

We are IntechOpen, the world's leading publisher of Open Access books Built by scientists, for scientists

6,900

Open access books available

186,000

International authors and editors

200M

Downloads

Our authors are among the

154

Countries delivered to

TOP 1%

most cited scientists

12.2%

Contributors from top 500 universities



WEB OF SCIENCE™

Selection of our books indexed in the Book Citation Index
in Web of Science™ Core Collection (BKCI)

Interested in publishing with us?
Contact book.department@intechopen.com

Numbers displayed above are based on latest data collected.
For more information visit www.intechopen.com



Local Metastasis in Head and Neck Cancer - an Overview

Suwarna Dangore–Khasbage

Additional information is available at the end of the chapter

<http://dx.doi.org/10.5772/60072>

1. Introduction

Head and neck cancer refers to epithelial malignancies of various parts of the orofacial region, which include paranasal sinuses, nasal cavity, pharynx and larynx, etc. These represent about 6% of all cancer cases and account for a number of new cancer cases and cancer-related deaths worldwide every year [1, 2]. Amongst those, oral cancer is the most common type of cancer. Squamous cell carcinoma is the most frequent single entity, constituting 95% of all oral malignancies [3].

Oral squamous cell carcinoma is an invasive lesion with the presence of perineural growth. It has a significant recurrence rate and frequently metastasizes to cervical lymph nodes. Since squamous cell carcinoma constitutes the preponderance of primary malignancies of the head and neck, it is by far the most common tumour that spreads to the cervical nodes [4]. Reports from the American Cancer Society indicate that, at the time of initial diagnosis, over 40% of patients with squamous cell carcinomas of the oral cavity and pharynx present with regional dissemination of the disease [5].

In oral cancer, tumour dissemination occurs via regional lymphatic to cervical lymph node in a predictable and sequential fashion. Oral cancer occurring in the posterior aspect of the oral cavity, oropharynx and inferior of the mouth tends to be associated with a higher incidence of spread to the lymph nodes at the time of diagnosis. Ipsilateral lymph nodes metastases are frequent. However, its spreading to contralateral nodes is more common with midline and posterior lesions [6].

The incidence of spread is influenced by the size of the tumour. Lesions classed as T1 may show a regional spread in 10 to 20% of cases, T2 lesions in 25 to 30% of cases and T3 to T4 tumours in 50 to 75% [6].

The determination of the presence or absence of metastases in the neck nodes is mandatory for cancer-bearing patients. This is because the therapeutic rational and prognosis depend on

the staging of the cancer. It is stated that the presence of metastatic node reduces the 5-year survival rate by 50%. Moreover, the presence of another metastatic node on the contralateral side further reduces the survival rate by 25% [7]. Patients with metastasis need more aggressive treatments. Therefore, it is important to assess as reliably as possible whether or not a patient has regional lymph node metastases.

The common cause of metastatic cervical lymphadenopathy is the spread from primary tumours in the head and neck region. However, in unusual cases, they represent secondary tumours from primary sites below the clavicles [3]. The diagnosis of such cervical neck tumours can be decided after a complete clinical and radiological examination, focusing on the organs or areas where there is a high chance of an existing primary tumour.

2. Mechanism of metastases in head and neck cancer

The most deadly aspect of any cancer is its ability to spread or metastasize. Metastasis is a complex process involving the detachment of cells from the tumour tissue, the regulation of cell motility and invasion, and the proliferation and evasion through the lymphatic system or blood vessels.

There are different views regarding the involvement of regional lymph nodes in metastasis. The nearby lymph nodes in tumour-bearing hosts are considered as anatomic barriers to the spread of tumour cells. On the contrary, another concept is that the lymphatic and lymphaticovenous shunts bypass the regional lymph nodes and allow both the lymphatic and haematogenous dissemination of malignant cells. [8].

Cancer cells have the ability to overcome the safeguards that are present in the body for the prevention of metastasis. It is necessary to understand what ways cancer cells have mutated in order to circumvent the body's defences and travel freely to other locations.

2.1. Lymphatic drainage in head and neck cancer

Several important groups of lymph nodes act as first echelon nodes of the oral cavity. The first lymph node encountered in the channel, which drains a particular submucosal or subepidermal lymph capillary plexus, is called the first echelon node. This is because it is here that pathogenic organisms or free tumour cells within the lymph fluid meet their first resistance to travel. A sentinel lymph node is defined as the first lymph node in a regional lymphatic basin that receives lymph flow from the primary tumour. Sentinel node imaging provides a "road map" of the lymphatic drainage from a tumour. However, it does not provide information regarding the presence or absence of cancer cells in those nodes.

Sometimes, lymphatic metastases do not first develop in the lymph nodes nearest to the tumour. This is known as skip metastases. The reason for this phenomenon could be venous lymphatic anastomoses or obliteration of lymphatics by inflammation or radiation. Due to the obstruction of the lymphatics by tumour cells, the lymph flow is disturbed and the tumour cells spread against the flow of the lymph. This causes retrograde metastases at unusual sites,

for example, metastases of carcinoma prostrate to the supraclavicular nodes. It is believed that lymph nodes in the vicinity of the tumour perform multiple roles – first, acting as an initial barrier filter and destructing tumour cells, while later providing fertile soil for the growth of tumour cells [9].

Cervical lymph nodes include the submental, prevascular facial and submandibular group of lymph nodes. Deep jugular lymph nodes include the jugulodigastric, juguloomohyoid and supraclavicular group of lymph nodes. Lymph nodes in the posterior triangle of the neck include the accessory chain of lymph nodes. The mucosa of the upper aerodigestive tract drains to the cervical lymph nodes in the lateral aspect of the neck. Tumours of the pharynx may drain to the parapharyngeal and retropharyngeal lymph nodes.

The Delphian lymph node is present in the central compartment of the neck and drains the larynx and perithyroid lymph nodes adjacent to the thyroid gland. Lymph nodes in the tracheoesophageal groove provide primary drainage to the thyroid gland, as well as the hypopharynx, subglottic larynx and cervical oesophagus. Lymph nodes in the anterior superior mediastinum provide drainage to the thyroid gland and the oesophagus. Furthermore, they serve as a secondary lymphatic basin for anatomic structures in the central compartment of the neck. Each anatomic subgroup of lymph nodes described above specifically serve as primary echelon lymph nodes, draining a specific site in the head and neck region. Thus, the location of a palpable metastatic lymph node may often indicate the source of a primary tumour [8].

