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The application of ultrasound contrast, 3D imaging and tissue harmonic imaging in the differential diagnosis of lymph nodes enlargement in children

Ultrasonographic imaging is a vastly used diagnostic method in children with lymph node enlargement. Due to new generations of more and more sensitive ultrasonographs it becomes possible to increase the number of criteria used in differentiating the diagnosis of lymph node enlargement. However, difficulties in differentiating reactive lymph node enlargement from proliferative or metastatic enlargement still persist. Current sonomorphological criteria (size, shape, echogenicity, presence of echogenic hilus) observed in 2D presentations are not sufficient for distinguishing benign and malignant lymph node enlargement. Introducing harmonic imaging (THI) of the lymph node enables the improvement of image contrast and better revealing of the echostructure of lymph nodes by reducing the amount of artefacts. Also application of the Doppler technique enabled assessment of the vascularisation and measurement of blood flow parameters in lymph node vessels as a differential criterion. The visualisation of vascular architecture inside a lymph node enabled defining various types of vascularisation, which are recognised as characteristic of benign and malignant lymphadenopathy. However, those criteria appeared to be insufficient to evaluate malignancy grade of enlarged lymph nodes, especially in lymph nodes with very small vascularisation visualised in Power Doppler mode. Application of contrast media in ultrasound imaging creates the hope of increasing efficiency of diagnostic ultrasonography in lymph nodes enlargement. Ultrasonographic contrast media cause the intensification of the Doppler signal even by 20 dB. It gives the opportunity of more detailed imaging of the lymph node vascularisation pattern.

OBJECTIVE

The purpose of the study was to define the usefulness of ultrasonographic contrast media (Levovist), 3D presentation and harmonic imaging in differential diagnosis of lymph nodes enlargement in children.

MATERIAL AND METHODS

32 children with cervical lymph nodes enlargement underwent examination with ultrasonography. Among the analysed cases, 10 children (31.25%) suffered from oncological diseases: 1 child (3.12%) had Hodgkin's disease, 9 children (28.12 %) – acute lymphoblastic leukaemia. In the remaining 22 cases (68.75%) lymph nodes enlargement appeared among other symptoms of generalised infection (pyrexia, leucocytosis, increased ESR). Among the analysed cases of cervical lymph nodes enlargement, 26 patients (81.3%) had multiple lymph nodes in a number of more than 5. In the remaining 6 cases (18.7%), lymph nodes were in amount of less than 5. In all the cases, the biggest lymph node or the lymph node with the most disturbed echostructure of the whole group was chosen for ultrasonographic examination. Examinations were done with a Sonoline Elegra sonograph using convex and linear probes, 7.5 to 9.0 Hz frequencies. In each patient, examination consisted of evaluation of lymph nodes in 2D, THI and 3D presentations and the Doppler technique before and after the application of a contrast medium. In the examinations, Levovist by Schering was used in concentration 300, the amount depending on patient's body mass.

The following comparative analyses were performed: 1) Sonomorphologic image of the lymph node before and after the application of Levovist using the harmonic mode, 2) Lymph node vascularisation pattern, using the Doppler Techniques before and after the application of Levovist using BURST-mode, 3) Visualisation of blood vessels architecture, type of lymph node vascularisation and the spatial picture of blood vessels in 3D presentation.

RESULTS

Morphometric features of lymph nodes revealed in ultrasonoghraphic images were the following:

Table 1. Size criterion

	Number of lymph nodes	%
Size according to coefficient S/L<0.5*	24	75
Size according to coefficient S/L>0.5*	8	25
Total	32	100

*S/L (short to long axis) coefficient

Table 2. Contour criterion

	Number of lymph nodes	%
Smooth contours	28	87.5
Polycystic contours	4	12.5
Total	32	100

Table 3. Echogenicity criterion

	Number of lymph nodes	%
Echogenicity homogeneously decreased with presence of hilus	19	59.37
Echogenicity homogeneously decreased with absence of hilus	3	9.37

Echogenicity non--homogeneously decreased with presence of hilus	3	9.37
Echogenicity non--homogeneously decreased with absence of hilus	7	21.87
Total	32	100

