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Superficial lymph nodes involved by lymphoma in modern gray-scale ultrasound imaging

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Summary

Background: Clinical evaluation by palpation of superficial lymph nodes involved by lymphoproliferative process is not sufficient. Ultrasound is a useful method of the initial differential diagnosis of lymph nodes. The aim was to assess the spectrum of ultrasound features of superficial lymphomatous nodes and possible diagnostic pitfalls.

Material/Methods: Fifty five lymph nodes in 55 patients were prospectively examined in ultrasound with application of blood flow imaging modes and modern imaging techniques. Only forty lymph nodes with histopathologically proven lymphoma were selected for this analysis (3 Hodgkin, 37 non-Hodgkin).

Results: 27.5% of the examined lymph nodes were longitudinal; 42.5% had an oval or round shape; 30% were oval-lobulated or lobulated. 32.5% of the nodes did not show an echogenic hilum, 20% had a normal hilum, and 25% - evidently abnormal. 12.5% of the nodes were anechoic. The general ultrasound impression of a reactive lymph node was presented by 37.5% of the lymphomatous nodes; 45% were suspicious. Among 26 patients with non-Hodgkin lymphoma with multiple lymph nodes involved, in 15 (58%) lymph nodes were modeling on each other.

Conclusions: Lymphomatous nodes reveal diverse ultrasound presentations: from appearances indistinguishable from benign reactive lymph nodes to features typical of metastases. Ultrasound internal structure of lymphomatous nodes may be anechoic, causing the possibility of confusion with a cyst, especially in case of a single lymphomatous node. Multiple lymphomatous nodes with non-Hodgkin lymphoma often model on each other assuming geometrical shapes.

Key words: lymphoma • lymph nodes • ultrasound • imaging

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Background

The evaluation of lymph nodes involved by lymphomas is an important clinical problem in hematology. Palpation is not sufficiently sensitive for superficial lymph node detection and does not provide a reliable differential diagnosis [1-3]. Among different imaging methods, ultrasound has the best resolution in superficial tissues, allows excellent lymph node visualization, even when not enlarged, and supports differential diagnosis between benign and malignant adenopathy [4, 5].

Previous studies suggested the possibility of overlapping ultrasound presentations of lymph nodes in different lymphadenopathies [6-8].

Table 1. Final histopathologic diagnoses in the excised lymph nodes.

			Number
non-Hodgkin lymphomas	**low-grade**	small lymphocytic lymphoma (SLL)	22
		nodal marginal zone lymphoma (MZL)	2
		plasma cell myeloma infiltration	2
		follicular lymphoma (FL) G1	1
		follicular lymphoma (FL) G2	1
		mantle cell lymphoma (MCL)	2
	high-grade	diffuse large B-cell lymphoma (DLBCL)	7
Hodgkin lymphomas			3

The aim of this study was to analyze ultrasound features of lymphomatous nodes in order to show the spectrum of ultrasound presentations and to find out the possible diagnostic pitfalls. To have reliable confirmation of the assessed lymph node status, the lymph nodes scheduled for diagnostic resection were chosen for detailed ultrasound study.

Materials and methods

Fifty five superficial lymph nodes in 55 patients were prospectively examined in ultrasound with application modern ultrasound gray-scale imaging techniques (tissue harmonic imaging, panoramic imaging, three-dimensional imaging). Siemens Elegra (Erlangen, Germany) ultrasound machine with a 7.5 MHz linear transducer was used.

Only the lymph nodes with finally diagnosed lymphomas were selected for this analysis. Forty patients turned out to be affected by lymphoma. The patient population comprised 27 men and 13 women, aged, on the average, 58 years (age range: 22-84). The diagnosis was established by histopathologic examination of the whole excised lymph node. Twenty six lymph nodes were cervical, 13 – axillary, and one inguinal. The same node, which was previously assessed with ultrasound, was excised to have unequivocal confirmation of the examined lymph node status. Final diagnoses included: 3 Hodgkin lymphomas and 37 non-Hodgkin lymphomas (30 low-grade, 7 high-grade) (Table 1).

