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Echography of metastatic nodes treated by radiotherapy

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Abstract

The purpose of this study was to evaluate whether the ultrasonographic appearances of nodal metastases in nasopharyngeal carcinoma (NPC) revert to normal after radiotherapy.

Serial ultrasonography was performed in 18 patients with palpable nodal metastases in the neck who underwent radiotherapy for NPC. All patients had a pre-radiotherapy baseline and another study at least one year after radiotherapy. The largest node in each patient was evaluated for any change in the ultrasonographic features following radiotherapy.

One year after radiotherapy nodes returned to normal size for their respective areas, the shape of the node and the echogenic hilus also reverted to normal. However, the nodes are more echogenic than nodes in normal subjects. This distinguishes these nodes from nodes not affected by radiotherapy. The histological basis for this observation is presumed to be the result of fibrosis.

At first glance the post-radiotherapy nodes may resemble normal nodes, however subtle changes within the node and adjacent soft tissues can be recognized on ultrasonography. During long-term follow-up, the appearance of nodes at sites previously uninvolved or any change in the appearance of nodes should alert the sonologist to the possibility of recurrence.

Key words: Ultrasonography; Nasopharyngeal neoplasms; Lymph nodes; Neoplasm metastasis; Radiotherapy

Introduction

Ultrasound has been shown to be valuable in the detection of subclinical cervical lymphadenopathy in malignant disease. It could, therefore, have a useful role in the monitoring of nodes following therapy. However ultrasonographic signs of malignancy take time to disappear and there may be new appearances associated with the effect of therapy. These features must be recognized so that persistent or new imaging signs are not interpreted as representing residual or recurrent disease.

We have, therefore, studied the effect of radiotherapy on cervical lymphadenopathy in NPC. This restriction to one primary tumour was intentional in order to achieve as homogeneous a patient group as possible.

Materials and methods

In this prospective study, serial ultrasonographic examinations were performed on 18 patients with palpable malignant nodes in the neck (proven by fine needle aspiration cytology (FNAC)) who had radiotherapy (60–66 Gy over 6–6.5 weeks) for NPC. All patients had a baseline (pre-radiotherapy) ultrasonographic examination. Sixteen patients had no local or regional recurrence during the follow-up period and were free of disease six months after the last ultrasonographic examination. All 16 patients had subsequent scans at a minimum of one year (12–14 months).

Two patients had recurrent disease during the course of their follow-up. One patient had local (nasopharyngeal) and regional (cervical lymph node) recurrence and the second had only regional recurrence. Neither had clinical evidence of distant metastatic disease.

Ultrasonographic examinations were performed on either an Aloka 650 (Tokyo, Japan) or a Diasonics VST Master Series (California, USA) US machine with a linear 7.5 and a sector 10 MHz transducer.

Although not all the lymph nodes in the same patient may react in the same way after radiotherapy, the largest node was looked at specifically. The position of the largest abnormal node in the first scan was documented and subsequent follow-up scans recorded the changes in this particular node.

In evaluating the largest abnormal node in each patient, the features recorded were established and well-known criteria. These were: position, shape and size of the node, internal architecture, nodal border, soft tissue oedema, nodal matting, intranodal necrosis, calcification and echogenicity. In evaluating size

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TABLE I
ULTRASOUND FEATURES OF THE CLINICALLY LARGEST PALPABLE NODE (NON-RECURRENT GROUP, N = 16) IN THE SERIAL SCANS

Ultrasound features	Number of lymph nodes (percentage)				*p* value (S = significant; NS = non-significant)
	Pre-RT		⩾1 year		Pre-RT vs ⩾ 1 year
S/L ratio < 0.5	7	(44%)	15	(94%)	0.008 S
Hilus present	1	(6.3%)	5	(31%)	0.125 NS
Echogenic area	0	(0.0%)	11	(69%)	0.001 S
Fascial plane preserved	16	(100%)	14	(88%)	0.500 NS
Homogeneous	13	(81%)	15	(94%)	0.500 NS
Unsharp nodal border	0	(0.0%)	11	(69%)	0.001 S

for the definition of metastatic nodes of ear, nose and throat cancers, 8 mm (maximum transverse diameter) is taken as the upper limit of normal (Bruneton and Normand, 1987). In this study the largest node was greater than 8 mm in size in all the patients.

