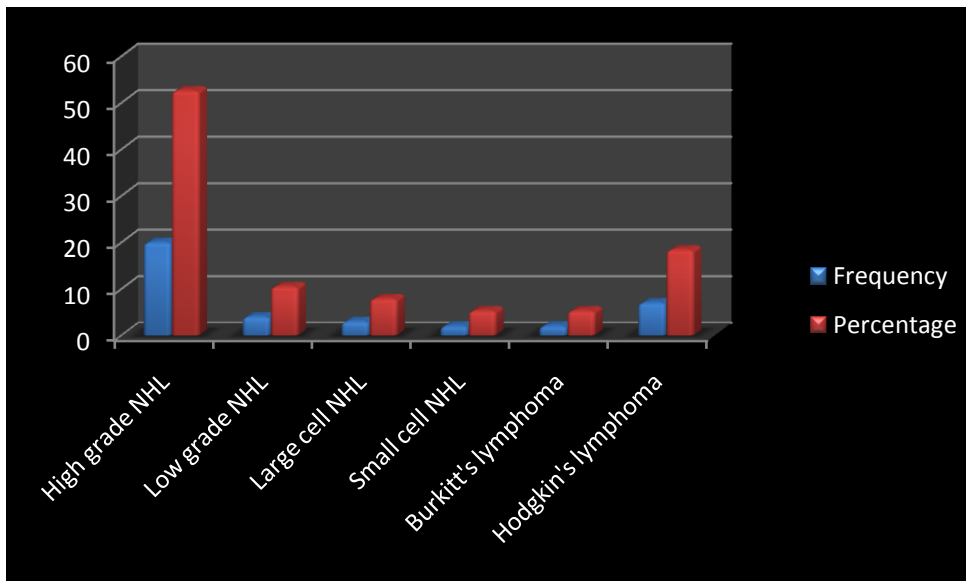


Fig. 2 Pathological types of lymphoma

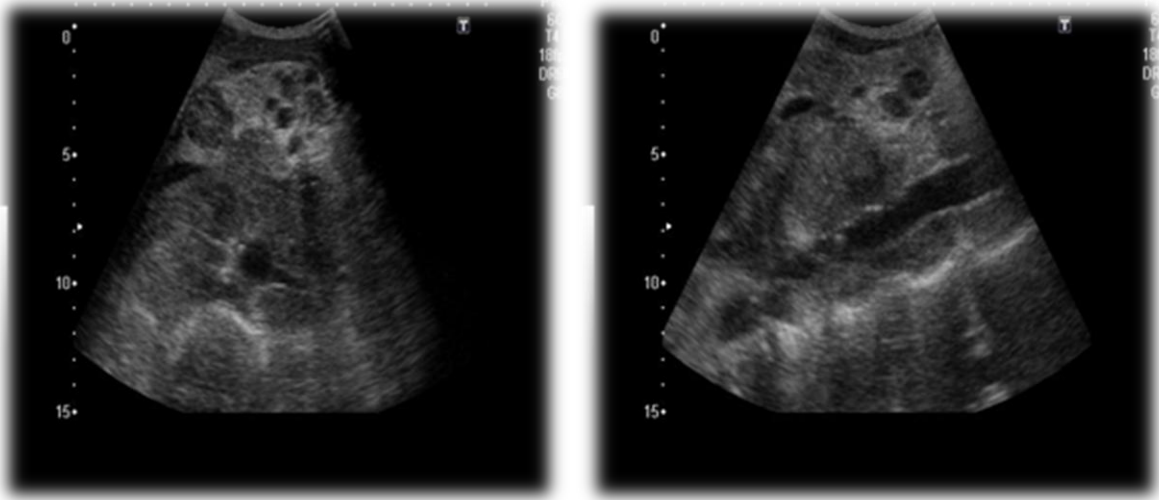


Fig. 3A & B; Paraaortic and conglomerate node encasing the vessels

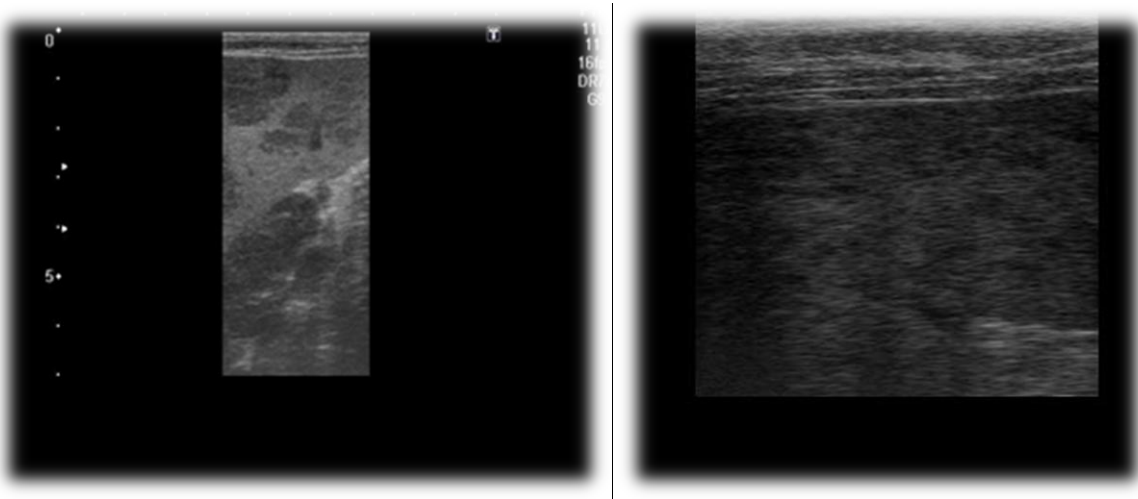