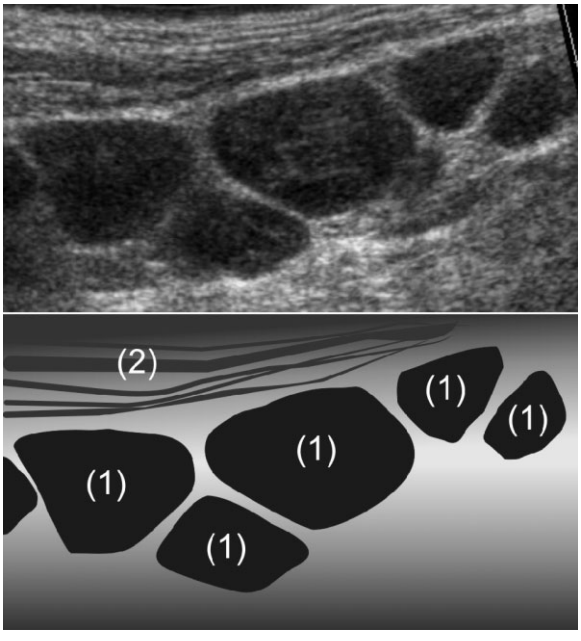

Figure 1. An ultrasound image and a scheme of multiple cervical lymph nodes modeling on each other and assuming geometrical shapes (1) in a 57-year-old male with a small lymphocytic lymphoma. (2) – sterno-cleido-mastoid muscle.

The histopathological diagnoses of lymphomas were established according to the WHO classification [9]. The division into 2 groups (depending on the aggressiveness of lymphoma were established according to The Non- Hodgkin's Lymphoma Classification Project [10].

The selected lymph node was primarily assessed in standard ultrasound gray-scale examination (assisted by tissue harmonic imaging), and subsequently a power Doppler or color Doppler mode was applied – detailed analysis of vascular pattern is the subject of another paper under review. The majority of patients underwent also evaluation in three-dimensional imaging and application of panoramic imaging (allowing to obtain longer than standard images).

The imaging protocol included the assessment of the whole area (neck, axilla, groin) and the detailed analysis of the lymph node intended for diagnostic excision. The evaluation criteria included the size, hilum, shape, echogenicity and internal homogeneity. The spatial arrangement of the lymph nodes was also taken into consideration in case of multiple lymph nodes.

The hilum was understood as an intranodal hyperechoic area which was seen to be continuous with the surrounding connective tissue.

Evaluation was performed by two experienced examiners reaching consensus.

Results

The average dimensions of the examined lymph nodes were: 21x10 mm. The smallest lymph node measured 8x6 mm; the biggest: 60x40 mm.

Table 2. Shape of the examined lymph nodes in ultrasound.

		longitudinal	oval or round	oval-lobulated	lobulated
non-Hodgkin lymphomas	low-grade	8	14	5	3
	high-grade	2	3	1	1
Hodgkin lymphomas		1	0	0	2

In none of the patients with Hodgkin lymphoma, multiple lymph nodes were modeling on each other.

Among 26 patients with non-Hodgkin lymphoma, multiple lymph nodes were involved in 15 (58%) and they were modeling on each other (Figure 1).

The shapes of the examined lymph nodes are presented in Table 2.

All the examined lymph nodes were hypoechoic. Five (12.5%) were anechoic.

Nine (22.5%) of the examined lymphomatous lymph nodes were inhomogeneous (Table 3). Multiple fine punctuate echoes scattered within a node or hiperechoic net pattern, and in one lymph node, anechoic areas gave the impression of internal inhomogeneity.

The appearance of the hilum in the examined lymph nodes is presented in Table 4.

The general ultrasound impression of a reactive lymph node was seen in 15 (37.5%) of the examined lymph nodes (Table 5) (Figure2). Eighteen (45%) of the examined lymphomatous nodes were suspicious in ultrasound (Figure3), while indeterminate ultrasound appearance was observed in 7 (17.5%).

Discussion

Ultrasound proved to be useful in differential diagnosis of superficial lymph nodes, helping to suggest their benign or malignant character [11-13].

Findings of our prospective study revealed diverse ultrasound presentation of involvement by lymphoma: from

Table 3. Ultrasound internal homogeneity of lymphomatous nodes.

		inhomogeneous	homogeneous
non-Hodgkin lymphomas	low-grade	6	24
	high-grade	2	5
Hodgkin lymphomas		1	2

appearances indistinguishable from benign reactive lymph nodes (Figure 2) to features typical of metastases (Figure 3).

The low number of lymph nodes assessed in our study is due to our attempt at obtaining very reliable ultrasound criteria of involvement by lymphoma through histopathological verification of the same node which was examined in ultrasound.

Lymphomatous nodes may mimic other lesions in ultrasound imaging, for example benign cysts, or benign, reactive lymph nodes [8,14]. Possible misdiagnoses may result in wrong treatment and the delay, or lack of treatment. Ultrasound appearance resembling other diseases or other pathologic lesions may be especially misleading in case of single lymph nodes involved by lymphomas.