Table 4. Vascularisation type criterion

	Number of lymph nodes	%
Presence of single hilus vessel	15	47
Presence of branching hilus vessel	11	34
Scanty peripheral vascularisation	3	9.4
Lack of vascularisation	3	9.4
Total	32	100

Ultrasonographic examination prior to contrast medium application of all examined lymph nodes revealed decreasing of echogenicity. In 10 lymph nodes decreasing of echogenicity had non-homogeneous character. After applying Levovist in sonomorphologic picture of the examined nodes homogenous type of intensifying of echogenicity was observed in 21 lymph nodes (65.62%) and non-homogeneous in 11 (34.38%). Heterogeneous intensity was shown in all cases, in which we could appreciate a non-homogeneous echogenicity of the node in 2D-mode and in 1 case, in which during examination with 2D-mode the node had homogeneously decreased echostructure. In 29 nodes (90.6%) after applying Levovist we could observe very intensive amplification of the signal in Power Doppler mode. In all lymph nodes on which Power Doppler examination was done before applying the contrast medium only a hilus vessel was visible. After applying Levovist branches of the hilus vessel appeared, in number from 3 to 7 of the main branches and in 4 nodes 5 additional branches were visible (Figs 1, 2).

Quantity evaluation of the vessels appearing after applying Levovist was undertaken with 3D-mode. Using the 3D presentation also enabled documentation of the geometric

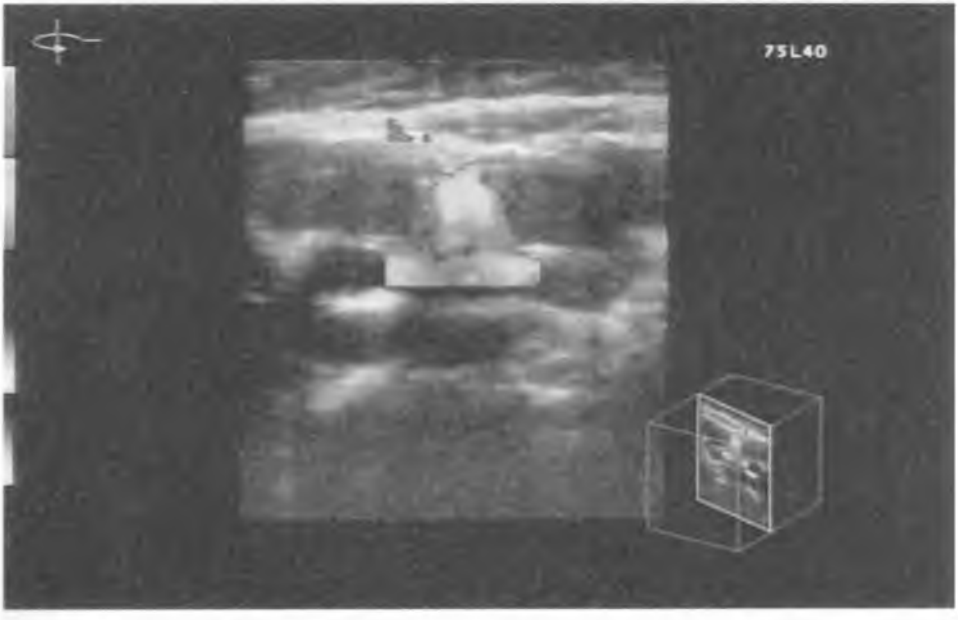

Fig. 1. Ultrasonographic image of a lymph node. Power Doppler mode, 3D presentation. Visualised the hilus vessel