2.2. Assumptions about the mechanism of metastases

Lymph node metastasis occurs by haematogenous or by lymphatic routes. The cancer mass has the same vascularity as that of healthy tissue. Thus, the cancer cells have access to the blood stream. The malignant cells are detached from the tumour mass and enter the body's circulation. Once in the bloodstream, the cancer cells circulate to other parts of the body. Similarly, the lymphatic system has channels throughout the body, like the circulatory system, through which a malignant cell can travel and metastasize.

If the cells travel through the lymph system, they may end up in nearby lymph nodes or spread to other organs. In circulation, the cancer cells may reach to any part of the body where they begin to grow and form a secondary tumour mass. This spread of cancer to a new part of the body is called metastasis. The spread of malignancy to nearby lymph nodes is called local or regional metastasis and the spread of the tumour to a distant organ is called a distant metastasis.

Cancer cells have to go through several steps in order to spread to new parts of the body:

- a. The loose cancer cells have to be able to break away from the parent tumour.
- b. They have to gain entry into the bloodstream or lymph system - this can carry them to another part of the body.
- c. They have to attach to the wall of a blood vessel or lymph vessel.

- d. They need to survive in a blood vessel or lymph vessel and move through it into a new organ.
- e. Malignant cells have to emerge from a blood or lymph vessel.
- f. They need to be able to multiply and grow to form secondary neoplasm at the new site.
- g. They need to be able to avoid attacks from the body's immune system.

There are various factors that may influence the mechanism of regional metastases and prevent tumour cells from developing lymph node metastases. These are:

1. The suppression of cellular immune response, in particular T cell function [7].
2. The microvascular invasion, grade of differentiation and tumour thickness in metastases of squamous cell carcinoma of the oral cavity [10].
3. The lymphatic vessel in and around the tumour tissue and lymph node metastasis in patients with oral squamous cell carcinoma. The dimension of lymphatic vessels is significantly greater in the tumour tissue than in the tumour-free tissue. This means that the function of lymphatic vessels appear to have increased in the tumour tissue, compared to the tumour-free tissue. This results in regional metastasis [11].

Reviews of literature recommend that there are multiple and diverse reasons for cervical lymph node metastases in head and neck cancer. However, by any means, the careful evaluation of these metastatic regional nodes is essential for appropriate treatment and to achieve the best outcome of the treatment. Certainly, a careful clinical examination must be carried out at the beginning of the journey regarding the evaluation of the status of cervical lymph nodes in head and neck cancer.

3. Clinical examination of lymph nodes in head and neck cancer

Customarily, all of the palpable cervical lymph nodes are considered as positive for regional metastasis in oral cancer. Thus, to treat all necks by considering the significant risk of having occult lymph node metastases is a traditional approach for the treatment of oral cancer. However, this approach often involves the unnecessary treatment of necks that ultimately prove to be pathologically free of cancer. Therefore, appropriate investigations should be carried out. These will help to determine the treatment plan, prognosis and morbidity by diminishing the possibility of unnecessary neck dissection.

The location, number, size, shape, tenderness, consistency and fixity to underlying structures are the criteria routinely used during a clinical examination of the cervical lymph nodes.

Usually, a 1 cm size cut-off in the largest axial diameter is used for metastatic disease. However, size is not a reliable marker of malignancy as small nodes can harbour small metastases that do not expand the node and conversely, benign nodes can be enlarged due to hyperplasia or inflammation. Thus, the nodes of less than 1 cm should also be carefully evaluated, particularly

if they are in expected drainage sites of the primary tumour. In clinical practice, the size of the lymph node is only considered useful when there is an increase in nodal size on serial examinations in a patient with a known primary tumour, which is highly suggestive of metastasis.

Metastatic disease can change the shape of the node by infiltrating nodal tissue and expanding the nodal capsule. Rounded nodes are more suspicious than oval nodes. As the disease progresses, ill-defined irregular margins in a lymph node are a sign of malignancy and may represent an extracapsular spread of tumour.

Metastatic lymph nodes are usually painless and thus, remain undetected by the patient until they reach considerable dimensions. Characteristically, these nodes are stony-hard and freely movable until the tumour cells penetrate the node capsule and invade the surrounding tissue. Then, they become fixed and the expanding tumour may amalgamate surrounding nodes into one larger, stony-hard and fixed mass. Sometimes, the small tumours in the nasal cavities, nasopharynx and larynx may go undetected. The only evidence of their presence is the metastatic tumour.

Oral cavity tumours usually cause metastasis in the submandibular and upper cervical regions. Rarely, lymph nodes in the posterior triangle may also be involved. The malignancy of the tongue base and tonsillar fossa is often the reason for metastatic lymphadenopathy in the posterior triangle of neck.



Figure 1. Ulceroproliferative growth with rolled edges, involving buccal and lingual vestibule and alveolar ridge in a 62-year-old male. There was a history of tobacco-lime quid keeping in the same region since 30 years of age.



Figure 2. Showing an enlarged (4 × 4 cm), hard and fixed submandibular lymph node in a patient with a malignancy of bucco- lingual vestibule and alveolar ridge (extra oral photograph of the same 62-year-old male, shown in Figure 1)

4. Clinical staging of cervical lymph nodes in head and neck cancer

In the 1940s, the tumour-node-metastasis (TNM) staging system was reported by Pierre Denoix. The TNM staging system is an anatomic staging system that describes the anatomic extent of the primary tumour, the involvement of regional lymph nodes and distant metastasis.

As head and neck cancers consist of tumours arising from a variety of anatomic sites, such as the oral cavity, nasal cavity, paranasal sinuses, nasopharynx, oropharynx, hypopharynx, larynx, oesophagus, thyroid gland, salivary glands, etc., and miscellaneous tumours, such as neurogenic tumours, it is impossible to generate a uniform staging system that would be relevant for all tumours arising in the head and neck region. In current practice, information obtained from the clinical examination and radiologic imaging is used to assign a clinical stage (cTNM). This is then used to stratify patients for a selection of therapy and to report outcomes of the treatment.