All lymphomatous lymph nodes examined in our study were hypoechoic – similarly to previous reports [14]. Five of 40 lymphomatous lymph nodes (12,5%) were very dark, without any internal echoes, giving the general ultrasound impression of a simple cyst in gray-scale. This possible ultrasound appearance may lead to misinterpretation of a lymphomatous node with a cyst, especially in case of a single lymph node involved (Figure 4).

However, using high-resolution ultrasound transducers, lymphomatous lymph nodes demonstrate more often

Table 4. Appearance of the hilum in lymphomatous nodes in ultrasound examination.

		linear	oval	narrow	lobulated	irregular	Indeterminate	no hilum
non-Hodgkin lymphomas	low-grade	8	3	3	3	3	1	9
	high-grade	0	0	1	0	1	1	4
Hodgkin lymphomas		0	0	0	1	2	0	0

Table 5. General ultrasound impression of the examined lymph nodes.

		benign (reactive)	indeterminate	suspicious
non-Hodgkin lymphomas	low-grade	14	4	12
	high-grade	1	2	4
Hodgkin lymphomas		0	1	2

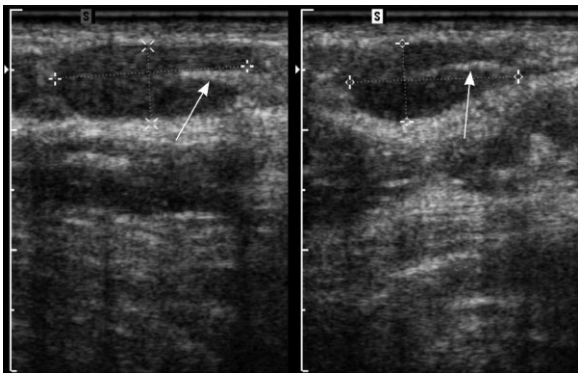

Figure 2. An ultrasound image (in two perpendicular planes) of a cervical lymph node (between markers) with ultrasound features of a reactive lymph node: longitudinal in shape with homogenous cortex and with a preserved hyperechoic linear hilum (arrow), in a 46-year- old male with a small lymphocytic lymphoma.

a heterogeneous pattern (68-86%) [14]. In our study nine (22.5%) of the examined lymphomatous nodes were inhomogeneous. The impression of internal inhomogeneity in our study was due to multiple fine punctuate echoes scattered within a node or fine hiperechoic net pattern, and in one lymph node anechoic areas (Figure 4). However, there were no gross inhomogeneities (e.g. large cystic areas or calcifications) in lymphomatous nodes in our study, nor in previous reports. This feature may be helpful in differential diagnosis with metastases, often containing anechoic areas, hyperechoic areas or calcifications [12, 15].

Normal or reactive lymph nodes tend to be longitudinal (flat oval) in shape [5, 16, 17]. In our study, 11 lymphomatous lymph nodes (27.5%) showed a longitudinal shape (Figure 2).

On the other hand, the majority of metastatic lymph nodes have rounded (broad oval or round) shape [5, 12, 13, 15, 18, 19]. Similarly to metastases also the majority of lymphomatous lymph nodes (77-86%) were described as rounded in shape [5, 14, 19]. Consistently with other reports, also in our study 17 lymphomatous lymph nodes (42.5%) showed an oval or round shape (Figure 4).

As far as we know, oval-lobulated and lobulated shapes have not been previously described in studies on superficial lymph nodes. Considering the fact that 12 (30%) of lymphomatous nodes in our study presented this feature (Figure 3), it is possible that lobulated shape might be one of the indicators of abnormality, but this observation requires comparison with large series of other lymph node pathologies. Including a lobulated shape into the spectrum of malignant lymph node features may support resemblance to an eccentric cortex widening described by Vassalo et al. and found only in malignant lymph nodes [5].

The appearance of a lymph node hilum is one of the key elements in differential diagnosis of superficial lymph nodes. The mere fact of the absence of the hilum is not differentiating, because it had been described in benign (reactive) lymph nodes, as well as in malignant ones (metastatic or lymphomatous) [5, 17-19].

