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Imaging Modalities in Squamous Cell Carcinoma of Head and Neck: A Review Article

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Abstract

Squamous cell carcinomas of head and neck region (HNSCC) are the epithelial cancers derived from the mucosal lining of oral cavity, nasal cavity, paranasal sinuses, nasopharynx, oropharynx, larynx and hypopharynx. All the structures in head and neck lies in close proximity with each other, so exact localization of carcinoma is really challenging which has been facilitated by use of imaging modalities and refinement by invention of newer imaging modalities. Each imaging modalities has their own pros and cons and has benefit in some way or other. USG (Ultrasonography) as imaging modality is cheaper, faster and easily accessible with no radiation hazards and most commonly useful for thyroid, salivary gland pathologies and also to assess neck nodes. USG and CT (Computed Tomography) have benefit not only as imaging modalities but to guide interventional procedure as core needle biopsy or FNAC (Fine Needle Aspiration Cytology). CT scan has benefit to evaluate the bony invasions, status of necrotic neck node and has minimal movement artifact. MRI (Magnetic Resonance Imaging) has benefit to know the extent of primary tumor, involvement of nearby soft tissue structures. PET (Positron Emission Tomography)/CT provides both functional and anatomical information about the presence and extent of tumor. It plays valuable role in the assessment of suspected recurrence of head and neck which has been biased by other conventional imaging modalities. CT scan, MRI and PET do not just have diagnostic and post treatment assessment roles but also play important role in treatment for assessing the volume and providing radiation delivery. Imaging modalities in the form of emerging functional techniques help to assess the cancer microenvironment and provide the background for researchers in the arena of cancer management.

Key Words: Head and Neck cancers; USG; CT Scan; MRI; PET Scan;

Background

The term “head and neck cancer” generally denotes the cancers arising from below the skull base to the region of the thoracic inlet. The epithelial carcinomas arising from the mucosal surfaces in these areas are mainly squamous cell in origin and the other histologic entities are less common. The squamous cell carcinomas of head and neck region (HNSCC) include cancers of the paranasal sinuses, the oral cavity, the nasopharynx, oropharynx, hypopharynx and larynx.

The HNSCC constitute around 4.6% of all the cancers worldwide. According to the GLOBOCAN 2018, more than 834,000 new HNSCC cases were diagnosed worldwide, comprising the eighth most common cancer, leading to more than 431,000 deaths in 2018.The most common sites of HNSCC comprise the oral cavity and larynx. [1]

There is a very large variation in the geographic distribution of HNSCC for different countries and regions. The incidences are relatively low in Western Europe and the USA and the high incidence regions include the countries of South East Asia, parts of

Africa and South America. The incidence of HNSCC rises with the age and are more common in men than women having a ratio of 3:1. [2]

The incidence of HNSCC in black males is almost double than that of the white males in the USA. [3] Tumors of the oral cavity and the base of the tongue are more common in India. In the Indian subcontinent, squamous cell carcinoma (SCC) of oral cavity may account for 50% of all cancers. The incidences and prevalence of nasopharyngeal and hypopharyngeal cancers are very high in Southeast Asia, Hong Kong, and southern China. [4]

The most common risk factors for HNSCC are alcohol and tobacco. Besides these, long term use of marijuana, occupational exposures to nickel, textile fibers, and woodworking are some of the uncommon risk factors. Dietary factors also contribute. The incidence of HNSCC cancer is highest in people with the lowest consumption of fruits and vegetables. Some head and neck cancers have viral etiologies. Epstein Barr Virus (EBV) infection is associated with nasopharyngeal cancer (NPC). Oncogenic Human Papilloma Virus (HPV), particularly type 16, has been established as a causative agent in up to 70% of oropharyngeal cancers mainly in younger patients who do not smoke or drink. The virus has a predilection for the lingual and palatine tonsils, accounting for the rise in tonsil and base of tongue (BOT) cancers. [5]

The local anatomy and the lymphatic supply of the head and neck region dictate the spread of the cancer in these sites. The common feature is muscle involvement by direct spread and spread along fascial plane to involve the adjacent soft tissue structures. Bone and cartilage act as barriers to spread and the invasion commonly occurs only when the disease is fairly advanced. Hematogenous spread occurs late in the course of disease and leads to distant metastasis. Lung is the most common site of involvement in 50% of metastatic diseases.[2]