Shape was assessed on the basis of short axis (SA) to long axis (LA) ratio. A SA/LA ratio greater than 0.5 indicates round nodes, less than 0.5 indicates oval nodes. Malignant nodes tend to be round with a SA/LA ratio greater than 0.5 (Tohnosu *et al.*, 1989).

We evaluated abnormalities of internal architecture which included cystic necrosis; coagulation necrosis and the presence or absence of a hilus. Coagulation necrosis appears as a highly reflective focus within abnormal nodes. It is less reflective than the normal hilus, and discontinuous from surrounding connective tissue (Sakai *et al.*, 1988). Cystic necrosis is seen as focal irregular areas of low reflectivity in a node. The normal hilus is seen as a linear, hyperechoic structure within a node and is continuous with the surrounding connective tissue (Sakai *et al.*, 1988; Evans *et al.*, 1993).

The soft tissues were analysed for oedema of the subcutaneous tissues and/or adjacent muscle; oedema being indicated by a diffuse decrease in reflectivity in adjacent tissues, and loss of fascial planes. Matting was defined as clumps of nodes adherent to each other with no normal echogenic connective tissues between.

McNemar's chi-square test was used to calculate the *p* values in Table I. Fishers exact test was used to calculate the *p* values in Tables II and III.

As this study involved a small number of patients, all statistical results should be viewed with caution. The reason for the small number of patients is due to non-compliance by patients. Often, when the patients knew that there was no evidence of local or regional relapse on their post-treatment clinical follow-up, the patients defaulted their ultrasonography.

Results

In the group of patients with no recurrence there were 12 males and four females ranging in age from 27 to 74 years.

At the baseline scan the largest node of each patient ranged in size from 8 mm to 21 mm (maximum transverse diameter). One year after radiotherapy these nodes measured 3 mm to 5 mm in their maximum transverse diameter with a mean reduction of 50 per cent in the long axis and 67 per cent in the short axis of the largest node.

Table I compares the various ultrasonographic features (described for malignancy) of the largest node (16 patients, non-recurrent group) in each

TABLE II
COMPARISON OF ULTRASOUND FEATURES BETWEEN THE STUDIED NODES (NON-RECURRENT GROUP, N = 8) AND THE UPPER CERVICAL NODES IN NORMAL CHINESE SUBJECTS (N = 287)

Ultrasound features	⩾ 1 year		Normal		*p value* (S = significant; NS = non-significant)
S/L <0.5	8	(100%)	273	(95%)	1.000 NS
Short axis > 8 mm	0	(0.0%)	12	(4.2%)	1.000 NS
Hypoechoic	8	(100%)	271	(94%)	1.000 NS
Hilus present	4	(50%)	238	(83%)	0.037 S
Echogenic area	4	(50%)	0	(0.0%)	<0.0001 S
Unsharp nodal border	5	(63%)	159	(55%)	1.000 NS
Fascial plane preserved	8	(100%)	287	(100%)	—

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TABLE III

COMPARISON OF ULTRASOUND FEATURES BETWEEN THE STUDIED NODES (NON RECURRENT GROUP, N = 8) AND THE POSTERIOR TRIANGLE NODES IN NORMAL CHINESE SUBJECTS (N = 454)

Ultrasound features	⩾ 1 year		Normal		*p* value (S = significant; NS = non-significant)
S/L < 0.5	7	(88%)	446	(98%)	0.147 NS
Short axis > 8 mm	0	(0.0%)	6	(1.3%)	1.000 NS
Hypoechoic	8	(100%)	450	(99%)	1.000 NS
Hilus present	1	(13%)	367	(81%)	<0.0001 S
Echogenic area	7	(88%)	0	(0.0%)	<0.0001 S
Unsharp nodal border	6	(75%)	134	(30%)	0.011 S
Fascial plane preserved	6	(75%)	454	(100%)	0.0003 S

patient, at the baseline, and follow-up (one year after radiotherapy) scans. Although different machines were used, the scanning frequency was unchanged and the morphological changes reported were unaffected by a change in the machine.

Tables II and III compare ultrasonographic appearances of normal nodes after radiotherapy (non-recurrent group) and nodes in normal Chinese subjects at a similar location (upper cervical, and posterior triangle).

