The value of qualitative and semiquantitative ultrasonographic findings in the differential diagnosis of lymphomatous superficial lymph node enlargements

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ABSTRACT

The value of the gray-scale (GSUSG), color Doppler (CDUSG), and power Doppler (PDUSG) ultrasonography in the differential diagnosis of lymphomatous superficial lymph node enlargements were evaluated. The study group consisted of 33 males and 16 females (5-74 yrs old, mean age 36.1 yrs) in whom physical examination had revealed superficial lymph node enlargements. All patients were investigated with Doppler USG (Sonoline Elegra Advanced, Siemens, Germany) using 7.5 Mhz linear transducer. Longitudinal/transverse dimensions (L/T) and hilar echogenecity of lymph nodes were evaluated with GSUSG. During the CDUSG and PDUSG examination, we classified the nodes into 3 patterns: type I, “hilar normal”; type II, “hilar activated”; and type III, “peripheral”. Pulsatility (PI) and resistivity (RI) indexes were calculated using CDUSG. Above parameters were analyzed to determine their differential diagnostic values using ANOVA based discriminant analysis, Student's-T test and ROC curve analysis. When clinical data and histopathological findings were combined, 27 subjects were diagnosed as lymphoma, and 22 cases were classified as lymphadenitis. Multiple comparison analysis of qualitative GSUSG and PDUSG features consisting of hilar echogenecity, L/T value and vascular type patterns was able to differentiate lymphomatous lymph nodes and lymphadenitis with 86.8% accuracy (p<0.001). On the contrary, semiquantitative features (RI, PI) were not able to classify lymph nodes (p>0.05). Semiquantitative RDUS parameters are not valuable in the differential diagnosis of lymphomatous superficial lymph node pathologies. Qualitative GSUSG and PDUSG features, on the other hand, may be used as an alternative work-up to cytological studies in patients in whom diagnostic surgical procedures cannot be performed. [Turk J Cancer 2004;34(4):156-162]

KEY WORDS:

Color Doppler, lymphomatous lymph nodes, ultrasonography
INTRODUCTION

Imaging methods in evaluation of lymph node pathologies play role in determination of lymph nodes pathologically, in decision of whether the nodes depend on dispersion of metastatic disease or not, in determination of extranodal extension and neighboring vital organ invasions and in observation of the patients’ responses to the medical treatment. In lymphoma, which is one of the most common causes of superficial lymphadenopathies, cervical region enhancement is frequently encountered and high-resolution ultrasonography (USG) is preferred over other imaging methods in determination of lymph nodes and in pursuit of the disease (1,2). On the other hand, USG evaluation of the lymph nodes can be insufficient due to technical limitations of the method and its dependence on the user. When USG and results of fine needle aspiration biopsy (FNA) are compared, it can be seen that USG still couldn’t reach the desired diagnostic level (3).

Gray-scale USG (DSUSG) is not sensitive enough in differentiation of malignant and benign lymph nodes (4,5) Application fields of color Doppler US (CDUSG) and power doppler USG (PDUSG) are rather broad and Doppler USG was suggested to be used for differentiation of benign and metastatic lymph nodes (6,7). However, there are limited number of studies concerning GSUSG and CDUSG usage for differential diagnosis of lymphomatous lymphadenopathies (8).

In this study, we investigated the values of GSUSG, CDUSG and PDUSG findings in differential diagnosis of superficial lymphomatous lymphadenopathies.