For many decades, the AJCC-UICC TNM staging system has been used worldwide for staging head and neck cancer [12, 13]. This system has been periodically revised for improvement. According to this, the cervical lymph nodes are divided into seven levels or groups, which are based on the extent and level of cervical nodal involvement by metastatic tumour. Although this classification of cervical lymph nodes is commonly used, especially by surgeons and oncologists, some important lymph nodes, such as parotid and retropharyngeal nodes, are not included in this classification.

Stage	Criteria
Nx	Regional lymph nodes cannot be assessed.
No	No regional lymph node metastasis.
N1	Metastasis in a single ipsilateral lymph node, < 3 cm in greatest dimension.
N2a	Metastasis in a single ipsilateral lymph node, > 3 cm but < 6 cm in greatest dimension.
N2b	Metastasis in multiple ipsilateral lymph nodes, none > 6 cm in greatest dimension.
N2c	Metastasis in bilateral or contralateral lymph nodes, none > 6 cm in greatest dimension.
N3	Metastasis in a lymph node > 6 cm in greatest dimension.

Table 1. N staging for all Head and neck sites except the nasopharynx and thyroid - AJCC/UICC 2002 [12, 13].

Stage	Criteria
Nx	Regional lymph nodes cannot be assessed.
No	No regional lymph node metastasis.
N1	Unilateral metastasis in lymph node(s), 6 cm or less in greatest dimension, above the supraclavicular fossa. *
N2	Bilateral metastasis in lymph node(s), 6 cm or less in greatest dimension, above the supraclavicular fossa. *
N3	Metastasis in a lymph node(s) > 6 cm and/or to supraclavicular fossa.
N3a	Greater than 6 cm in dimension.
N3b	Extension to the supraclavicular fossa. *

*Midline nodes are considered ipsilateral nodes.

Table 2. N staging for tumours of the nasopharynx - AJCC/UICC 2002 [12, 13].

Stage	Criteria
Nx	Regional lymph nodes cannot be assessed.*
No	No regional lymph node metastasis.
N1	Regional lymph node metastasis.
N1a	Metastasis to Level VI (pretracheal, paratracheal and prelaryngeal/Delphian lymph nodes).
N1b	Metastasis to unilateral, bilateral, or contralateral cervical or superior mediastinal lymph nodes.

*Regional nodes are the central compartment, lateral cervical, and upper mediastinal lymph nodes.

Table 3. N staging for tumours of the thyroid - AJCC/UICC 2002 [12, 13].

The **TNM** staging system is widely used to assess prognosis, determine treatment and compare results from different protocols. However, it has a few pitfalls. The palpable lymph node in the neck does not always mean that it is metastatic and a non-palpable does not always mean that it is non-metastatic. They may contain micrometastases and may be discovered on a histological examination, which were thought to be normal on palpation and imaging.

One or more non-painful nodes in asymptomatic patients or patients with an already diagnosed malignancy in the T1-T2 stage in satellite or non-satellite locations are considered as risky nodes. Furthermore, in patients with an already diagnosed malignancy in the T3-T4 stage, three or more > 2 cm nodes in a satellite location are called end-stage nodes [14].

TNM staging systems are based on clinical findings. However, imaging should be a necessary part of this staging or it should always be used to support the staging. If the imaging complements the clinical examination, the following staging conversions can occur: N0 will become N1 neck, N1 will become N2 neck, N1 will become N3c neck or N0 will become N3c neck [15].

5. Diagnosis and investigations for metastatic lymph nodes in head and neck cancer

Imaging plays an important role in the evaluation of disease in the cervical lymph nodes and should be a part of any thorough workup of patients with head and neck cancer. The continuous advances in techniques have led to the increased sensitivity of the imaging modalities in the detection of lymph nodes. Various imaging techniques are used for the detection of enlarged nodes, including ultrasound, Colour Doppler ultrasound, computed tomography, magnetic resonance imaging positron emission tomography (PET), lymphoscintigraphy and USG-guided fine-needle cytology, etc. Each imaging modality has advantages and disadvantages [16].

5.1. Ultrasound and colour doppler ultrasound examination of neck in head and neck cancer

Ultrasound (US) is a non-invasive, easily accessible and comparatively cheaper imaging modality, which is used for the evaluation of cervical lymphadenopathy. The sonologist is often the first person to identify the presence of an abnormal node. Several studies have shown that sonography has a markedly higher sensitivity than palpation for the detection of enlarged lymph nodes in patients with suspected regional lymph node metastases, particularly in the presence of severe postoperative scarring. The use of sonography also allows the assessment of the infiltration of blood vessels and organs, such as the thyroid gland, by adjacent nodal metastases and an accurate follow-up of patients receiving chemotherapy or radiation therapy [17].

The AJCC classification for cervical lymph nodes in head and neck cancer is not specific for the ultrasound examination. This is because some lymph nodes in the classification, such as prelaryngeal, paratracheal and upper mediastinal nodes, may not be accessible via ultrasound. In 1986, Hajek et al. established another classification of cervical lymph nodes in order to

simplify ultrasound examinations of the neck. According to this, the cervical lymph nodes are classified into eight regions based on their location in the neck, as shown in Figure 3 [18].