Both the patients with proven recurrences were male (40 and 42 years of age). In the first patient malignant nodes were seen in right upper cervical chain and left posterior triangle. The largest node measured 18 mm in the right upper cervical chain. Clinical examination six months after completion of radiotherapy showed that the node reduced in size. However one year after radiotherapy echographically suspicious new nodes were seen within the right parotid gland and in the submental area. FNAC was positive for tumour recurrence. Recurrent tumour was also histologically confirmed in the right nasal cavity and ethmoid sinus.

In the second patient the largest node measured 9 mm (maximum transverse diameter) in the pre-radiotherapy scan, and was hypoechoic with no obvious calcification or intranodal necrosis. Six months after completion of radiotherapy the node measured 8 mm in maximum transverse diameter, and was hypoechoic, and elliptical in shape. One year after radiotherapy the node measured 6 mm in maximum transverse diameter and was hypoechoic with no intra-nodal necrosis. However, the shape of the node reverted to round (S/L ratio >0.5). FNAC done under ultrasonographic guidance confirmed the echographic suspicion of recurrent nodal disease. Examination of the nasopharynx and biopsy were negative for malignancy. A neck dissection confirmed the malignant nature of the node.

Discussion

Post-radiation induration makes detection of lymph nodes less sensitive. Even if a node can be palpated this cannot identify the presence of active disease within the node. Ultrasonography with its superior sensitivity and specificity (Baatenberg de Jong *et al.*, 1989), easy availability, and low cost is therefore the ideal imaging modality for following up neck nodes after radiotherapy. However, following radiotherapy, ultrasonographic criteria for malignant nodes are still present in many of the nodes at three months, thus limiting its usefulness in predicting persistence or recurrence in the early post-radiotherapy period (Ahuja *et al.*, 1996). Despite this limitation ultrasonography is still attractive as the imaging modality of choice for long-term follow-up, particularly as it easily evaluates features that may help to identify recurrent disease such as size, shape, distribution of nodes and echocharacter. In order to perform a long-term follow-up, it is essential to be familiar with post-radiation changes in the nodes (Bruneton and Normand, 1987), and the time frame over which these changes occur.

We were interested:

(1) To see the effect of radiotherapy on established and well-known features such as the size and shape of the nodes, internal architecture, nodal border, calcification, nodal matting and echogenicity;

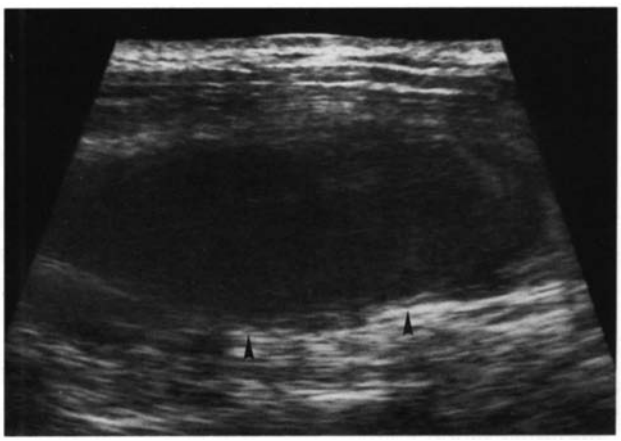

FIG. 1

Pre-radiotherapy longitudinal sonogram showing a hypoechoic, heterogeneous malignant node (arrowheads) in the posterior triangle.

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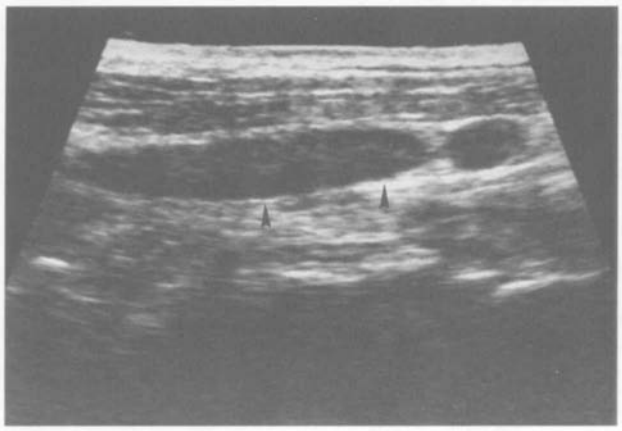

FIG. 2

One year post-radiotherapy longitudinal sonogram (same node as in Figure 1) showing a reduction in the size of the node (arrowheads). The transverse diameter at this time was less than 8 mm, however the node still remains hypoechoic compared to adjacent muscle.