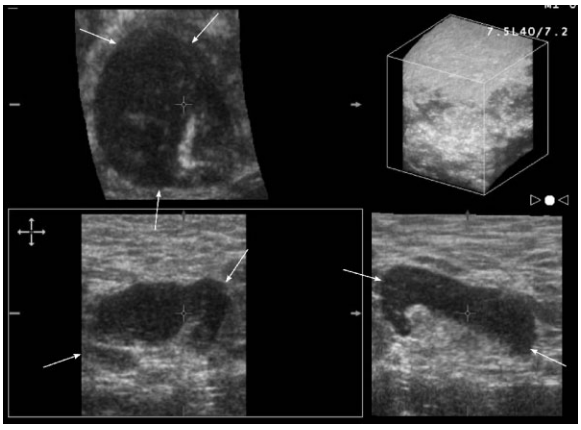

Figure 3. An ultrasound three-dimensional image of an axillary lymph node (arrows) with ultrasound features of a malignant lymph node: lobulated in shape with thickened cortex and irregular, star-shaped hilum, in a 58-year-old male with a small lymphocytic lymphoma.

In our study, 32.5% (13/40) of the lymphomatous lymph nodes did not show an echogenic hilum in ultrasound (Figure 4).

In other 2 cases (5%) in our study, the presence of a hilum was indeterminate: in the central area of a lymph node a faint thin echoic structure was observed, and it was equivocal whether it represents a slit-like hilum or an internal inhomogeneity of other origin.

A linear hilum, continuous with the perinodal connective tissue, considered characteristic of normal lymph nodes [20], was found in 20% (8/40) of lymphomatous lymph nodes in our study (Figure 2).

If the hilum is visible in ultrasound in metastatic lymph nodes, it may be distorted, suggesting a lymph node involvement by malignant disease. According to Yang et al., metastatic lymph nodes showed a significantly higher percentage (55%) of abnormal hilum than benign nodes [13].

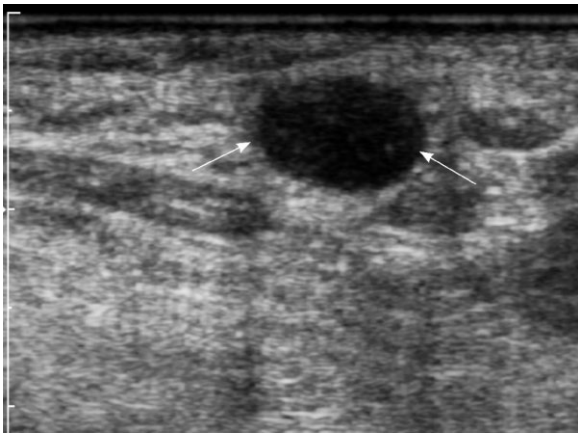

Figure 4. An ultrasound image of a lymph node (arrows) presenting in gray scale almost like a simple cyst: oval, anechoic, without the hilum, with posterior acoustic enchancement, in a 50-year-old male with a small lymphocytic lymphoma. The only sign suggesting possible solid nature of the lesion are very fine punctuate echoes inside.

In our study, the hilum was irregular in six lymph nodes (15%), and seven lymphomatous lymph nodes presented oval and lobulated hilum shapes (17.5%). Oval and lobulated hilum shapes were displayed by lymphomatous lymph nodes in the axilla. The meaning of this feature should be further studied and compared with benign, reactive or inflammatory lymph nodes.

A very narrow, slit-like hilum was found in 46% of metastatic lymph nodes and in 51% of lymphomatous lymph nodes in the study of Vassalo et al. [5].

In our study, only 10% (4 of 40) lymphomatous nodes showed a very narrow hilum. Therefore, a very narrow and irregular hilum may be considered abnormal, suggestive of malignancy: primary or secondary.

The general ultrasound impression of a reactive lymph node was observed in 37.5% (15/40) of the examined lymphomatous nodes (Figure 2). 45% (18/40) were suspicious in ultrasound – possibly malignant (Figure 3). Indeterminate ultrasound appearance was seen in 17.5% (7/40).

The important element of ultrasound differential diagnosis in case of detection of multiple superficial lymph nodes is their mutual spatial relationship. Non-Hodgkin lymphomas were described previously to model on each other, assuming geometrical shapes [21]. In our study, 58% of non-Hodgkin lymphomas (15 patients from 26 patients with multiple lymph nodes) presented ultrasound appearance compared with a "stone hedge" (Figure 1). On the other hand, in none of the patients with Hodgkin lymphoma multiple lymph nodes were modeling on each other in our study. These results are consistent with conclusions of other authors.

Conclusions

Lymphomatous nodes reveal diverse ultrasound presentation: from appearances indistinguishable from benign reactive lymph nodes to features typical of metastases.

Ultrasound internal structure of lymphomatous lymph nodes may be anechoic, causing the possibility of confusion with a cyst, especially in case of single lymphomatous lymph nodes.

Non-Hodgkin multiple lymphomatous lymph nodes often model on each other, assuming geometrical shapes.

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