Fig .4A & B ; Multiple hypoechoic lesions of spleen in different lymphoma patients

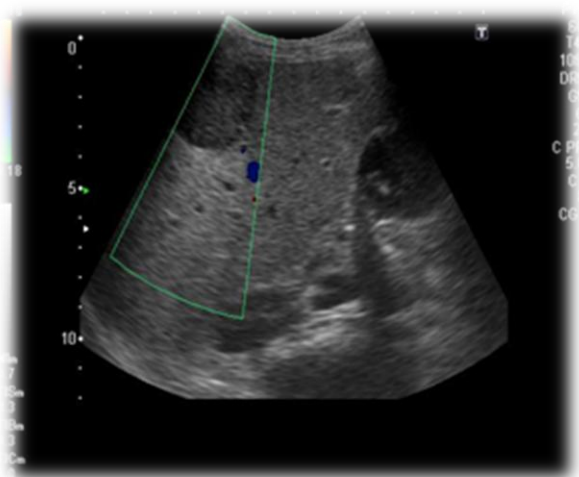
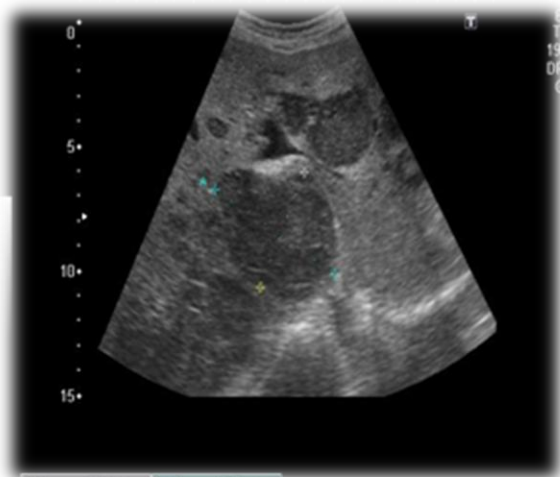
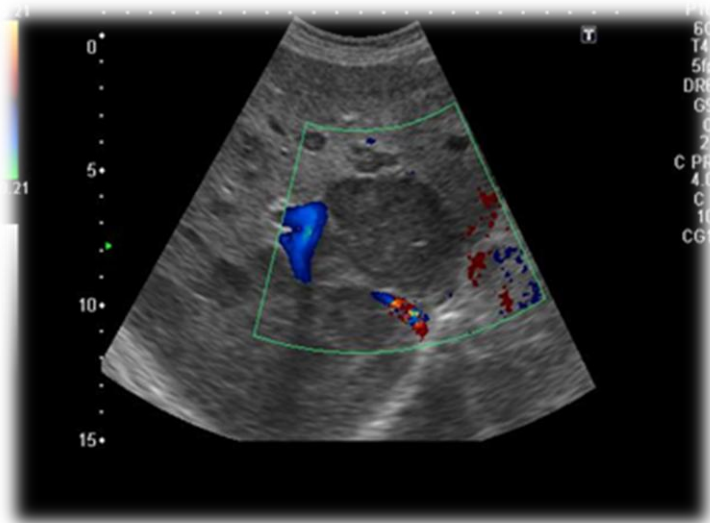