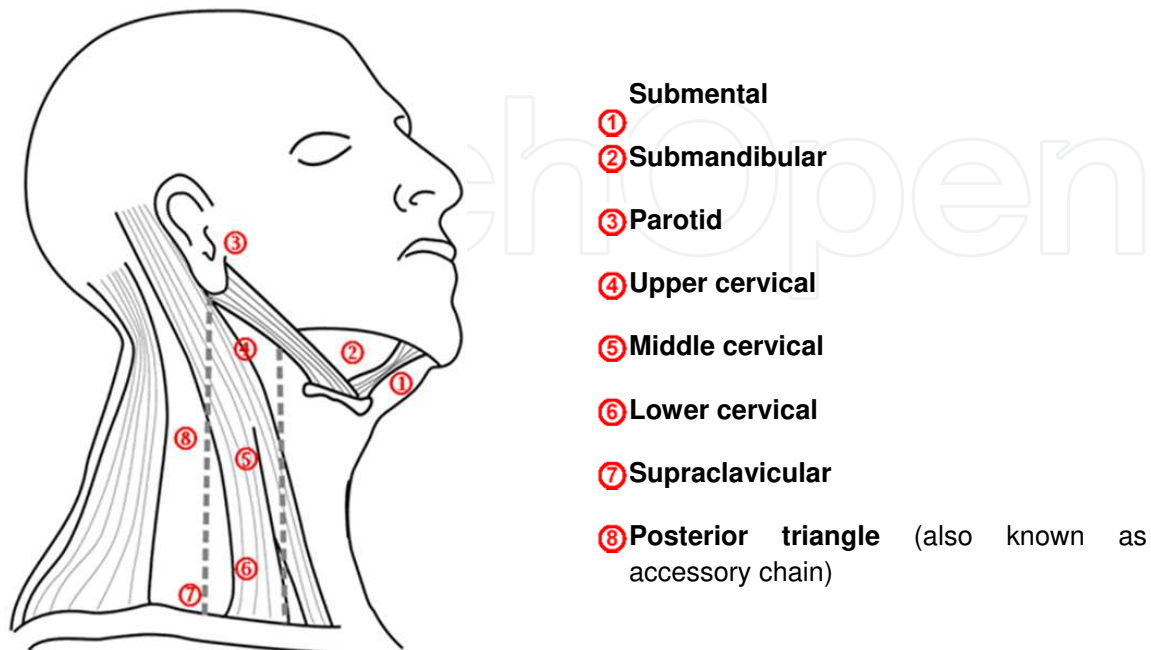


Figure 3. Classification of cervical lymph nodes for US examination [18].

In an ultrasound examination of neck lymphadenopathy, the distribution, size, shape, nodal border, echogenic hilus, intranodal necrosis and calcification are the evaluated features.

The size of normal cervical lymph nodes differs with the location in the various regions of the neck and thus, it cannot be used as an absolute criterion for the diagnosis of metastatic lymphadenopathy. The inflammatory nodes can be as large as malignant nodes, whilst a malignancy can be found in small nodes. It has been reported that the lymph nodes in the upper neck tend to be larger than those in the lower neck.

The shape of lymph nodes is usually assessed by the short axis diameter: long axis diameter (S:L ratio). A lymph node with an S:L ratio less than 0.5 is oval in shape, whereas an S:L ratio greater than or equal to 0.5 indicates round node. An oval node indicates normality, whereas malignant nodes tend to be round in shape as shown in Figure 4 and 5.

There is a difference in the border of malignant and reactive or normal nodes. The metastatic and lymphomatous nodes have sharp borders, whereas unsharp borders are seen in reactive or normal nodes. The presence of a sharp border in malignant nodes is believed to be due to the infiltrating tumour cells replacing the normal intranodal lymphoid tissue. This causes an increase in the acoustic impedance difference between the lymph nodes and surrounding tissues.

As far as the presence of hilum is concerned, the absence of it in a lymph node is a sign of metastasis or malignant lymphadenopathy, as shown in Figure 6 and 7.



Figure 4. Sonogram showing oval reactive lymph nodes.



Figure 5. Sonogram showing round metastatic or malignant lymph node.

In an ultrasound examination of lymph nodes, sonologists examine intranodal necrosis and calcification. However, these examinations contribute little to the diagnosis of malignant characteristics of lymph nodes. The reason for this is that intranodal necrosis may be present in other conditions like tuberculous lymphadenopathy. Similarly, intranodal calcification also does not aid the diagnosis of malignant lymphadenopathy. This is because there are other well known causes of lymph node calcification including BCG vaccination, sarcoidosis, cat scratch disease, tuberculosis, lymphoma and fungal infections, which have been previously treated with radiation therapy.

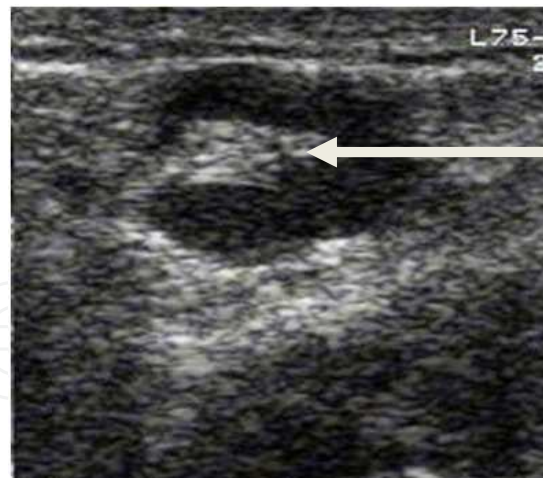


Figure 6. Sonogram depicting intact hilum suggestive of benign lymph node.

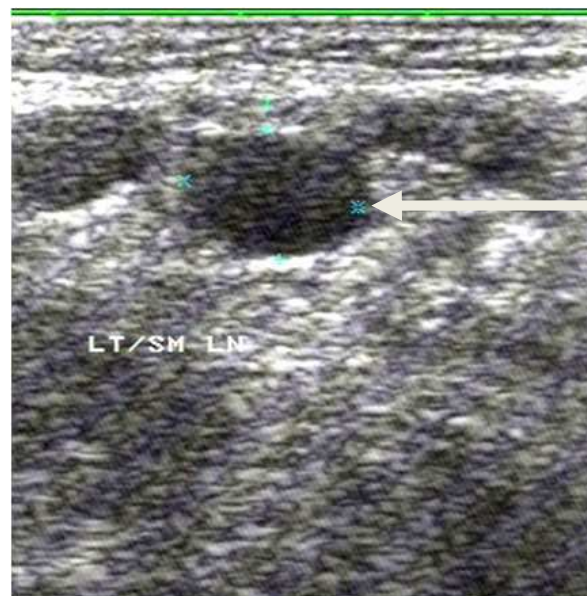


Figure 7. Sonogram showing metastatic lymph node depicting absence of hilum.

One of the advancements in ultrasonography, Colour Doppler ultrasound, can be used to define the morphologic and vascular characteristics of lymphadenopathies. Colour Doppler sonography provides information about the presence of intranodal vascularity and estimates the intravascular resistance. In Colour Doppler sonography, the pattern of vascular flow and presence of high intranodal vascular resistance have been used as key features to differentiate benign from malignant nodes.

The status of the vasculature of the lymph nodes provides additional information in the sonographic examination of cervical lymph nodes. The vascularity of the lymph node gives direction for diagnosing the cause of lymphadenopathy. This is because vascularity is directly related to the actual pathology present within the lymph node.