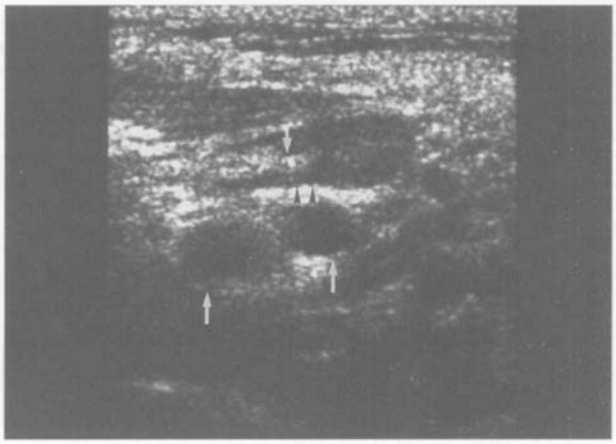

FIG. 4

One year post-radiotherapy transverse sonogram (same node as in Figure 3) showing a marked reduction in the size of the node (arrowheads) and a normal looking hilus (small white arrows). Large white arrows show the carotid bifurcation.

(2) to determine if the ultrasonographic appearances of malignant nodes revert to normal;

(3) to see if the ultrasonographic appearances of normal nodes after radiotherapy was any different from normal nodes in a similar location in the non-irradiated neck.

(4) to determine the post-radiotherapy changes in the soft tissues of the neck.

Coagulation necrosis and nodal matting have been seen in three and 11 per cent of all NPC nodes respectively (Ahuja *et al.*, 1995), but were not observed in this study and hence we are unable to comment on the effect of radiotherapy on coagulation necrosis and matting.

All the nodes were hypoechoic and one showed the presence of calcification, but these features did not change following radiotherapy. The nodes remained hypoechoic compared to adjacent soft tissues, however, when compared to normal nodes, nodes one year after radiotherapy were slightly more echogenic. This is best appreciated when comparing the echogenicity of the node with the echogenicity of the adjacent sternomastoid muscle. Radiotherapy invariably increases muscle echogenicity so a relative increase in echogenicity compared with the muscle does suggest a real increase.

Although it has been well established that as a indicator of benignity or malignancy size appears to be of little value (Solbiati *et al.*, 1988; Sutton *et al.*, 1988; Vassallo *et al.*, 1992), for the prediction of metastatic nodes of ENT cancers 8 mm is taken as the cut-off point (Bruneton and Normand, 1987). In this study one year after radiotherapy none of the nodes were greater than 8 mm in maximum transverse diameter (range 3 to 5 mm) and none of the nodes increased in size. One year following radiotherapy, in the non-recurrent group there was a 50 per cent reduction in size in the long axis and 67 per cent in the short axis of the largest malignant node (Figures 1 and 2). This decrease in size of nodes following radiotherapy is important in the follow-up of these patients. Clinical examination is often

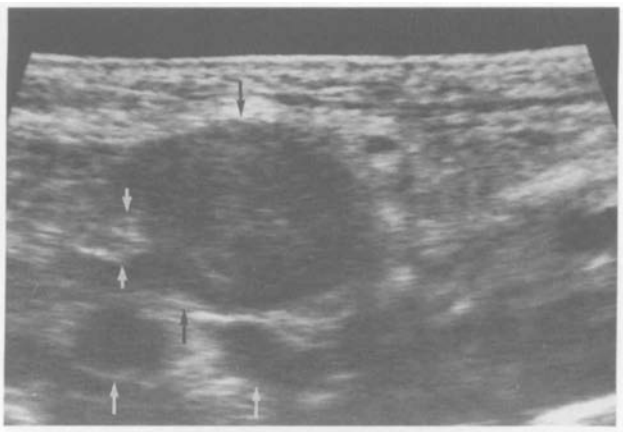

FIG. 3

Pre-radiotherapy transverse sonogram of a malignant node (black arrows) in the upper cervical chain (large white arrows show the carotid bifurcation). Note the eccentrically located hilus (small white arrows).

