Cervical Lymph Node Metastases in Neck Malignancy – An Ultrasonographic and Histopathological Comparative Study

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Objectives: Different approaches have been made to differentiate benign from malignant cervical lymphadenopathy by Ultrasound examination. Assessment of nodal status is essential in patients with head and neck carcinomas as it predicts prognosis and helps in the selection of treatment options. The present study was designed to evaluate the role of ultrasonography in the assessment of malignant cervical lymph nodes. Grey scale Ultrasound assesses the nodal size, shape, border, internal architecture (echogenicity and necrosis). The vascular pattern of lymph nodes is evaluated with Color Doppler Ultrasound.

Methods: 117 cervical masses evaluated by ultrasonography in 83 patients over a period of 29 mounths (between January 2008 and June 2010) were evaluated for the presence of intranodal vascular pattern, which was considered benign when it traversed through the node without disruption.

Results: Of the 117 cervical tumors evaluated, 73 were found to be malignant on pathologic review. Malign vascular markings were present in 93/117 lymph nodes evaluated. The presence of malign vascular pattern had a sensitivity of 97.3% and a negative predictive value of 91.7%. Malignant Gray scale Ultrasound martkings had a sensitivity of 23.3% and a positive predictive value of 100%.

Conclusions: The presence of normal intranodal blood flow was associated with a benign diagnosis in 91.7% of the masses evaluated. The addition of this Color Doppler Ultrasound finding improves the ability of ultrasonography to predict the likelihood of malignant involvement.

Keywords: ultrasound examination, lymph nodes, positive predictive value, malignant tumors

Introduction

Colour Doppler Ultrasound (CUDS) is a valuable tool in the differentiation of benign from malignant lesions within parenchymal organs. Evaluation of enlarged lymph nodes is another application of CUDS. CUDS is a sensitive non invasive imaging technique capable of detecting vessels as small as those found in lymph nodes.

Assessment of nodal status is essential in patients with head and neck carcinomas as it predicts prognosis and helps in the selection of treatment options. In patients with proven head and neck carcinomas, the presence of a unilateral metastatic node reduces the 5-year survival rate by 50%, whereas the presence of bilateral metastatic nodes reduces the 5-year survival rate to 25% [1].

Metastatic cervical lymph nodes from head and neck carcinomas are usually site specific with respect to the location of the primary tumour. Besides metastases, lymphoma is also a common malignant disease and head and neck involvement is relatively common [1]. Clinically, lymphomatous cervical lymph nodes are difficult to differentiate from other causes of lymphadenopathy including metastatic nodes. As the treatment options differ, accurate identification of the nature of the diseases is essential.

Ultrasound (US) is sensitive compared to clinical examination (96.8% and 73.3% respectively) in patients with head and neck cancer [1].

The present study was designed to evaluate the role of ultrasonography in the assessment of malignant cervical lymph nodes. Grey scale ultrasound assesses the nodal size, shape, border, internal architecture (echogenicity and necrosis). The vascular pattern of lymph nodes is evaluated with CUDS.

Material and methods

In this prospective study, ultrasound patterns of neck masses were evaluated.

The neck was divided into 12 levels (six bilaterally)[2] and into eight regions according to their location in the neck established by Hajek et al. [3].

A total of 83 patients were included in the study with ages ranging from 19 and 78 years. The mail to femail ratio was 4:1.

On histological examination fifty patients were diagnosed with malignant tumors and 33 with benign lesions. At those patients we analized 117 neck masses. On this 117 cervical tumors 73 were malignant and 44 benign masses. Malignant masses consisted of the following diagnoses: lymphoma (N=8), metastasis of laryngeal carcinoma (N=40), metastasis of undifferentiating carcinoma (N=14), metastasis of malignant melanoma (N=6), metastasis of tyroidian cancer (N=3) and metastasis of lung cancer (N = 2). Benign lesions consisted of: 2 lipomas, 1 thyrogossal duct cyst, 1 branchial cleft cyst, 14 normal lymphoid nodes, 7 lymphoid reaction, 3 sinusoid histiocitosis, 1 submandibular sialadenitis, 1 submandibular sialolithiasis, 5 pleomorphic adenoma, 1 dermoid cyst, 1 ectopic thyroid,

Table I. Morphological characteristics compared to pathologic results / biopsy

N = 117	Echo-genicity	Border	Shape	Size	Necro-sis	Vas-cular pattern	Six charac-teristics
True positive	71	25	62	57	34	71	12
True negative	10	38	24	20	44	22	44
False positive	34	6	20	24	0	22	0
False negative	2	48	11	16	39	2	61

1 thyroidian node, 2 nodal tuberculosis, 2 nodal toxoplasmosis and 2 cases of Warthin tumor. The distribution of masses by cervical regions are shown in Figure 1.