The characteristic event in tumour formation is angiogenesis. The morphologic and haemodynamic changes that occur in tumour vessels help to differentiate between malignant and benign lymph nodes in a Colour Doppler evaluation. In malignant or metastatic nodes, vascular structures are usually deformed due to the destruction caused by tumour infiltration and neovascularization induced by angiogenesis factor [19].

Tumour neovascularity has a particular set of characteristics. The vessels in the tumour are abnormal and show an irregular course without the progressive diminution in calibre. Furthermore, they may demonstrate arteriovenous shunting and bizarre thin walled vessels lined by tumour cells may end in amorphous spaces. The characteristic feature of tumours stimulating the growth of new vessels assists in the evaluation of metastatic nodes via Doppler sonography. The tumour vessels have a relative paucity of smooth muscle in their walls, compared to their calibre. This lack of muscular elements is reflected in the low impedance to flow, leading to a high diastolic flow and, in some tumours, the absence of systolic/diastolic flow variation [19, 20].

Both the angioarchitecture and haemodynamic differ among various cervical nodal diseases. Blood vessel morphology in metastatic nodes is usually deranged as internal nodal architecture, which is destroyed by neoplastic infiltration. Small arteries in metastatic nodes may be destroyed by tumour tissue, whereas inflammation causes the dilatation of intranodal vessels due to local humoral agents. All of these intranodal vascular alterations aid in the differentiation of malignant lymph nodes by CDUS. This is because reactive or benign nodes tend to have prominent hilar/central vascularity and metastatic or malignant nodes have peripheral or no vascularity [21]. See Figure 8 and 9.

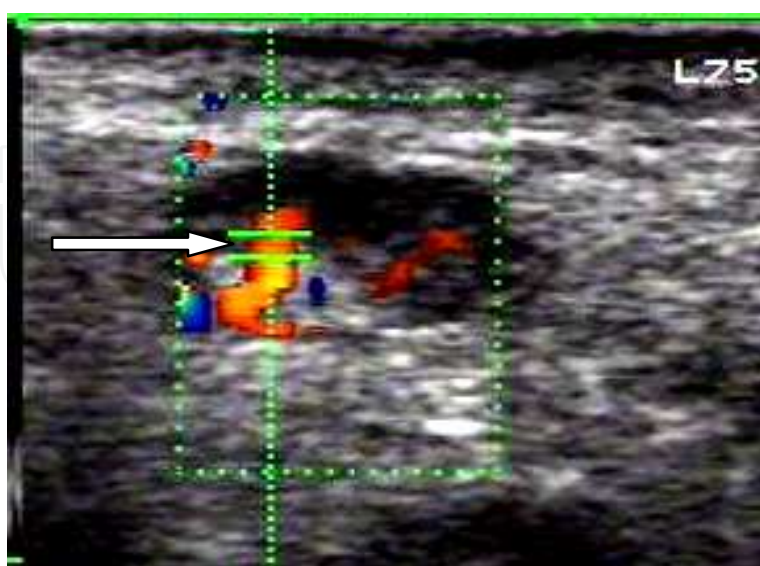


Figure 8. Color Doppler sonogram showing a lymph node with central vascular flow.

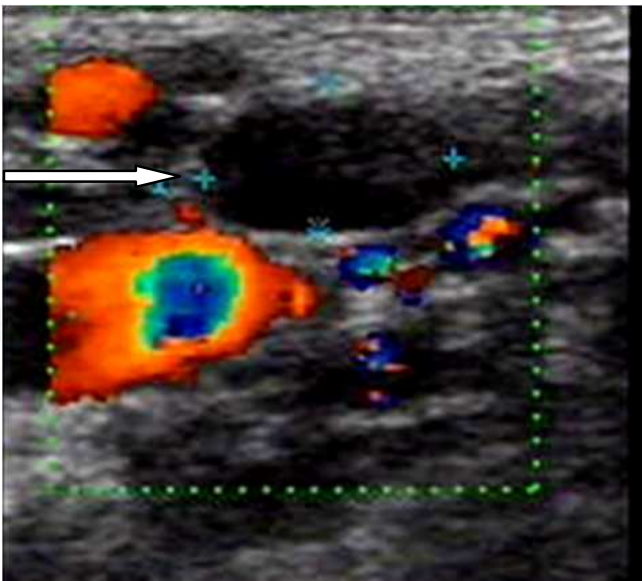


Figure 9. Color Doppler sonogram showing a lymph node with absence of vascular flow.

In advanced stages of the disease, tumour cells grow and replace a large portion of the lymph node. When the lymph node is totally replaced by the tumour cells, the tumour cells compress vessels in the lymph node. This vascular compression by the tumour cells increases vascular resistance, causing an increase in resistive index. These higher resistive indices can be observed in the metastatic/malignant lymph nodes by CDUS [21], as shown in Figure 10.

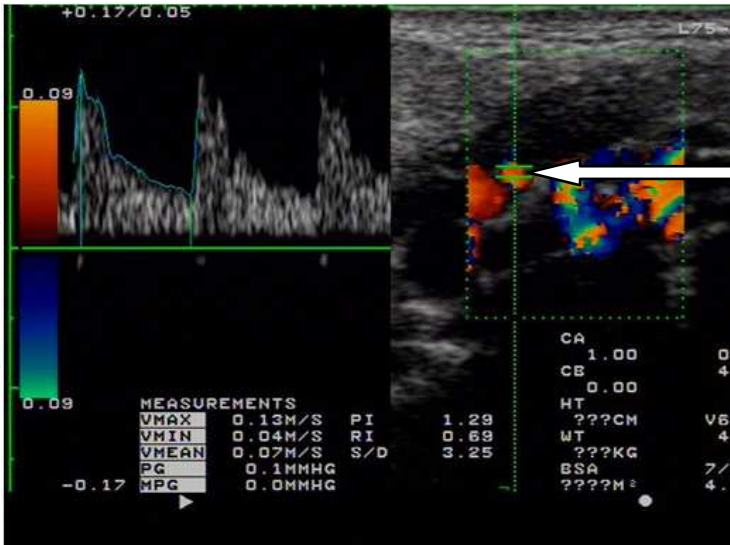


Figure 10. Colour Doppler sonogram with Doppler spectral waveform, showing a malignant cervical lymph node with peripheral Colour Doppler flow and a high resistivity index and pulsatility index.