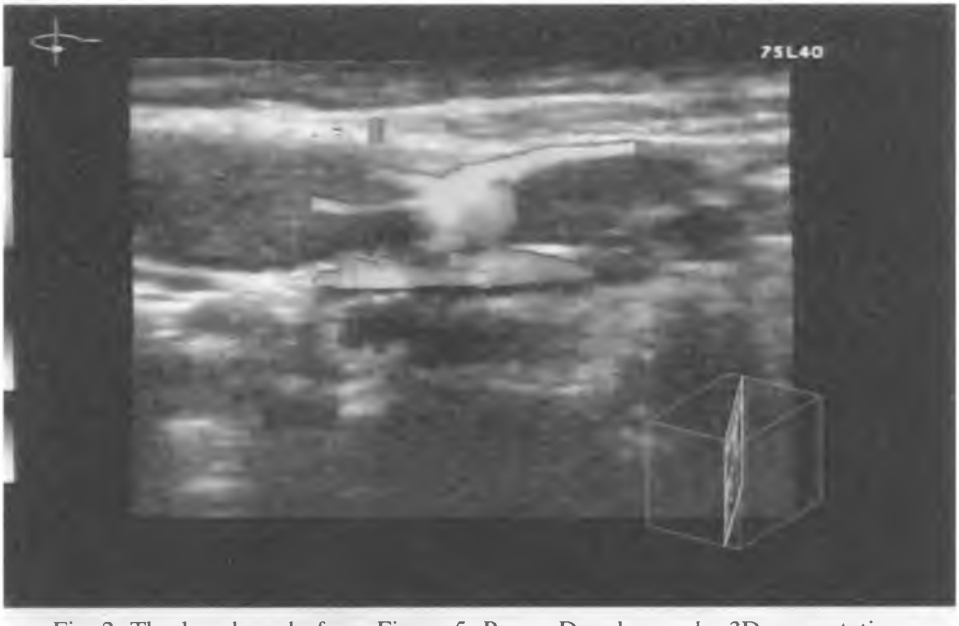

Fig. 2. The lymph node from Figure 5. Power Doppler mode, 3D presentation. With the use of other dimension in 3D mode. Visualisation of 3 additional branches of the main vessel

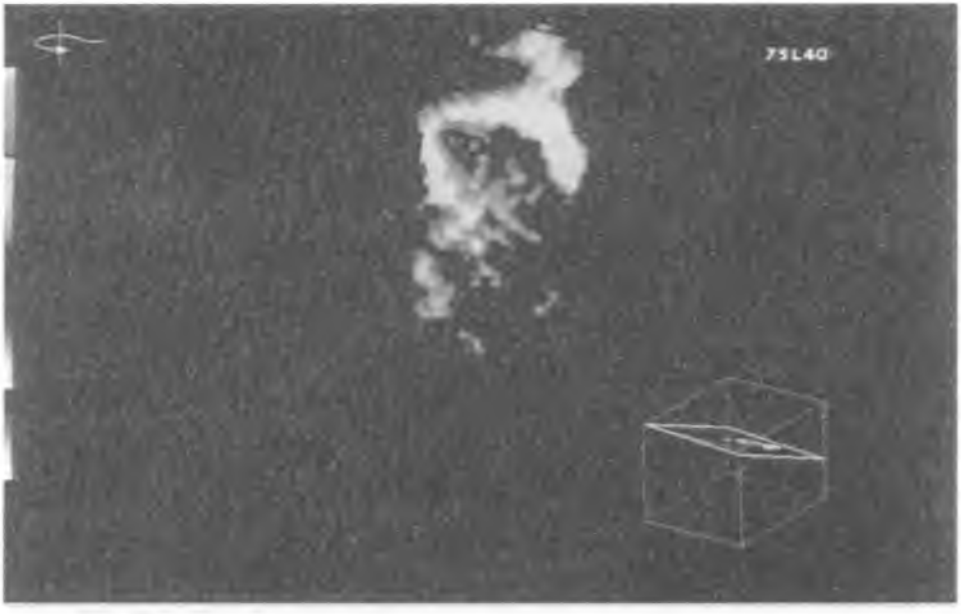

Fig. 3. Visualisation of a lymph node vessels in 3D presentation, with Power Doppler mode