MATERIALS AND METHODS

49 cases, 33 male and 16 female, between the ages of 5-74 (mean: 36.1, DF: 19.5), who were found to have superficial lymphadenopathies in cervical, axillar and inguinal regions with physical examinations were included in the study (Table 1). Cases with lymphadenopathies were evaluated with CDUSG without a preliminary preparation following a B-mode USG performed in supine position. In all cases after USG investigation, diagnosis were provided with FNA, surgical specimen pathology, clinical/laboratory correlation and sonographic examination. A decrease in the size of the lymph node or its disappearance most early in two months were interpreted to be in favor of benignity. Sonographic studies were conducted with scanner (Siemens, Sonoline Elegra Advanced) equipped with broadband (frequency bands, 7-10 MHz) linear array transducer. Color Doppler parameters were adjusted for detection of low-velocity or low-volume flow or both. The pulse repetition frequency as 800 kHz; band pass filter was set at 62 and/or 75 Hz; and high levels were adjusted for both color-versus-echo priority and color persistence. The further increase depiction of vessel continuity, the power Doppler mode was also used.

In all cases, the biggest of the lymph nodes was evaluated with respect to size, echo structure and relationship with adjacent tissues. For size criteria of the nodes, the largest axis, that is the longitudinal diameter, and the one perpendicular to it in the broadest region, that is the transverse diameter, were considered and the ratio of the former to the latter was calculated to obtain Sombiati Index (2,5,9-11). Limit value of this index was accepted as 1.5 or 2 and its value in differential diagnosis was investigated. When echo structure was the point in question, besides absence of echogenic hilus, decrease in hilar echogeneity and distortion were also accepted as pathology. Central echogenicity loss and strong cortical hipoechogeneity were considered to be in favor of malignity (Figures 1, 2).

Fig 1. Gray scale sonography image shows of fatty hilus and cortex in a lymph node. A final diagnosis of benign lymph node
Vascular patterns were classified into 3 groups (type I, type II and type III) as in Giovagnorio et. al. (3) type I, “hilar normal” (a single vascular pole with the eventual presence of small branches); type II “hilar activated” (a single vascular pol, wider and longer than the previous one, with some large branches); and type III, “peripheral” (the presence of peripheral vessels arranged into single poles with multiple irregular and tortuous centripedal branches) (Figures 3-5). Following these morphological evaluations, spectral wave analysis was performed by taking into consideration the fastest arterial signal in the biggest lymph node detected in CDUSG. Resistivity index (RI) and pulsatility index (PI) were repeated continually there times in spectral wave analysis by considering highest peak systolic velocity (Figure 6).

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### Table 1

<table>
<thead>
<tr>
<th>Localisation</th>
<th>Lymphoma</th>
<th>Benign</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cervical</td>
<td>18</td>
<td>9</td>
<td>27</td>
</tr>
<tr>
<td>Axillary</td>
<td>9</td>
<td>8</td>
<td>17</td>
</tr>
<tr>
<td>Inguinal</td>
<td>4</td>
<td>5</td>
<td>9</td>
</tr>
<tr>
<td>Total</td>
<td>31</td>
<td>22</td>
<td>53</td>
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</tbody>
</table>

Fig 1. Power Doppler sonogram of an 1.7-cm-long laterocervical lymph node. A final diagnosis of lymphoma was made at subsequent biopsy. A rounded shape and hilar activated (type II) vascular pattern with evidence of a large feeding artery with increased flow are shown.

Fig 2. Gray scale sonography image shows of nonechogenic hilum in a lymph node. A final diagnosis of lymphoma.

Fig 3. Power Doppler sonogram of an 2-cm-long axillary region lymph node. A final diagnosis of reactive adenitis was made at subsequent biopsy. A normal sonographic appearance and a normal hilar (type I) pattern are shown.

Fig 4. Power Doppler sonogram of an 1.7-cm-long laterocervical lymph node. A final diagnosis of lymphoma was made at subsequent biopsy. A rounded shape and hilar activated (type II) vascular pattern with evidence of a large feeding artery with increased flow are shown.
For statistical analysis Student T-test, ROC curve analysis and ANOVA-based discriminant analysis were used.

**RESULTS**

Using clinical data and tissue and cell specimens obtained with FNA and surgical methods 27 lymphoma and 22 lymphadenitis cases were diagnosed.