Fig. 5 A, B & C; Non vascular variable sized liver lesion in two patients

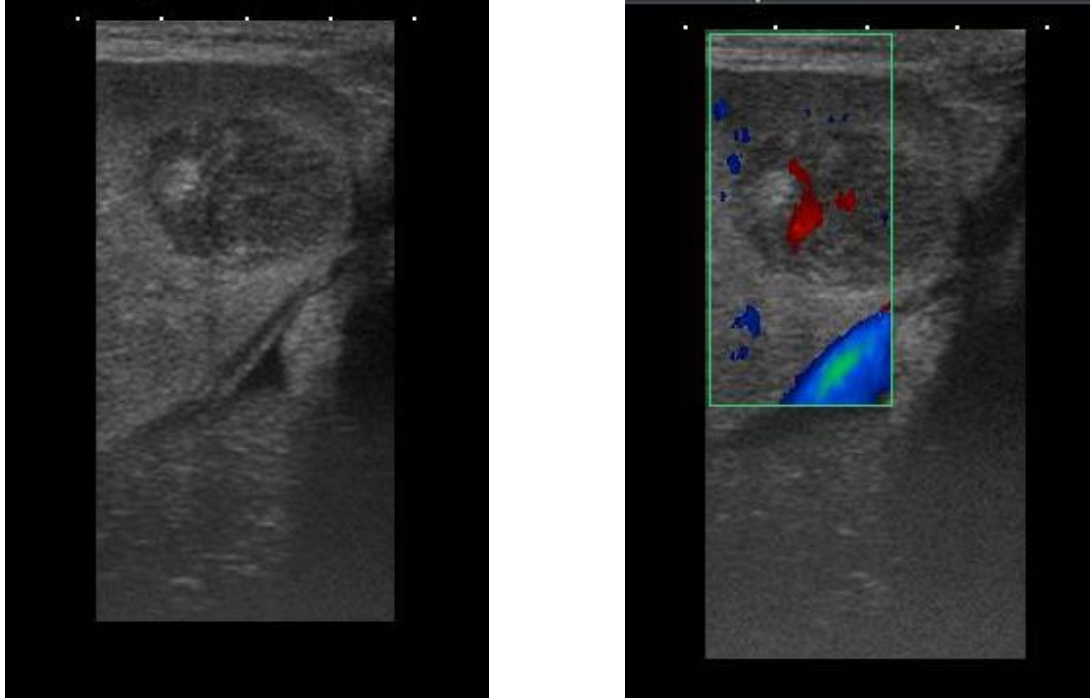


Fig. 6 A & B; Renal involvement in a patient with confirmed lymphoma in other sites(well defined , vascular and hypoechoic lesion)