Although Colour Doppler evaluation cannot replace the histopathological procedure in knowing the status of cervical lymphadenopathy, it plays a definite role as an adjunct to the

clinical evaluation of cervical lymphadenopathy and proves its value as an important investigation [22].

5.2. Role of CT or MRI in diagnosis of local metastases in head and neck cancer

The radiographic evaluation of the status of lymph nodes is routinely performed on the basis of size, morphology, shape and margins of the nodes.

Several studies have described the radio-morphologic characteristics of lymph node metastases in computed tomography (CT) and in magnetic resonance imaging (MRI). In computed tomography, the presence of a central hypodensity in a lymph node metastasis of a squamous epithelial carcinoma is considered a sign of nodal necrosis. In magnetic resonance imaging, a central necrosis appears in the T1-weighted as a central hypointensity and in the T2-weighted image as a central hyperintensity [23].

On a CT and MRI, axial scans are usually performed. These only demonstrate the nodes in the transverse plane, where they tend to appear round or oval. Although images can be reconstructed to coronal and sagittal plane, it is time consuming and in a CT, the resolution of images is usually lower. Nodal shape does not have any value in the differentiation of reactive from malignant nodes on a CT and MRI [24].

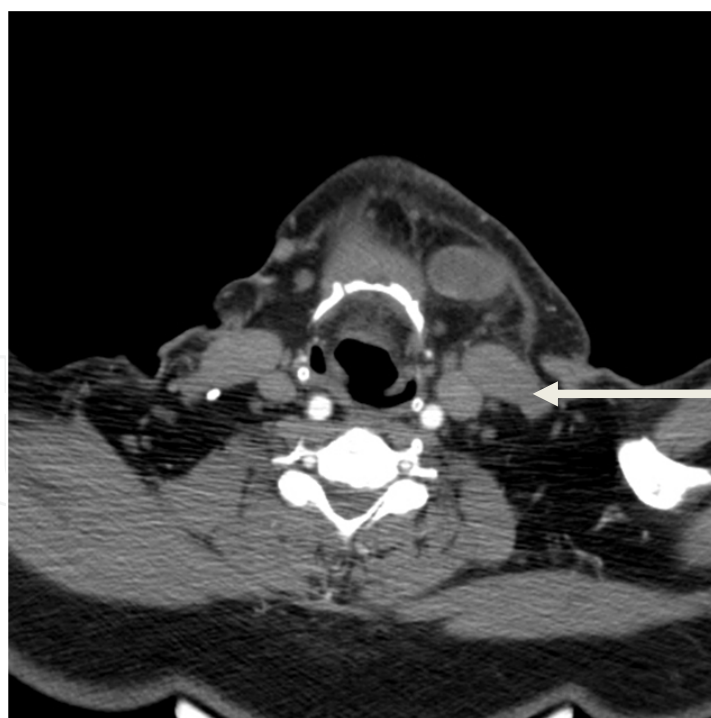


Figure 11. A CT scan of a skull with contrast reveals: homogeneously enhancing lesion present in the left buccinator space, left submandibular and left jugulodigastric region lymphadenopathy. These are suggestive of a malignant lesion.

It is important to estimate the status of regional lymph nodes in cancer of any body part. In head and neck cancer, various imaging modalities should also be performed for the detection of local metastases. This is because imaging is more accurate than clinical examination. However, the assessment of nodal disease by imaging can be challenging for the radiologist. This is because there are multiple sites to review and differing opinions regarding the criteria for abnormal nodes. Hoang et al. [25] have mentioned a systematic four-step approach for the evaluation of metastatic cervical lymph nodes on cross-sectional neck imaging.

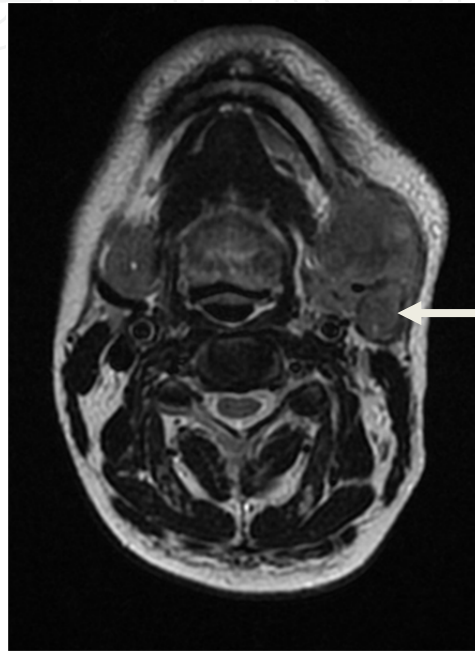


Figure 12. MRI reveals intense enhancing soft tissue mass involving gingiva, alveolus, submandibular gland and mandible suggestive of malignant lesion. It also reveals well-defined enhancing soft tissue lesion suggestive of lymphadenopathy (Axial view - T2-weighted image).

In doubtful cases of CT or MRI criteria, ultrasound is an excellent second-line tool, which can be used for evaluating these suspicious nodes and can also guide fine-needle aspiration to obtain cytology.

In oncology, the use of 18-fluorodeoxyglucose (FDG) PET has grown rapidly. This is a metabolic imaging tool that provides information beyond the anatomical constraints of conventional imaging. It can establish whether or not enlarged lymph nodes contain a tumour or are reactive. In 2005, Hain stated that PET has found more than 40% of metastases in lymph nodes smaller than 1 cm. However, the disadvantage of PET is that false positives can be found in infected nodes [26].

Kubicek et al. stated that PET and PET/CT scans have the potential to improve treatment outcomes by providing improved lymph node staging and prognostic factors [27].

Lymphoscintigraphy has been used to evaluate lymph node function. It is less invasive for delineating drainage and can help to visualize changes in the function [28].