While echogenic hilus was determined in 4 of lymphoma cases (14.8%), it was not seen in the remaining 23 (85.2%). Similarly, in 8 of the benign lymph nodes (36.4%) echogenic hilus was absent whereas in 14 (63.6%) it was seen (Table 2). A statistically significant relationship was found between hilar echogeneity and diagnosis.

![Fig 5. Power Doppler sonogram of an 2.5-cm-long laterocervical lymph node. A final diagnosis of lymphoma was made at subsequent biopsy. Irregular margins, heterogeneous echo texture with hypoechoic areas, and a peripheral (type III) vascular pattern with evidence of abundant atypical peripheral flow are shown.](image1)

![Fig 6 (A,B). (A): Increased hilar vascularity and RI and PI values can be seen with power Doppler sonogram, (B): Increased peripheric vascularity with no hilar echogenecity and RI and PI findings of a cervical lymphadenopathy in a Hodgkin lymphoma case. In both cases no difference in RI and PI values](image2)

<table>
<thead>
<tr>
<th>Echogenicity</th>
<th>Lymphoma (n)</th>
<th>Benign (n)</th>
<th>Total (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Echogenic hilum</td>
<td>7</td>
<td>18</td>
<td>25</td>
</tr>
<tr>
<td>Non-echogenic hilum</td>
<td>24</td>
<td>4</td>
<td>28</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>31</strong></td>
<td><strong>22</strong></td>
<td><strong>53</strong></td>
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</table>
Mean L/T values were found as 2.3 cm (SD: 0.5) and 1.7 cm (SD: 0.3) in benign lymph nodes and lymphoma cases, respectively. L/T size ratios of benign lymph nodes were higher than those of lymphomas and the threshold value was calculated as 1.95 cm. Taking this value into consideration, specificity and sensitivity of L/T ratio in differential diagnosis of benign and lymphoma cases were found as 73.3% and 66.7%, respectively.

Vascular pattern was determined in all lymph nodes investigated. Type I pattern was identified in 5 (18.5%), type II in 20 (74.1%) and type III in 2 (7.4%) of all the cases with lymphoma. While type I pattern was identified in 15 (68.2%) and type II in 7 (31.8%) of benign cases type III pattern was not identified. A 75.5% diagnostic differentiation was obtained (p<0.001) in discriminant analysis performed considering vascular patterns (Table 3).

Mean RI values were 0.58 (SD: 0.22) for benign lymph nodes and 0.58 (SD: 0.21) for lymphoma cases. On the other hand, mean PI values were 1.16 (SD: 0.36) in benign lymph nodes and 0.96 (SD: 0.38) in lymphoma cases. There was no statistically significant difference when mean RI and PI values of lymph nodes of lymphoma cases and those of benign lymph nodes were compared (p>0.05) (Figure 7).

Multiple comparison analysis of qualitative GSUSG and PDUSG features consisting of hilar echogenicity, L/T value and vascular type patterns was able to differentiate lymphomatous lymph nodes and lymphadenitis with 86.8% accuracy (p<0.001).

**DISCUSSION**

Doppler USG, a noninvasive and an easy to apply method in evaluation of lymph nodes, is hopeful in determination of vascular distribution (3). To our knowledge, at present all authors agree that a single vascular pole with linear and regular branches is a sign of benignity, whereas multiple peripheral poles with distortion and displacement of the internal vessels generally indicate malignancy (8,12-18). Although this assumption makes it possible to differentiate, in most cases, a normal node from a neoplastic one, apparently there have been no attempts to differentiate between the 2 main classes of neoplastic nodes, lymphomatous and metastatic. There exist many studies evaluating nodal blood flow with Doppler USG in addition to imaging methods such as CT and MRI which are both used in determination of metastatic lymph nodes and in differential diagnosis of superficial lymphadenopathies in lymphoma cases (19). However, as far as we know CDUSG investigation aimed at differentiating lymphomatous and benign lymph nodes is reported only in one study (3).
Vascular patterns were evaluated with CDUSG and PDUSG in 3 groups; presence of one vascular structure in hilus (type I hilar normal), presence of a long and wide vascular branching structure in hilus (type II hilar active) and presence of a peripheric hilar vascular structure showing a number of tortoise and irregular branches (type III peripheral) (3). In their study type I hilar normal vascular structure was found in inflammatory benign lymph nodes and type II hilar active vascular structure in lymph nodes related to lymphoma.