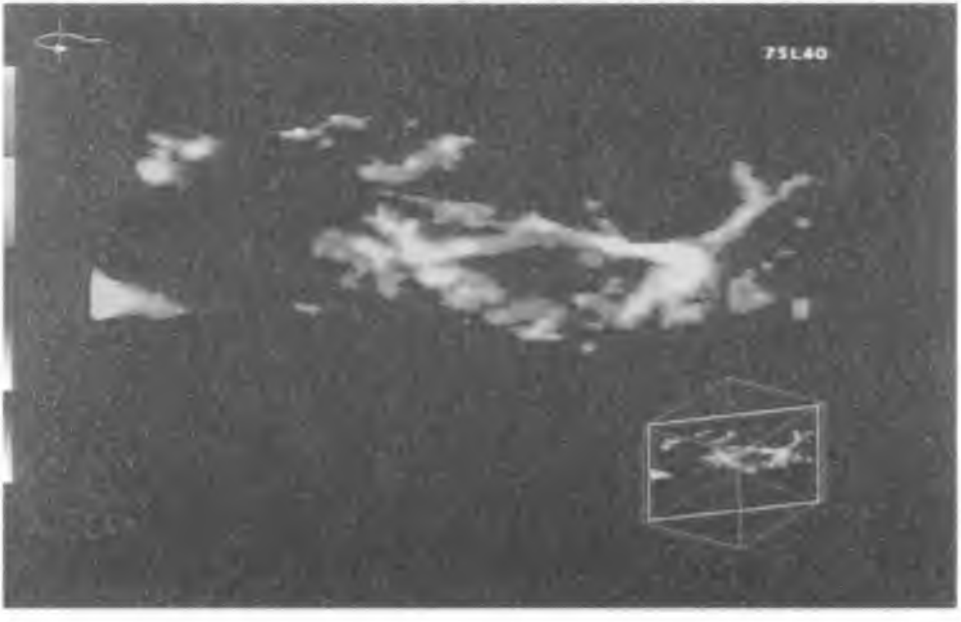

Fig. 4. Visualisation of a lymph node vessels in 3D presentation, with Power Doppler mode

Fig. 5. Image of a lymph node vascularisation after application of Levovist in BURST-mode. Pointing intensifications during first seconds

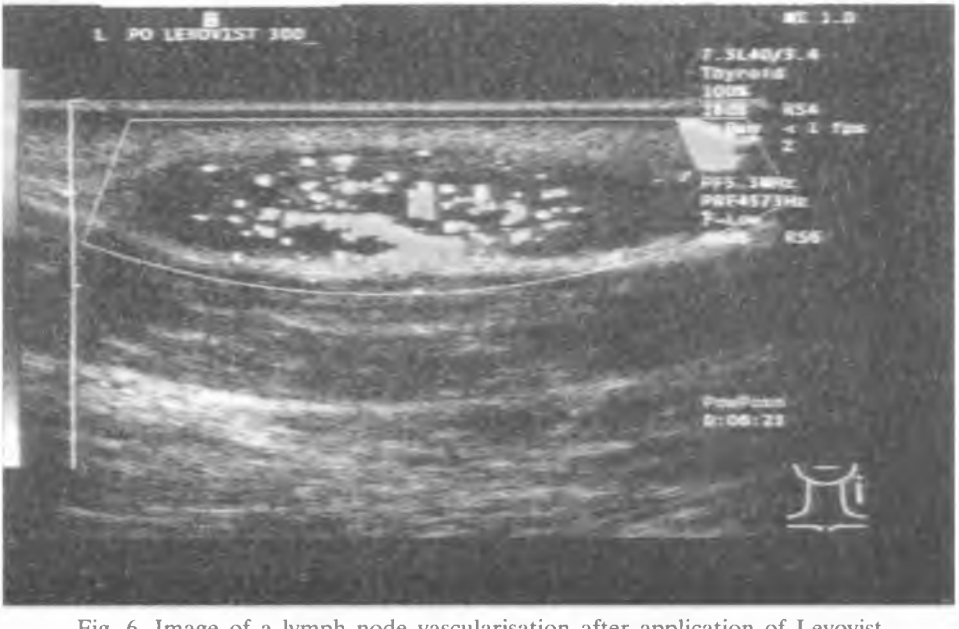

Fig. 6. Image of a lymph node vascularisation after application of Levovist in BURST-mode. Maximum of pointing intensifications

pattern of blood vessels in the node (Figs 3, 4). Among 3 cases of the examined nodes, in which in Power Doppler mode before applying contrast medium the vascularisation was invisible, 2 of the nodes (6.25%) did not reveal any blood vessels also after applying Levovist. In the other 1 node (3.12%) a single peripheral vessel was shown.

The duration of intensification of the signal in the examined lymph nodes was estimated with BURST-mode and lasted from 10 s. (appearing single echoes of intensification) to 300 seconds (vanishing of the last pointing echo of intensification). The largest intensification (the greatest amount of pointing echoes of intensification) was observed in the time from 30 to 120 seconds (Figs 5, 6).