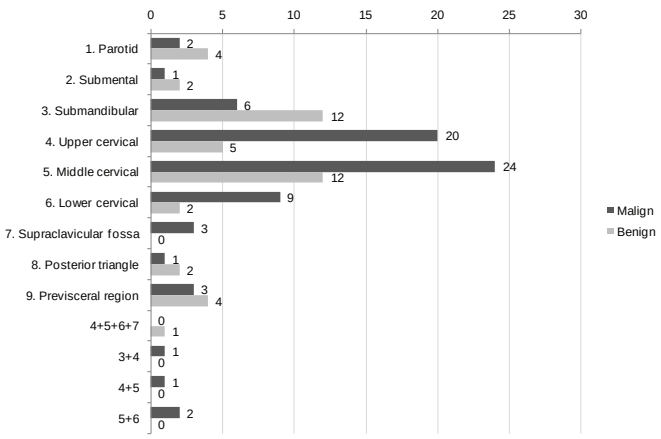

Fig. 1. Assessment of neck masses according to their region

Ultrasonography was performed using a 10 mHz linear transducer (Philips HD +11XE). The subject lay supine on the couch with the shoulders supported by a pillow and the neck hyper extended. Scans were obtained with the transducer placed transversely and longitudinally and measurements made in the plane that showed a maximum cross sectional area. The ultrasound findings documented were nodal site, number, internal architecture, relation to surrounding structures and vessels.

The Gray scale US features included in this study were (1) echogenicity, (2) border, (3) size, (4) necrosis and (5) shape. The sixth characteristic was the evaluation of vascular pattern of the lession. Nodal blood flow was considered benign when he passes throught the center of the lymph node without disruption. Nodes were classified for each of the six characteristics as either malignant or benign in nature. The malignant features were hypoechoic echogenicity, sharply demarcated border, size >15 mm, round contour, presence of necrosis and abnormal vascular pattern. Benign features were considered to be the oposite of these findings.

Initial confirmation of neck masses was done by biopsy or surgical resection.

The study protocol was approved by our institutional review board, and all patients gave written informed consent. An Excel table was used for the centralization and data analysis. The Ultrasound results were correlated using the GraphPad In Stat 3 statistics software (version 3.06), by chi-square or Fisher tests. The obtained values were considered statistically significant in case of $p < 0.05$ and a 95% confidence level.

Negative and positive predictive values were used to assess the performance of sonographic examinations in the detection of metastatic nodes. The negative predictive value (NPV) is the percentage of nodes interpreted on sonograms as negative for malignancy that were histopathologically proved not to be malignant. The positive predictive value (PPV) is the percentage of nodes interpreted at sonography as positive for malignancy that were histopathologically proved to be malignant. We also calculated the sensitivity (true-positive results/[true-positive results + false-negative results]) and specificity (true-negative results/ [true-negative results + false-positive results]). The accuracy was calculated by the following formula: (true-positive results + true-negative results)/total number of nodes.

Results

The individual criteria for detection of malignancy on US were compared with the histopathological findings.