Imaging

One of the indispensable parts of the management of HNSCC is the role of imaging, without which overall management of these cancers are almost impossible. Its major contributions, in the field of cancer, are in diagnosis, staging, selection of therapy, contouring and guiding the delivery of radiation beam in radiation therapy, assessment of treatment, detection of recurrence, and predicting survival outcomes. Interventional radiology helps in establishing diagnosis by guided aspiration or tru-cut biopsy. Modern imaging modalities, including ultrasound (USG), computed tomography (CT), magnetic resonance imaging (MRI), positron emission tomography (PET) and radionuclide scans, have dramatically enhanced the process of diagnosis and staging as well as the evaluation for tumor recurrence in the head and neck cancers. [6] Imaging is the backbone of radiotherapy planning and treatment delivery. CT scan is, now, the basic tool for the contouring of volumes of targets in the planning of radiotherapy. Similarly, MRI and PET scan are potentially helpful for this purpose. Kilovoltage and megavoltage imaging machines integrated in the Linear Accelerators aid in the proper delivery of radiation to the targets. Each imaging modality has its own limitation and benefit depending on the specific types and specific situations of cancer. Individual modalities have their own pros and cons. [7]

Ultrasonography (USG) is a very useful tool which, along with fine needle aspiration cytology (FNAC) and core needle biopsy, allows rapid imaging assessment for those with an undiagnosed neck lump or suspected metastatic disease in the neck. [8] USG comfortably differentiates solid from cystic lesions[1]and delineates thyroid and salivary gland pathologies. [9] Similarly, it can detect small and occult pathological nodes that could not be found during manual examinations. [10] It can recon the invasion of nodal mass into the adjacent blood vessels and organs. Similarly, it can be used to do the follow-up of patients getting radiation and chemotherapy. [11] USG provides one-stop service; it's readily available, portable and cheaper. However, ultrasonography may fail to localize the deeper pathologies. [7]

The cross-sectional modalities such as CT and MRI are useful to better evaluate the entire extent of the pathology.[7]CT is a robust and fast technique of imaging which offers excellent details on bony structures but has low soft-tissue contrast.[12] contrast enhanced CT is best suited to define the primary tumor and to identify bony invasion but can also be used for guiding tissue biopsy. [6]

CT is superior to MRI because of its speed, easy access, and patient tolerance. [9] Modern technologies have enabled scan to rapidly acquire images without movement artefact which is very useful for head and neck cancer patients having difficulty with breathing, swallowing secretions and lying flat.[10] Because of lower image degradation from breathing and swallowing during examination malignancies of the oropharynx, larynx, and hypopharynx are primarily imaged with CT. [6] CT guided fine needle aspiration or tru-cut biopsy of deep-seated tumors such as mass of parotid gland, foramen ovale, maxillary sinus, infratemporal fossa, middle cranial fossa, Meckel cave, nasal cavity, nasopharynx, sphenoid ridge and the parapharyngeal space can be a beneficial alternative option to US-guided biopsies. CT is also preferred for the evaluation of metastatic lymph node necrosis. However, ionizing radiation and need for iodinated contrast agents, which is contraindicated in those with severe renal impairment, are disadvantages of CT scan. [9]

MRI is largely guided by proton density and paramagnetic materials such as blood products and melanin and indicates biochemical tissue characteristics.[10] Because of inherent superior soft tissue contrast resolution, multiplanar imaging capability and lack of radiation, MRI is better in specific situations.[6,7] It is best suited to delineate the primary tumor extension and infiltration or invasion into adjacent tissues.

It also offers a wide range of additional imaging techniques

such as apparent diffusion coefficient maps for the quantification of cellular density, arterial spin labeling, intravoxel incoherent motion, and dynamic contrast enhancement to determine the quality of tumor blood vessels. [10] MRI has some significant disadvantages such as requirement of long time for imaging acquisition (which leads to motion degradation), metallic implant noncompliance (pacemakers), patient intolerance, and use of gadolinium contrast. Meaningful artifacts can be caused by swallowing, while doing MRI of head and neck region, which can limit the evaluation of the nearby tissues. [9] MRI has strengths for tumor localization and assessing for tumor extension through T1- and T2-weighted imaging. T1-weighted multiplanar postcontrast fat-suppressed images concede to reveal the potential perineural invasion of cancer. MRI is the primary imaging tool to image sinonasal, nasopharyngeal and salivary gland malignancies because of its superior anatomic detail in the absence of motion. MRI can reveal cancer infiltration into the nearby soft tissue specifically in the skull base, perineural invasion, intracranial involvement, sinus of Morgagni and pharyngobasilar fascia.[9] MRI is used to assess the laryngeal cartilage involvement in case of equivocal findings on CT and to better define the margins of the tumor.[7] Sometimes all forms of imaging including PET-CT fail to detect very small primaries, specifically of tonsil and base of tongue which often give bigger cervical lymph node metastases, and can be detected only after biopsy or tonsillectomy. For these situations, MRI with Short-T1 Inversion Recovery (STIR) sequences is the choice of investigation.[10]