Among 32 examined lymph nodes histopathological evaluation was performed in 9 lymph nodes: 1 lymph node in child with Hodgkin's disease, 1 lymph node in a child with symptoms of acute inflammation and 7 lymph nodes in children with laboratory evidence of mild lymphadenopathy. Only in the case of Hodgkin's disease in histopathological examination specific alterations were revealed. In all other cases the result of histopathological examination showed mild lymphadenopathy.

DISCUSSION

According to many authors the lymph nodes, which do not reveal any vascularisation in Power Doppler mode are the nodes considered to be benign. (7, 8) Due to intensification of ultrasound signal coming from blood vessels, Levovist enables better visualisation of the lymph node vascularisation. Among the nodes examined in the study in three cases the vascularisation was invisible in Power Doppler mode. After application of Levovist in one of the examined nodes (3.12%) a single peripheral vessel was shown. According to Mäurer et al. the lack of both hilus blood flow and peripheral vascularisation might appear in malignant nodes (7). In our case the lymph node was found in a patient with benign lymphadenopathy. Application of Levovist enables defining the vascularisation pattern due for visualisation of the vessels primarily invisible in Power Doppler mode. One of the patterns recognised as malignant is the presence of focal lack of vascularisation. Among the cases analysed in our study such lymph nodes were found. However, histopathological verification in all the cases was impossible.

Determining the correlation between histopatological and ultrasonographic results in the cases of enlarged lymph nodes in children analysed in the study was difficult. It was connected with a comparatively small number of performed biopsies (1 node in the case of Hodgkin's disease, 1 node in benign lymphadenopathy and 7 lymph nodes in the children with laboratory evidence of acute inflammation). Merely the node taken from a child with Hodgkin's disease revealed the presence of neoplasmatic cells. In the ultrasonographic examination with the 2D-mode it demonstrated homogeneously decreased echostructure, without the presence of the hilus. In Power Doppler presentation we could observe a single vessel in the hilus. After applying Levovist, non-homogeneous

increase of echogenicity could be noticed with an isolating area of weak intensification, which was not visible before applying the contrast medium. After application of Levovist the branches of hilus vessel appeared in Power Doppler mode. We could also observe 5 additional branches of the hilus vessel. Although in that node in the histopathological examination the presence of neoplasmatic cells was noted, it might not be assumed that the ultrasonographic image obtained is patognomic for malignant lymphadenopathy. Analogical features of ultrasonographic picture were revealed in 2 examined lymph nodes, in which during histopathological examination the presence of neoplasmatic cells was not noted. It is also confirmed by many other authors that the pattern of vascularisation with the presence of hilus vessel with or without peripheral branches is characteristic rather of reactive nodes (8). The only differentiating point between benign and malignant lymphadenopathy among analysed cases in our study was the finding of non-homogeneous intensification after application of Levovist in Hodgkin's disease's node. However, it could also be an effect of both infiltration of neoplasmatic cells and the shallow area of regressive changes (necrosis), which can be found both in benign and malignant lymphadenopathy (5). Non-homogeneous decrease of echogenicity of lymph nodes both before and after the application of the contrast medium was observed also in 3 nodes of the children with laboratory evidence of inflammation, and in 1 node in the child with lymphoblastic leukaemia. Unfortunately, in those cases histopathological examination was not performed.

In the case of leukaemias in children with laboratory evidence of neoplasmatic process, biopsy is renounced assuming that at least some part of lymph nodes are infiltrated by neoplasmatic cells. The ultrasonographic picture of lymph nodes in children with leukaemias varied. In 1 case it was the node with non-homogeneous decrease of echogenicity with the presence of hilus, the remaining 8 nodes showed homogeneously reduced echogenicity with the presence of hilus. After the application of Levovist, in all 8 cases homogeneous increase of echogenicity of the node was observed. Changes of echogenicity and an image of vascularisation shown in the examined nodes in the children with lymphoblastic leukaemia were also discovered in the cases of nodes in the children without any laboratory evidence of a neoplasmatic process.

CONCLUSIONS

The analysis of obtained ultrasonographic images performed in the study allowed to draw the following conclusions:

1. Change of echogenicity of the lymph node after the application of contrast media enables better visualisation of a non-homogeneous structure of the node. Revealing the areas of the node with non-homogeneous

intensity might correspond to regressive changes or infiltrations of neoplasmatic cells.