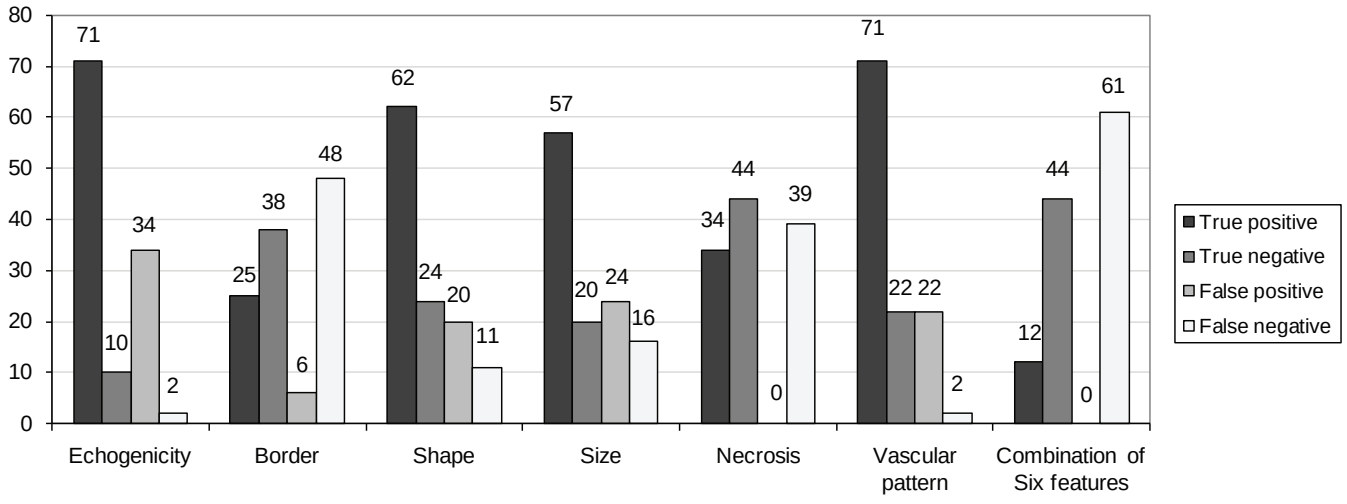

Fig. 2. Assessment of neck masses according to their region

Size

On US, size of the nodes detected ranged from 0.7 × 0.3 cm to 5.7 × 4 cm (longitudinal diameter x axial diameter). All nodes considered positive for malignancy on US had an axial diameter of > 1.5 cm while those negative for malignancy were < 0.5 cm. On histopathological exam (HPE) all nodes positive for malignancy had an axial diameter of > 1.5 cm while those negative were < 0.4 cm. A diameter > 15 mm was present in 81 of the 117 (69.23%) masses. Of the 81 tumors found to have a diameter >15 mm, 57 (70.37%) were found to have malignant pathologic results. Of the 36 nodes that did not demonstrate a diameter >15 mm, 20 (55.55%) was found to be benign on pathologic review. Thus, using univariate analysis, the size criteria had a sensitivity of 78.1% and a specificity of 45.5% with a PPV of 70.4% a NPV of 55.6% and an accuracy of 65.8% (p = 0.0075).

Shape

Of the 82 nodes detected on US, 62 (75.61%) were found positive for malignancy on HPE and 35 masses were found negative on HPE: of these, 11 (31.42%) were round and 24 (68.57%) were oval. The shape of the lymph node was assessed by the L/S (long axis/short axis) ratio (Solbiati-(L/T-) indices). Normal lymph nodes are usually elliptical with an L/T ratio of >2 whereas metastatic nodes tend to be rounder and L/T is below 2. A round contour was present in 82 of the 117 (70.08%) tumors. Thus, using univariate analysis, contour recorded a sensitivity of 84.9% and a specificity of 54.5% with a PPV of 75.6%, a NPV of 68.6% and an accuracy of 73.5% (p = 0.000006).

Echogenecity

Metastatic lymph nodes are typically hypoechoic to skeletal muscle. Hypoechoic echogenicity was present in 105 of the 117 (89.74%) neck masses. Of these, 71 (97.26%) were found to have malignant pathologic results. Of the 12 masses that did not demonstrate hypoechoic features, 10 (83.33%) were found to be benign on pathologic review. Thus, using univariate analysis, echogenicity features demonstrated a sensitivity of 97.3% and a specificity of 22.7% with a PPV of 67.6% , a NPV of 83.3% and an accuracy of 69.2% (p = 0.0005).

Necrosis

Of the nodes detected on US and found positive on HPE, 34 (46.57%) showed necrosis. Thus, using univariate analysis, the necrosis criterion had a sensitivity of 46.6% and a specificity of 100% with a PPV of 100% a NPV of 53% and an accuracy of 66.7% (p = 0.0000).

Extra-Capsular Spread (ECS)

A sharply demarcated border was present in 31 of the 117 (26.5%) tumors. Of the 31 nodes found to have a sharply demarcated border, 25 (80.64%) were found to have malignant pathologic results. Of the 86 tumors that did not demonstrate a sharply demarcated border, 38 (44.18%) were found to be benign on pathologic review. Thus, using univariate analysis, border features proved a sensitivity of 34.2% and a specificity of 86.4% with a PPV of 80.6% and a NPV of 44.2%. P value was 0.0144 (considered significant) and accuracy was 53.8%

In our patient population, benign vascular markings were present in 24 of the 117 (20.51%) cervical masses evaluated. Of the 24 nodes found to have benign vascular pattern, 22 (91.66%) were found to have benign histopathologic results (Table I). Of the 93 nodes that did not demonstrate benign vascular markings, 71 (76.34%) were found to be malignant on pathologic review (p = 0.0001). Thus, using univariate analysis, lack of benign vasculature demonstrated a sensitivity of 97.3% and a specificity of 50%. Lack of benign vasculature was found to have a positive predictive value of 76.3%, whereas the presence of benign vasculature had a negative predictive value of 91.7%. The accuracy in this case was 79.5%. Chi test was 0.000000.