The advancement of imaging technologies has supplemented the morphological techniques with functional capabilities which are of value to assess the microenvironment of cancer such as its metabolism, pH, angiogenesis and hypoxia. These techniques have the potential to improve the prediction of the cancer behavior and response to treatment, evaluate new drugs, monitor early cancer response during treatment and identify residual/recurrent cancer. In the era of shifting of management strategies of HNSCC from surgery to organ preserving chemoradiotherapy, role of these techniques is becoming more pronounced. [13] PET and radionuclide imaging provide the functional information which combined with the structural imaging modalities (CT scan/ MRI) help in better evaluation of the pathology.[7] Integrated PET/CT has been established as an important diagnostic technique for staging and therapy assessment in advanced head and neck cancers. The sensitivity of PET scan, for the detection of small lymph nodes, is higher than CT scan or MRI. Also, in therapy assessment PET/CT has been shown to differentiate early responders from non-responders. However, 18F-FDG is known not to be specific to cancer cells, and inflammatory or physiologic uptake has to be considered as a differential diagnosis. Moreover, it can miss the changes in cystic lymph nodes. For this reason, for the accurate diagnosis of cystic lymph node metastases contrast enhanced PET/CT scan is recommended. [12] Evaluating the patient with malignant cervical adenopathy from an unknown primary is one of the main, up-front indications. PET scan detects an occult primary in approximately one third of cases. [10] PET/CT is very beneficial in the evaluation of doubtful reoccurrence of cancer when there are considerable, confusing post treatment changes on other imaging modalities. PET/MRI, although not widely available, holds promise in patients with head and neck malignancy, but research and availability are limited compared with other imaging modalities.[6]

Detection of nodal metastasis by imaging is more accurate than clinical examination thus, it has become routine to perform CT, MRI or PET scan as workup for head and neck cancer. The criteria regularly utilized during a clinical examination of the nodes are their location, number, size, shape, consistency, fixity to underlying structures and tenderness. Generally, node's largest axial diameter of 1 cm size is considered the cut-off size for metastatic disease, but size is not a reliable marker because small nodes can have small metastasis, while benign nodes can have larger than 1 cm size. Therefore, if the lymph node lies in expected drainage site of the primary tumor and has size less than 1 cm, it should not be ignored and should be evaluated carefully. [14,15]

A normal lymph node has kidney like shape covered by smooth capsule. The shape of the nodes gets altered by the metastasis as it expands the nodal capsule and becomes rounded thus rounded lymph nodes are more suspicious to have metastasis than oval nodes. Ill-defined irregular margins in a lymph node are a sign of malignancy and may represent an extracapsular spread of tumor. Generally, metastatic nodes are painless, non-tender and firm to stony hard in consistency. They are freely mobile until the cancer cells penetrate the capsule and infiltrate the nearby tissues. Then, they become fixed and the expanding tumor may amalgamate surrounding nodes into one larger, stony-hard and fixed mass. [6,7]

The morphology of nodes can be changed by the metastatic disease by substituting normal fatty hila causing calcifications, hyperenhancement, cystic changes or necrosis. Necrosis in node is most valuable sign of metastasis in the presence of primary cancer in the head and neck region having specificity of 95-100%. [16] Nodal metastasis from head and neck can be exclusively necrotic or cystic. Thyroid cancer and HPV related head and neck cancers can cause purely cystic metastasis while papillary and medullary thyroid cancers commonly cause calcified metastatic nodes. Mucinous adenocarcinoma, treated lymphoma and less commonly tuberculosis are the other causes of nodal calcification. [7, 17]

The American Joint Committee on Cancer (AJCC) Staging classifies the lymph nodes as level I through level VII. Level I refer to nodes in the submandibular and submental region. Levels II, III, and IV refers to lymph nodes along the anterior cervical chain. Level V is those nodes in the posterior compartment. Level VI nodes are in the visceral compartment of the neck, whereas level VIIs are in the superior mediastinum. Retropharyngeal nodes and parotid nodes are not included in this system and they may be overlooked during reporting the scans and these two groups may not be palpable on clinical examination. Nasopharyngeal cancers drain to the retropharyngeal and parotid nodes and thyroid cancers can

drain to the retropharyngeal nodes. The other nodes that should be reviewed carefully are the superficial nodes when a skin cancer is the primary tumor which metastasizes to level V and superficial nodes, such as parotid, posterior auricular, facial, and occipital nodes. [7]