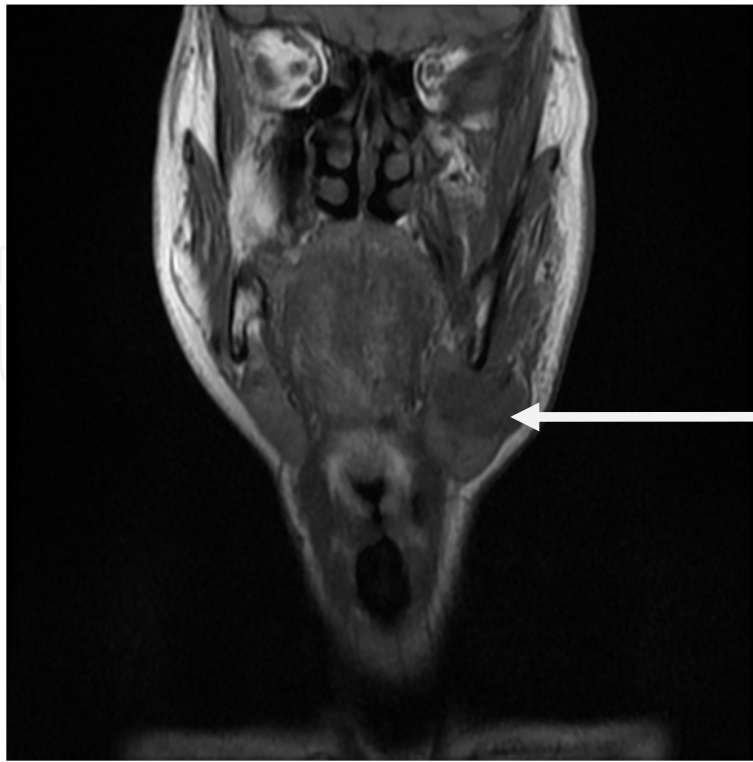


Figure 13. MRI reveals intense enhancing soft tissue mass involving gingiva, alveolus, submandibular gland and mandible, suggestive of a malignant lesion. It also reveals a well-defined enhancing soft tissue lesion, suggestive of lymphadenopathy (coronal view - T1-weighted image).

Elsewhere in the body, lymphangiography and lymphoscintigraphy are useful as these investigations provide a combination of anatomic and physiological information about lymph nodes. However, these are of no use in the neck. Both of these are invasive and can be technically difficult. MR imaging performed after the administration of superparamagnetic iron oxide particles, another hybrid of anatomic and physiological assessment, has still not been fully evaluated and is not widely available. Metabolic (functional or physiological) imaging with fluorine-18-fluorodeoxyglucose positron emission tomography is new and promising. The limited anatomic detail that positron emission tomography provides will likely require correlation with CT or MR imaging to make it widely useful.

Several studies suggested that new and highly sensitive investigations, in particular immunohistochemistry, molecular analysis, polymerase chain reaction (PCR) and serial sectioning of cervical lymph nodes, have increased the detection rate of micrometastases in head and neck cancers [29].

In addition to imaging techniques, the use of biomarkers studied on a protein, DNA or RNA level may be useful for the assessment of regional metastasis in head and neck squamous cell carcinoma [30].

FNAC and biopsy are considered confirmatory tests for the diagnosis of lymphadenopathy but these have a certain lacunae. For example, Ying et al. [18] stated in their review that it is difficult to collect adequate tissue volume from small lymph nodes and from post-irradiation

nodes. According to them, it has been reported that 15% of specimens from US guided FNA did not provide an accurate diagnosis due to an uncertain diagnosis or inadequate sample. In the neck, FNA is usually difficult in a lymph node that is situated in the deep submandibular area.

Sato et al. [31] stated that puncturing the metastatic node with a needle could not be indicated in all situations because of the risks of micro dissemination of cancer cells, rupture of the capsule of the metastatic node and infection after FNAB.

6. Treatment related significance of cervical lymphadenopathy in head and neck cancer

Localized tumours that do not metastasize have the best prognosis. Cancers that have metastasized usually indicate a later stage disease and treatment becomes more complicated, with poorer outcomes. During the surgical treatment of a tumour, the nearby lymph nodes are also removed. This is because these are frequently the first sites of the cancer metastasis.

Current treatment strategies in oral cancer rely on staging based on the imaging techniques to detect regional metastasis. However, no strategies challenge the gold standard of histopathological examination of the neck dissection [32]. Nevertheless, various imaging modalities may direct the surgeons to convert the treatment plan to choose a more conservative neck dissection or, after frozen section control, to convert the treatment to a more radical dissection.

In conclusion, the presence of local metastases influences the treatment and prognosis of head and neck cancer. The traditional approach of treating all necks by considering the significant risk of having occult lymph node metastases may result in the unnecessary removal of regional lymph nodes, which ultimately prove to be pathologically free of cancer. Imaging plays a vital role in detecting the status of regional lymph nodes. For each and every patient of head and neck cancer, pretreatment imaging should be a protocol used to help to decide the appropriate treatment. Imaging performed before surgical treatment will aid in reducing mortality and morbidity.

7. Conclusion

In conclusion, the traditional approach in head neck cancer is to treat all necks by considering the significant risk of having occult lymph node metastases. Unfortunately, this approach often involves the unnecessary treatment of necks that ultimately prove to be pathologically free of cancer. So, we recommend the policy that for each and every patient of head and neck cancer, careful thorough evaluation should be performed by means of various imaging modalities. This will help to decide most appropriate treatment as well as reduce overall morbidity.

Author details

Suwarna Dangore-Khasbage

Address all correspondence to: Dangore_suwarna@redffmail.com

Oral Medicine and Radiology, SPDC, Datta Meghe Institute of Medical Sciences, Wardha, India