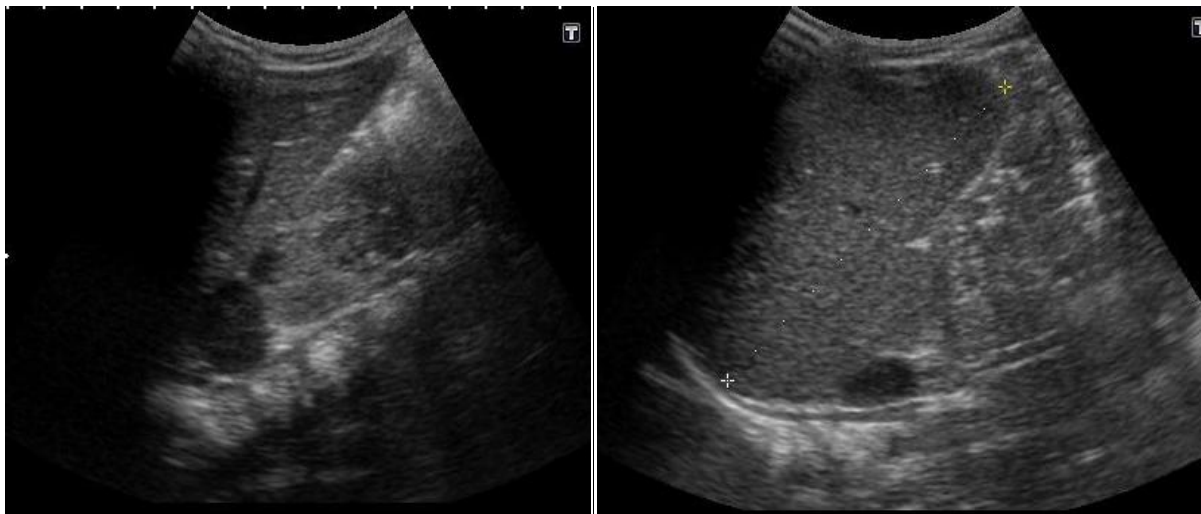


Fig . 7A & B; Bilateral adrenal gland in a patient confirmed with lymphoma

7. Discussion And Recommendation

7.1 Discussion

Lymphoma, solid tumor of the immune system, commonly involve organs which contain lymphoid cells, specially at the onset nodal and splenic involvements are more common in Hodgkin disease, whereas extranodal involvement is more frequent in non-Hodgkin lymphomas. In HD, lymph node involvement is usually the only manifestation of disease, whereas in NHL nodal disease is frequently associated with extranodal sites of tumor. At presentation, differences also exist between the patterns of lymph node involvement in HD and NHL. Among the patients we examined. (15)

Nodal involvement is confirmed based on change in size related to the specific site involved (17, 18). Based on size our series showed nodal involvement to be the most common site involved in about 62 % of cases either in combination with other extra nodal site or alone (table2). Castellino et al and Goffinet also found similar finding where lymph node involvement as a common site (20, 21). In the abdomen different lymphnode groups are involved either alone or in combination. Mesenteric nodes are commonly involved in this series followed by the retroperitoneal and parasolid organs. This finding is in agreement with studies done by Castellino et al and Goffinet et al where retroperitoneal nodes are involved in 25–35% of patients with HD and 45–55% of patients with NHL while mesenteric lymph nodes are involved in more than half the patients with NHL and less than 5% of patients with HD (20, 21). It has been shown that usually patient develop retroperitoneal or mesenteric nodal involvement which gradually extend to other lymphnode. Patients in our situation usually come late so most of them (39%) showed combination of lymph node region involvement.

US pattern of lymphnodes both at superficial sites like the neck and abdomen has long been studied. Description of the pattern and echo texture, appearance of the hilum, shape and size

of the node, degree and nature of vascularity and resistivity index and etc have been done(17, 38).