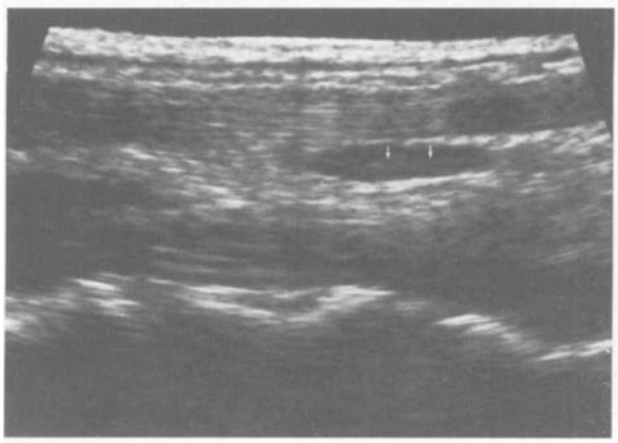

FIG. 5

Longitudinal sonogram of a node in the posterior triangle one year after radiotherapy. Note the areas of increased echogenicity within the node (arrows) and the absence of the hilus.

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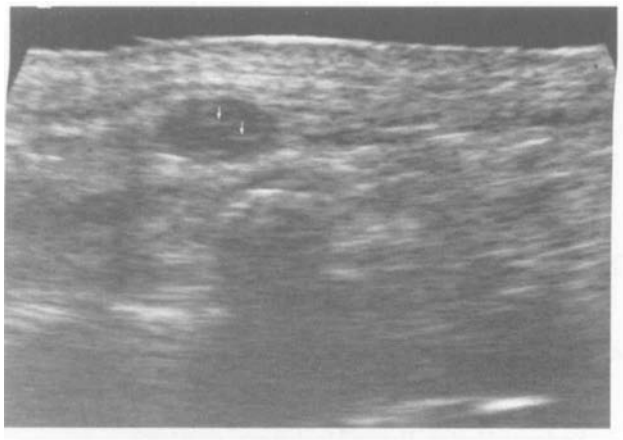

FIG. 6

Longitudinal sonogram of a node in the posterior triangle one year after radiotherapy. Note the faint, discontinuous echogenic lines within the node (arrows). This probably represents post-radiotherapy fibrosis.

unable to evaluate this serial reduction after radiotherapy due to post-radiation induration. An increase in size is probably more important in surveillance for recurrent disease. Although FNAC would be the next logical step, following radiotherapy to neck nodes it is often difficult to obtain positive samples (Wei *et al.*, 1990) and an excision biopsy is often necessary.

It has been shown that benign nodes tend to have a S/L ratio <0.5 and malignant nodes >0.5 (Vassallo *et al.*, 1992). Only one out of 16 nodes (6.2 per cent, non-recurrent group) still had a S/L ratio greater than 0.5 one year after radiotherapy. In this patient the last study was done 12 months after radiotherapy. In the patients who had their last examination more than 13 months all the nodes showed a normal shape. The follow-up of shape is also an important criterion as a change in shape from oval to round may indicate recurrent disease as seen in one of our cases.

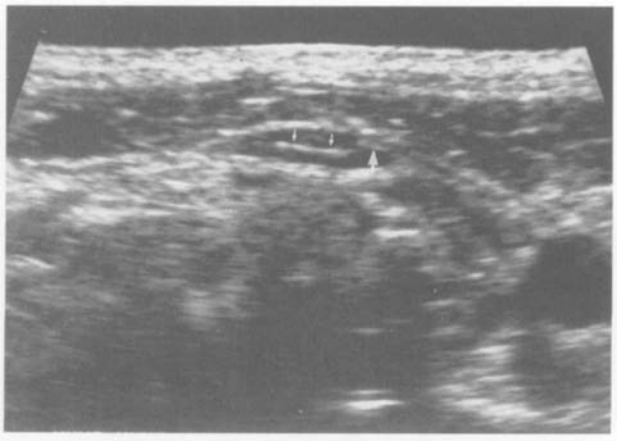

FIG. 7

Longitudinal sonogram of a normal node in the posterior triangle showing a dense echogenic line within the node (small arrows) continuous with adjacent connective tissues (large white arrow). Compare this appearance to the nodes in Figures 5 and 6.

It has also been established that lymph nodes with well-delineated boundaries are more likely to be malignant compared to nodes with poorly delineated borders (Shozushima *et al.*, 1990). In this study five out of 16 (31 per cent, non-recurrent group) still had sharp borders one year after radiotherapy.

In our experience malignant nodes from NPC are commonly seen in the upper cervical area and posterior triangles. This distribution of nodes is carefully mapped on the first scan and on follow-up. The appearance of an abnormal node at a site previously uninvolved may be the first indication of recurrent disease, and this was also seen in one of our cases.