References

- [1] Parkin D, Bray F, Ferlay J and Pisani P: Global Cancer Statistics, 2001. *CA Cancer J Clin* 2005; 55: 74-108.
- [2] Argiris A, Karamouzis M, Raben D and Ferris R: Head and Neck Cancer. *Lancet*. 2008; 371: 1695-1709.
- [3] Ravmond L. Warpeha. Masses in the Neck. In: Wood NK, Goaz PW (5th ed). *Differential Diagnosis of Oral and Maxillofacial Lesions*. St Louis, MO, Mosby-Year Book, 2005; 521-539.
- [4] Okura M, Aikawa T, Sawai N, Lida S and Kogo M. Decision Analysis and Treatment Threshold in a Management for the N0 Neck of the Oral Cavity Carcinoma. *Oral Oncol* 2009;45: 908-911.
- [5] Sheng-Po Hao, Shu-Hang NG. Magnetic Resonance Imaging Versus Clinical Palpation in Evaluating Cervical Metastasis from Head and Neck Carcinoma. *Otolaryngol Head Neck Surg* 2000; 123: 324-327.
- [6] B. Epstein et al. Oral cancer. In: *Burket's Oral Medicine. Diagnosis and Treatment*, 10th edition. 2003; 194-234.
- [7] Okura M, Kagamuichi H, Tominaga G, Lida S, Fukuda Y, Kogo M. Morphological Changes of Regional Lymph Node in Squamous Cell Carcinoma of the Oral Cavity. *J Oral Pathol Med* 2005; 34:214-219.
- [8] Santin AD. Lymph Node Metastases. The Importance of the Microenvironment. *Cancer* 2000; 88:175-179.
- [9] Mohan H. *Text Book of Pathology*. 5th Edition. Jaypee Brothers, Medical Publishers (P) Ltd, New Delhi. 2005; Pg. No. 442-467.
- [10] Martinez-Gimeno C, Moro Rodriguez E, Navarro C, Lopez Varela C. Squamous Cell Carcinoma of the Oral Cavity: A Clinicopathologic Scoring System for Evaluating Risk of Cervical Lymph Node Metastasis. *Laryngoscope* 1995; 105: 728-733.

- [11] Nakayama A, Ogawa A, Fukuta Y, Kudo K et al. - Relation Between Lymphatic Vessel Diameter and Clinicopathologic Parameters in Squamous Cell Carcinomas of the Oral Region. *Cancer* 1999; 86: 200-206.
- [12] Edge SB, American Joint Committee on Cancer. *AJCC Cancer Staging Manual*, 7th ed. New York, NY: Springer-Verlag, 2010: 648.
- [13] Greene FL, Page DL, Fleming ID, et al. American Joint Committee on Cancer. *AJCC Cancer Staging Manual*. 6th ed. New York, NY: Springer; 2002.
- [14] Giovagnorio F, Caiazzo R and Avitto A. Evaluation of Vascular Patterns of Cervical Lymph Nodes with Power Doppler Sonography. *Journal of Clinical Ultrasound*, 1997; 25: 71-76.
- [15] MacIntosh RB. Classification and Staging of Oral Cancer. *Oral and Maxillo - Facial Surgery Clinics of North America* 1997; 9(3): 283-296.
- [16] Jonas A. Castelijns, and Michiel W. M. van den Brekel. Detection of Lymph Node Metastases in the Neck: Radiologic Criteria. *AJNR* 2001; 22: 3-4.
- [17] Vassallo P, Wernecke KJ, Roos N and Peters PE. Differentiation of Benign from Malignant Superficial Lymphadenopathy: The Role of High-resolution US. *Radiology* 1992; 183: 215-220.
- [18] Ying M and Ahuja A. Sonography of Neck Lymph Nodes. Part I: Normal Lymph Nodes. *Clinical Radiology* 2003; 58:351-358.
- [19] Kenneth J.W. Taylor, Isabel Ramos, Darryl Carter, Steven S. Morse, Daniel Snower and Caren Fortune. Correlation of Doppler Ultrasound Tumor Signals with Neovascular Morphologic Features. *Radiology* 1988; 166: 57-62.
- [20] Ahuja AT, Ying M, Yuen YH and Metrewali C. Power Doppler Sonography of Metastatic Nodes from Papillary Carcinoma of the Thyroid. *Clinical Radiology* 2001; 56: 284-288.
- [21] Dangore-Khasbage S et al. Utility of Color Doppler Ultrasound in Evaluating the Status of Cervical Lymph Nodes in Oral Cancer. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2009;108:255-263.
- [22] Dangore SB et al. Evaluation of the Efficacy of Colour Doppler Ultrasound in Diagnosis of Cervical Lymphadenopathy. *Dentomaxillofacial Radiology*. 2008; 37: 205-212.
- [23] Maurer J, Willam C, Steinkamp HJ, Knollmann FD and Felix R. Original Investigations. Keratinization and Necrosis Morphologic Aspects of Lymphatic Metastases in Ultrasound. *Investigative Radiology* 1996;31: 545-549.
- [24] Ahuja A and Ying M. An Overview of Neck Node Sonography. *Investigative Radiology* 2002; 37(6): 333-342.

- [25] Hoang JK, Vanka J, Ludwig BJ and Glastonbury CM. Evaluation of Cervical Lymph Nodes in Head and Neck Cancer with CT and MRI: Tips, Traps, and a Systematic Approach. *AJR* 2013; 200:W17–W25.
- [26] Hain SF. Positron Emission Tomography in Cancer of the Head and Neck. *British Journal of Oral and Maxillofacial Surgery*. 2005; 43: 1-6.
- [27] Kubicek GJ, Champ C, Fogh S, Wang F, Reddy E, Intenzo C, Dusing RW, Machtay M. FDG-PET Staging and Importance of Lymph Node SUV in Head and Neck Cancer. *Head & Neck Oncology* 2010; 2:19.
- [28] Sato T, Morita Y, Kawabata Y, Noikura T, Yamaguchi K, Sugihara K and Matsune S. Clinical Evaluation of Lymphoscintigraphy with a New Technetium Compound for Metastatic Cervical Lymphadenopathy. *Dentomaxillofacial Radiology* 2000; 29: 230-237.
- [29] Ferlito A, Shaha AR and Rinaldo A. The Incidence of Lymph Node Micrometastases in Patients Pathologically Staged No Cancer of Oral Cavity and Oropharynx. *Oral Oncology*, 2002; 38: 3-5.
- [30] Takes RP. Staging of Neck in Patients with Head and Neck Squamous Cell Cancer: Imaging Techniques and Biomarkers. *Oral Oncology* 2004; 40:656-667.
- [31] Sato N, Kawabe R, Fujita K and Omura S. Differential Diagnosis of Cervical Lymphadenopathy with Intranodal Color Doppler Flow Signals in Patients with Oral Squamous Cell Carcinoma. *Oral Surg, Oral Med, Oral Patho, Oral Radio, Endod*. 1998; 86: 482-488.
- [32] Som PM. Detection of Metastasis in Cervical Lymph Nodes: CT and MR Criteria and Differential Diagnosis. *Am J Roentgenol*. 1992;158: 961.