Various studies showed that US & CT abdominal nodal involvement is seen as homogenous discrete masses that often surround mesenteric arteries and veins. They can grow so large that it encases the mesenteric vasculature and displace abdominal organs (Fig 3) (15, 16, 17, 19, 29, 30, and 36). The present series also showed 54 % of the lymph nodes showed homogenous discrete hypoechoic echo appearance . Those cases involving the mesentery showed conglomerate multiple nodes surrounding the vessels (sandwich sign (Fig 3) most are hypovascular.

Spleen like nodal lymphoma, is the common site involved. Munazza et al and Goerg et al showed that spleen is involved in 30–40% of patients with HD & NHL at the time of presentation(15,16,39). Unlike the above studies, splenic involvement in our series is about 29% of case less than that of the liver involvement(Fig 1). The result in our study may have slight from the one mentioned because of predominant histology of NHL type . Splenomegally and splenic lesions detected in our series on 56 and 30 % respectively . However, in agreement with the studies non specific splenic enlargement and multiple hypoechoic small deposits is the common finding (Fig 4). Splenomegally in splenic lymphoma is suggested to be secondary to the microscopic and diffuse involvement as they are difficult to identify on cross-sectional imaging, while focal splenic deposits occur in only about 10–25% which appear on Imaging as solitary mass, military nodules, or multiple masses, all of which tend to have hypoechoic or non specific. Even though splenomegally is thought to indicate lymphomatous splenic involvement, however, studies showed splenomegally does not necessarily indicate involvement; 33% of patients have splenomegally without infiltration and, conversely, 33% of normal-sized spleens are found to contain tumor following splenectomy. (15, 16, 39) .There for Clinicians must be aware of this fact and be cautious in staging patients.

In early studies, the sensitivity of ultrasound and CT for the detection of splenic involvement was extremely low (about 35%), although in a more recent study ultrasound was more sensitive

than CT in detecting nodules down to 3 mm in size (63 vs. 37%) (36). Detection of small focal nodules has improved with the advent of multi detector CT (MDCT) and powered contrast medium injection, with optimal splenic parenchymal opacification. MRI with super paramagnetic iron oxide may improve the diagnostic accuracy but is seldom undertaken to assess splenic status. However, FDG-PET can detect splenic disease more accurately than CT or gallium scintigraphy. In the past, the poor sensitivity of imaging for the detection of splenic involvement in HD necessitated staging laparotomy with splenectomy but the development of effective combination chemotherapy with good salvage regimens has led to this practice being abandoned

Hepatic lymphoma usually occurs in the setting of systemic lymphoma in both HL and in NHL. Rarely, it may be a primary lesion, almost always of the NHL large cell type. In our series it is the most frequently involved abdominal organ even higher than the spleen 35% (Fig 1.)

In an autopsy series the liver is often a secondary site of involvement by Hodgkin's and non-Hodgkin's lymphoma, the disease tends to be diffusely infiltrative and undetected by sonography and CT. Non specific Hepatomegally can be the only finding. However several patterns of hepatic involvement including, hepatomegaly, which is suggestive of diffuse liver infiltration, Multifocal hepatic masses resemble metastatic disease, Miliary lesions (<1 cm in diameter) mostly seen in Hodgkin disease, Lymphomatous infiltration may be seen extending from the porta hepatis along the margins of the portal veins resulting in periportal patchy, irregular areas (11,15,16). Unlike other studies our series showed higher percentage (35%) of liver involvement . However the US findings is similar with these studies where 53% of patients have non-specific hepatomegally while 25% showed hypoechoic few or multiple variable sized lesions on US (Fig 5).

The uniform cellularity of lymphoma without significant background stroma is thought to be related to its hypoechoic appearance on sonography (16).