In our study, identified type I pattern in 18.5%, type II pattern in 74.1% and type III pattern in 7.4% of lymphoma cases. Type I and type II patterns were present in 68.2% and 31.8%, of benign cases, respectively. While type III pattern was present in 2 of lymphoma cases it was not seen in benign ones. A 75.5% diagnostic differentiation was obtained (p<0.001) in differential analysis performed considering vascular patterns.

It was shown in various studies, that CDUSG could be used in differential diagnosis of lymph node pathologies because of structural differences of tumoral tissue in metastatic lymph nodes and presence of peripheric subcapsular vessels depending upon angiogenesis (9,20-24). Peripheric subcapsular vessels are rarely encountered in lymphoma except some malign subgroups. Similarly, in our study, type III peripheral vascular pattern was determined only in 2 of all lymphoma cases.

Some studies pointed out the clinical usefulness of CDUSG in discrimination of metastatic superficial lymph node enhancements from those of benign related lymph nodes using spectral wave patterns. For malignant lymph nodes high RI and PI values are reported to be an indication of increased peripheral resistance and peripheral vascular obstruction, respectively (25-27). This difference was thought to be based on compression of the vessels by tumor cells and/or tumor angiogenesis. According to Maurer et al. (25) although malignant lymph nodes tend to show higher RI and PI values, the high frequency of false results prevent trustable differential diagnosis. In our study, we didn’t find a statistically significant difference when we compared lymph nodes of lymphoma cases and mean RI and PI values of benign lymph nodes.

Despite new diagnostic criterions of USG, size of the lymph node and necrosis are still the most important radiological ones. While some researchers use level and number of the nodes as a criterion, some others use its shape. Shape of a lymph node is determined by measurements taken vertically (maximum longitudinal or minimal axial diameter) (25). Na et al. (9) found L/T ratio greater than 2 in 14% of lymphomas and in 74% of benign lymph nodes and smaller than 2 in 85% of metastatic lymph nodes. Vassallo et. al. (28) proved the superiority of high resolution sonography by showing increased L/T value and eccentric enlargement of nodal cortex to be useful parameters for discrimination of benign nodes from metastatic ones. We also found higher mean L/T size ratios in benign lymph nodes than those of lymphomas and calculated the threshold value as 1.95 cm. A 73.3% sensitivity and a 66.7% specificity were found with L/T ratio in differential diagnosis of benign and lymphoma cases.

As a result, if neoplastic process progresses, lymph node gains a spheric appearance due to an increase in node size. Original node structure shows defeats due to tumor infiltration, desmoplastic reaction and necrosis (10). In this stage either a decrease or an increase can be seen in vascularisation under influence of angiogenic factors. Vascular resistance differences determined by CDUSG investigations are attributed to expansion of vascular patterns and to decrease in resistance in inflammations. On the other hand, compression of vascular structures by tumoral cells are accepted in tumor neovascularization. In addition, presence of smooth muscles in tumor vascular structure walls not as much as normal is also thought to lead changes in flow resistance (29). It was reported that obtained CDUSG parameters depend on biological structure of tumor vascularisation and this biological structure depends on various factors such as histological types of tumor cells, degree of nodal invasion and arteriovenous structure of neovascularisation (10).

In our present study, we conclude that type patterns in vascular structures and L/T ratios of lymph nodes obtained by USG investigations of superficial lymphomatous lymph nodes give worthwhile results in differentiation of benign and lymphoma related lymph nodes.
References