A combination of these six malignant features was present in 16.43%(12) of the nodes evaluated. This combination demonstrated a sensitivity of 16.4%, a specificity of 100%, and a PPV of 100%, NPV of 41.9%, Accuracy of 47.9% (p = 0.0020) (Fig. 4). Chi test value was 0.004527.

Discussion

Different approaches have been made to differentiate benign from malignant cervical lymphadenopathy by Ultrasound examination. In Gray-scale sonography, assesment of l/s ratio has proven to be a major advance in the sonographic differentiation of enlarged nodes, achiving an accuracy of up to 95% [4].

Color Doppler is the modality of choice for the assessment of vascular pattern (VP). By comparison hilar and non-hilar patterns appear highly specific for benign and metastatic nodes respectively [5–7]. Tumor infiltration of a node distort the normal vascular pattern, which is composed of an artery and vein that enters throuth the node at the hilum [8]. In our study we found that the lack of benign vascular markings had a sensitivity of 97.3% and a NPV of 91.7%. Thus, when malignant vascular pattern was seen, 76.3% of lessions was associated with a malign lymph node. Unfortunately, malign vasculature was found in only 79.49% of lymph nodes that were evaluated. This means that the lack of benign pattern flow has a relatively poor PPV (76.3%) as a single marker. Dangore-Khasbage S. et al in a prospective study evaluated 70 cervical lymph nodes in 30 known primary oral cancer patients with CDUS during a period of 8 months and the CDUS evaluation was found to be highly significant with a sensitivity of 92.90% and a specificity of 84.21%, after comparing the CDUS findings with histopathologic results [9]. The overall accuracy of VP improves further when combined with size, shape and other grey-scale features. Tschammler A. et all in their study found a specificity of 77% and a sensitivity of 96% of CDUS [10] examination.

In our study other features such as echogenicity, shape, necrosis and vascular pattern demonstrated sensitivities of 97.3%, 84.9%, 46.6% and 97.3% and PPV values of 67.6%, 75.6%, 100% and 76.3% respectively. Among these features necrosis was highest PPV value. Other studies have shown varying levels of accuracy for the US features of echogenicity, border, necrosis and size. In their paper Yanrong ZHANG et al. [11] reported a sensitivity of 59.8%, specificity of 76.5% and accuracy of 67.1% for the round shape, values real closet to our results. Extracapsular spread is characterised by irregular nodal borders on US. Steinkamp et al. examined 110 patients with N-all HNSCC for ECS with US and reported a sensitivity of 79% with a specificity of 82% which was comparable to CT and MRI [12].

Ahuja's group looked at VP and grey scale features in 101 metastatic nodes from a mixed population of tumours and 72 non-metastatic nodes [6]. Using a minimum of three features to denote malignancy (abnormal internal echogenicity, deranged internal architecture and an L/T of <2.0), grey-scale alone had a sensitivity of 95% and specificity 83%. By comparison, VP had a sensitivity of 90% and specificity of 100%. However, when VP and greyscale parameters were combined (four features of malignancy), both sensitivity and specificity reached 100%.

We found that, by utilizing six features of malignancy, we could achieve a PPV of 100% which means that 100% of lymph nodes with all six malignant caracteristics are true malignant at histopathologic results. In our study p values obtained by chi square test is < 0.05 which means that malignant features/pathologic results association is statistically significant.

US was uselful in diagnosing malignancy using axial diameter or size only if the size was <0.5 cm or >1.5 cm. Nodes ranging in size between these two figures were not accurately assessed. All nodes showing necrosis on US were positive for malignancy. Absence of necrosis was seen in both benign and malignant nodes. No reactive nodes showed necrosis. US was only able to detect 25% of necrotic nodes in this study, but it is diagnostic of malignancy.

Conclusions

Sonography is a useful imaging tool in the assessment of cervical lymph nodes.

Color-Doppler ultrasound is a recently introduced method which makes it possible to evaluate intra- and perilesional vascularization and to perform a hemodynamic study of the area being explored. CDUS is a reliable and reproducible method which can provide a useful adjunct to conventional ultrasound, increasing diagnostic accuracy in cervical masses. The identification of metastases in lymph nodes of the neck has a major effect on the prognosis and treatment of head and neck cancer.

We conclude that ultrasonographic examination of cervical lymph nodes can yield important information regarding the diagnosis.

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