Gastrointestinal tract can be involved in both secondary and primary lymphoma. Secondary gastrointestinal involvement is common because of the frequent origination of lymphomas in

the mesenteric or retroperitoneal nodes and the abundance of lymphoid tissue in the gastrointestinal tract. Multiple sites are typically involved. Unlike to our series (6%), report of up to 50 % involvement has been described. The stomach, followed by duodenum, small bowel and large bowel are involved in that order of incidence (16). The relatively low GI involvement seen in our series can be explained by the use of only one imaging modality i.e. Ultrasound, which is relatively insensitive to detect less obvious gastrointestinal wall changes compared to CT. Primary gastrointestinal lymphoma is the most common extranodal manifestation of non-Hodgkin lymphoma, accounting for up to 20% of all cases (27, 28).

In our series only 6% of patients have GI involvement as seen by US (1 case has CT). The findings are focal thickening and polypoid mass with dilatation of the bowel loops in two cases and diffuse thickening of the wall. One out of four cases showed no extra GI pathology or palpable superficial or intrabdominal nodes or organomegally and Ultrasound did not show abdominal node involvement. Even though according to Dawson et al (24) diagnosis of primary GI lymphoma need a normal CXR, normal WBC count and absence of other organ involvement at laparotomy, we suspected one of our patient has primary lymphoma.

Patterns of GI involvement in lymphoma can be Infiltrative pattern radiologically seen as circumferential wall thickening, polypoid which appear as a submucosal mass or ulcerative lesions often seen as large cavitating lesions as multiple discrete submucosal nodules. Our case showed the former two appearances .

The genitourinary system specially the kidney is often affected by extranodal spread of lymphoma, and is said to be the second most commonly affected anatomic entity next to the hematopoietic and reticuloendothelial organs

Reports from autopsy series describe foci of lymphoma in the kidneys in approximately one-third of cases. Unlike the autopsy series, only 3%–8% of patients undergoing routine evaluation for staging or during the course of therapy show renal involvement The finding in our series is in agreement to the literature where 6% cases of renal involvement is seen. With also similar US findings where two patients showed focal solitary and multiple hypoechoic cortical lesion

(Fig 6)and one patient showed perirenal infiltrates encasing the kidney . No one of our patient's undergone biopsy to proved renal involvement. However, Literature suggests when renal involvement by lymphoma occurs in the setting of disseminated disease positive renal finding can be considered renal involvement of lymphoma (31, 32).

ADRENAL GLANDS are unusual sites for primary lymphoma but involved in 4% of patients with NHL. At autopsy, however, the adrenal gland has been found to be involved in 25% of the cases of disseminated NHL, may present as a solid mass or masses; however, the most /common presentation is of diffuse bilateral enlargement of the adrenal gland.(13) In our case there was only one patient with bilateral adrenal involvement which appeared as hypoechoic adrenal masses(Fig 7).

Eventhough multiple information can be extracted from the study there were few limitation in undertaking this study i.e limited numbers of lymphoma proved patients and possible modifications in the findings of patients who were scanned after initiation of treatment. Other difficulty was inability to get adequate information from patient record.

7.2 Recommendations

- By optimizing our ultrasound protocol radiologists can give optimal information on patterns and sites of involvement of lymphoma which helps in diagnosing , staging and follow up of lymphoma patients.
- We recommend the treating physicians to give full clinical information, other important imaging and laboratory findings in their requests which guides examining radiologist area of focus and describe changes in appearance of findings.
- From this study we can see that in resource limited areas like where we are practicing ultrasound has great value in imaging of lymphoma patients. So we recommend the radiologists to write full report of patients finding which should which organs are involved , pattern of involvement , size of lesions specially lymph nodes and also vascularity of lesions

8. Conclusion

The current study demonstrated different ultrasound patterns of abdominal lymphoma and study showed younger and male population predominated in the prevalence. Lymph nodes are most common sites of involved.

Abdominal organs were also affected in the majority of patients and liver was most involved from those.

From those patients who had pathologic result most of them have NHL type of lymphoma.

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