2. Applying contrast media enables better visualisation of the vascularisation of the lymph node.

3. Ultrasonographic examination with Levovist enables the localisation of the vessels which were not shown in conventional Doppler mode.

4. With the use of the 3D mode, we obtain a better picture of the vessels architecture in the lymph node with a possibility for quantitative evaluation of new lymph vessels revealed after Levovist.

5. Determining the correlation between histopathological and ultrasonographic results with the use of new imaging methods THI, 3D and contrast media in Power Doppler mode examinations will increase the diagnostic efficacy of ultrasonography in the differentiating of enlarged lymph nodes in children.

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SUMMARY

The application of Power Doppler mode examination introduced the assessment of vascularisation and measurement of blood flow parameters in lymph node's vessels as a differentiating criterion of benign and malignant lymphadenopathy. However, those criteria appeared insufficient in evaluation of the malignancy grade of enlarged lymph nodes, especially in the cases of lymph nodes with invisible or scantly visible vascularisation in Power Doppler mode. Introducing contrast media in ultrasonographic examinations enabling intensification of the Doppler signal even by 20 dB creates the hope of increasing diagnostic efficacy of ultasonography in evaluation of vascularisation in lymph nodes enlargement. The purpose of the study was to define the usefulness of ultrasonographic contrast media (Levovist), 3D presentation and harmonic imaging in differential diagnosis of lymph nodes enlargement in children. 32 children with cervical lymph nodes enlargement underwent examination with ultrasonography. In the examinations, Levovist by Schering was used in concentration 300, the amount depending on patient's body mass. The analysis of results obtained in the study revealed that application of contrast media enables better visualisation of lymph node vascularisation. Localisation of the vessels which were not shown in conventional Doppler mode enables visualisation of the vessel architecture in the lymph node and better defining of vascularisation pattern. Application of the new methods of THI and 3D imaging and contrast media in Power Doppler examinations increases the diagnostic efficacy of ultrasonography in differentiating lymph nodes alternations.

Zastosowanie ultrasonograficznych środków kontrastujących, obrazowania 3D oraz THI w diagnostyce różnicowej powiększonych węzłów chłonnych u dzieci

Zastosowanie badań dopplerowskich wprowadziło ocenę unaczynienia i pomiaru parametrów przepływu krwi w naczyniach węzła jako kryterium różnicowe limfadenopatii łagodnej i złośliwej. Jednak kryteria te okazały się niewystarczające w ocenie stopnia złośliwości powiększonych węzłów chłonnych, zwłaszcza w przypadkach węzłów chłonnych o niewidocznym w badaniu PD lub jedynie śladowym unaczynieniu. Wprowadzenie do badań ultrasonograficznych środków kontrastujących, powodujących wzmocnienie sygnału dopplerowskiego nawet o 20dB, stwarza nadzieję zwiększenia skuteczności diagnostycznej ultrasonografii w ocenie unaczynienia powiększenia węzłów chłonnych. Celem niniejszej

pracy było określenie przydatności zastosowania ultrasonograficznych środków kontrastujących (Levovistu) opcji 3D oraz obrazowania harmonicznego w diagnostyce różnicowej powiększenia węzłów chłonnych u dzieci. Badania ultrasonograficzne przeprowadzono u 32 dzieci, u których stwierdzono powiększenie węzłów chłonnych szyi. W badaniach został zastosowany Levovist firmy Schering w stężeniu 300, w ilości zależnej od masy ciała pacjenta. Analiza wyników badań przeprowadzonych w niniejszej pracy ujawniła, że zastosowanie środków kontrastujących umożliwia lepsze uwidocznienie unaczynienia węzła chłonnego. Zlokalizowanie naczyń, które nie zostały uwidocznione w konwencjonalnym badaniu dopplerowskim, umożliwia uwidocznienie architektoniki naczyń w węźle chłonnym oraz dokładniejsze określenie wzorca unaczynienia. Zastosowanie nowych metod obrazowania THI, 3D oraz środków kontrastujących w badaniach dopplerowskich zwiększa skuteczność diagnostyczną ultrasonografii w różnicowaniu zmian w węzłach chłonnych.