Evaluation of SCC of neck node with unknown primary (UPSCC) has always been challenging. UPSCC is the condition when the primary cancer is not identified but lymph node or nodes within the head and neck region that are not solely in the supraclavicular fossa harbor squamous cell carcinoma. [18] Almost 4% of metastatic lymph nodes at the head and neck region present as unknown primary. Oropharyngeal cancers, mainly that of tonsil and the base of tongue, are the most common sites concealing an occult primary tumor in these situations.[19] It is figured out that more than 90% of UPSCC are caused by human papilloma virus related oropharyngeal squamous cell carcinoma. [20,21]

The location of cervical lymph node metastases may suggest the location of the primary tumor. Tumors of the lip and oral cavity usually metastasize to lymph nodes in levels I to III, whereas metastases to the nodes at level II-IV or centrally at level VI are usually from oropharynx, hypopharynx, larynx, and the thyroid gland. Almost half of the metastases which are confined only to level IV or supraclavicular regions have primary cancers arising from the tissues located at the thoracic, abdominal or pelvic cavities and or lower extremities. Level V neck nodes metastases usually have primary from nasopharynx or skin at the vicinity. Midline structures such as nasopharynx, base of tongue and hypopharynx usually gives bilateral cervical lymph node metastases. [22] Since OPSCC is the most common primary tumor for unknown primaries, the initial recommended testing on a nodal fine-needle aspiration sample is immunohistochemistry for p16. If p16 is negative, then Epstein-Barr virus (EBV)–encoded RNA should be sought at in situ hybridization to detect an occult NPC. If p16 is positive but primary at oropharynx is not found at the imaging such as CT, MRI or PET/CT scans or tonsillectomy, it is advisable to perform HPV in situ hybridization because p16 can be positive in up to 30% of skin cancers. If the primary site is supposed to be skin, then the metastatic node can be evaluated for ultraviolet light DNA damage which helps to distinguish its originality from unknown mucosal primary site. [23]

Other imaging techniques for evaluating cervical nodes are Color Doppler USG, [24] diffusion-weighted MRI(DWI), perfusion imaging with dynamic contrast-enhanced MRI(DCE-MRI), and CT perfusion. [25] Color doppler USG helps to interpret the characteristics of blood vessels and morphology of the enlarged lymph nodes. Usually, reactive or benign nodes tend to have prominent hilar/central vascularity and metastatic or malignant nodes have peripheral or no vascularity. Though the value of histopathological examination to know the status of enlarged neck nodes cannot be replaced by color doppler, it has definitive complimentary role in the clinical evaluation of the nodes and has been proved to be an important investigation. [26] In a meta-analysis that compared FDG PET with CT, MRI, or sonography, FDG PET increased sensitivity for nodal metastases from 79% to 85% and increased specificity from 80% to 86%. [27]

Management

The management of a patients diagnosed with HNSCC is a complex process requiring a multidisciplinary approach, and depends on a number of factors such as the exact tumor location, staging, age, performance status and the general medical condition of the patient. The goals of treatment are to eradicate the cancer, maintain adequate physiologic function, and achieve a socially acceptable cosmetic result. The understanding of head and neck cancers and their management has undergone a major paradigm shift during the past decades. [28] The available treatments are surgery, radiation therapy, chemotherapy, targeted therapy and immunotherapy. Patients, presenting with early stage diseases (stage I and II) are generally treated with single modality either with surgery or radiation therapy and the patients who present in locally and or regionally advanced disease (stage III-IVB) are managed with combined modality treatment comprising surgery, radiotherapy and or chemotherapy.[29] The patients with metastatic and recurrent HNSCC are offered palliative therapy, which could be symptomatic, analgesics, chemotherapy, radiotherapy, targeted therapy, and immunotherapy or sometimes salvage surgery. If patient's performance status permits, generally chemotherapy becomes the initial palliative treatment.[30]

Conclusion

Imaging in the management of head and neck cancers has important rolesin the diagnosis, exact localization of the tumors, selection of the treatment modality, and guidance for contouring and radiation delivery during radiotherapy, treatment assessment and recurrence. Each modality whether its USG, CT scan, MRI or PET, has its own specific role and though the newer modality gets invented, importance of each modality has not been replaced by others. Choice of use of imaging modality depends on certain factors like physicians' need, availability of imaging technologies and economic condition of the patients. The advancement in head and neck cancer imaging from morphological to functional techniques is going to improve the cancer management with alteration and evaluation with newer treatment modalities on individualized basis and its future in head and neck cancer management that will be guided by imaging.

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