As an indicator of benignity the presence of a reflective vascular hilus has been of limited value (Evans *et al.*, 1993). In this study in only one patient (6.2 per cent, non-recurrent group) was the vascular hilus seen in all three examinations (Figures 3 and 4). In four patients (25 per cent) the hilus was not seen in the pre-radiotherapy scan but was clearly present in studies one year after radiotherapy. In 11 patients (69 per cent) the hilus was not seen on the pre-radiotherapy and follow-up studies. In these patients in scans done one year after radiotherapy the nodes showed areas of increased echogenicity and a faint, discontinuous line through the node (Figures 5 and 6). This was best appreciated on longitudinal scans through the node and was never continuous with adjacent soft tissues in any plane. It most probably represents fibrosis rather than the true vascular hilus (Rubaltelli *et al.*, 1990) (Figure 7). This feature is recognized by pathologists but we were unable to find any reference in the literature describing the histology.

Because the echographic appearance of normal nodes is different in different areas of the neck (Ying *et al.*, 1996), the post-radiotherapy appearances after one year in the non-recurrent group were compared with ultrasonographic appearances of cervical nodes at similar sites (upper cervical region and posterior triangle, Tables II and III) in normal Chinese subjects (Ying *et al.*, 1996). In the upper cervical area and posterior triangle there was no significant difference in the shape, and size. An important point to note was that there was no shrinkage (severe atrophy) of the irradiated nodes. Although nodes in both groups are hypoechoic compared to other soft tissues the post-radiotherapy nodes in both areas are brighter. In the upper cervical area the nodes showed a true vascular hilus in only 50 per cent (compared to 83 per cent in the normal group), and in the posterior triangle only in one patient (12 per cent, compared to 81 per cent in the normal group). In the others, the nodes showed the increased echogenicity (thin, echogenic fibrosis) previously mentioned. In the posterior triangle nodes generally have sharp borders (Ying *et al.*, 1996), however, following radiotherapy the majority of nodes in this study had unsharp borders. This is also a probable effect of radiotherapy on nodes.

Compared to nodes one year post-radiotherapy in the nonrecurrent group, metastatic nodes in both the patients with recurrence were solid, hypoechoic, homogeneous, sharply outlined, round (S/L ratio >0.5) and did not show the presence of an echogenic hilus. The larger measured 18 mm in transverse diameter and the smaller 6 mm in diameter.

Other than changes in the cervical nodes, radiotherapy also produces changes in the soft tissues such as cutaneous thickening (Bruneton and Normand, 1987) and soft tissue oedema and induration (Ahuja *et al.*, 1996). Following radiotherapy soft tissue oedema is an expected change, however, after one year the fascial planes remained blurred only in three (17 per cent) patients, particularly in the posterior triangle. Similar soft tissue changes in the posterior triangle have been previously described for infective nodes particularly tuberculous adenopathy (Ahuja *et al.*, 1995).

It must be noted that, although at first glance the post-radiotherapy nodes may resemble normal nodes, subtle changes within the node and adjacent soft tissues can be recognized. During the long-term follow-up, the appearance of nodes at sites previously uninvolved or any change in appearance (increase in size, change in shape or the development of intranodal necrosis) of nodes should alert the sonologist to the possibility of recurrence.

Conclusion

One year following radiotherapy there was a 50 per cent reduction in size in the long axis and 67 per cent in the short axis of the largest malignant node of each patient. All these nodes returned to the normal limits for size for their respective area and did not show shrinkage below normal values. The shape of the node also reverted to normal.

Following radiotherapy the echogenic hilus reverts to normal in a minority of patients. In most patients the nodes demonstrate a thin, discontinuous, faint echogenic line not continuous with the surrounding soft tissues. This most probably represents fibrosis.

Although all the nodes still remain poorly reflective compared to surrounding soft tissues, post-radiotherapy nodes are slightly more echogenic compared to the adjacent sternomastoid muscle than normal nodes compared with their adjacent muscle.

Soft tissue induration still persists in a small percentage of patients (12 per cent) one year after radiotherapy particularly in the posterior triangle.

Ultrasonographic features that help to identify residual/recurrent disease are increasing size or no reduction in size after radiotherapy, change in shape from oval to round and the appearance of nodes at a previously uninvolved site. FNAC or excision biopsy may then be necessary.

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