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Excision of submandibular gland during neck dissection in case of Oral squamous cell carcinoma –Critical Review

[1]Shaikh Amjad, PhD scholar, Dept of oral and maxillofacial Surgery, Datta Meghe Institute of Medical Sciences, Deemed to be University, Wardha, Maharashtra

[2]Rajiv M. Borle, Prof and Hon. Vice Chancellor, Datta Meghe Institute of Medical Sciences, Deemed to be University, Wardha, Maharashtra

[3]Nitin Bhola, Prof and Head, Dept of Oral and Maxillofacial surgery,Datta Meghe Institute of Medical Sciences, Deemed to be University, Wardha, Maharashtra

Corresponding Author: Shaikh Amjad, PhD scholar, Dept of oral and maxillofacial Surgery, Datta Meghe Institute of Medical Sciences, Deemed to be University, Wardha, Maharashtra.

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Introduction

Neck dissection has proved to be an essential and central procedure in the treatment of head and neck cancer. Paramount among the challenges and controversies facing the head and neck surgeon is the proper treatment of the neck i.e. Neck Dissection, in the cases of Head and Neck malignancy. Neck Dissection is a procedure that is designed to remove metastastic cancer involving the cervical lymph nodes. The first conceptual approach for removing nodal metastasis was made by Kocher;[1] he described the removal of the lymph nodes located within the contents of the submandibular triangle for gaining access to carcinoma tongue. Radical neck dissection involving the en bloc removal of lymph nodes and surrounding soft tissue structures popularized by Crile [2] and Martin [3] was the dominant surgical procedure for removing suspected or obvious metastasis to the cervical lymph nodes for much of the twentieth century.

Recent trends toward cosmetic and functional preservation have resulted in the development of more conservative treatment strategies. Treatment often involves surgical excision of the affected area followed by radiation therapy. Radiotherapy treatment of the head and neck has significant associated morbidity, out of which xerostomia is a common complication. Post radiotherapy xerostomia was first described by the French radiobiologist Jean Bergonie.[4] Murdoch-Kinch et al.[5] reported that submandibular gland salivary function decreases significantly after a mean dose of >40 Gy of radiation exposure. As the submandibular glands are responsible for a significant amount of the basal salivary flow. [6]

Squamous cell carcinoma of the oral cavity is one of the most common tumors of the head and neck region. [7] Current surgical treatment includes wide surgical excision of the primary lesion with appropriate neck dissection. Neck metastases are most frequently observed in levels I-II-III, but rarely in level-IV. [8] The submandibular glands are located in level-1b where rich lymphatic tissues surround them. Lymphatic metastases are common to this area, especially in floor of mouth (FOM) and tongue cancers. According to Rouviere, there are 5 lymph node groups in this region: preglandular, prevascular, retrovascular, retroglandular and intracapsular. [8] DiNardo added the "deep submandibular node" to this group. [9] Among these, the perivascular nodes (comprising prevascular and retrovascular nodes) are the most important because they are the primary afferent draining nodes of the oral cavity. Perivascular node involvement in FOM and tongue cancers is seen in about 5-7% of cases. [10]

Although tumor metastasis to the gland is uncommon, SMGs are frequently excised as a part of neck dissection because of their proximity to the primary lesion and afferent lymph nodes. However, the SMG is not a tissue without function; it secretes the majority of unstimulated saliva, especially during the night. [11] Saliva has many functions such as lubrication, buffering, immune defence, tooth enamel remineralisation and aiding mastication. Excision of submandibular glands may lead to xerostomia, which causes serious discomfort and a variety of problems in the oral cavity. Preservation of at least one gland will prevent these complications[12]; however, there is no consensus about the preservation of the submandibular glands in oral cavity tumours. [13]

Refinements in Selective Neck Dissection Nomenclature

Although it is well appreciated that patients with oral tongue cancer have a high risk of nodal involvement even for those with small primary lesions without clinical evidence of positive nodes, the extent by which the risk remains high for each neck level is controversial. Skip metastases to level IV may be a potential problem, and many surgeons prefer to include this region when performing an elective selective neck dissection.[14] However, the terminology to describe the neck dissection procedure for this situation is vague. Some prefer to apply the term *supraomohyoid neck dissection* because this is the standard elective procedure typically used for oral tongue cancer. But this is inaccurate because supraomohyoid neck dissection was intended to include only levels I through III. Others prefer to use the term *extended supraomohyoid neck dissection* or *anterolateral neck dissection*, which more accurately outlines the removal of levels I through IV. Unfortunately, acceptance of these additional terms adds complexity to the nomenclature system and runs the risk of adding confusion.[15]

The 1991 neck dissection classification system did not provide an accurate description of procedures in which the surgeon chooses to preserve certain sublevels. For example, the buccinator nodes may represent the primary echelon nodal basin for oral cavity cancers involving the buccal mucosal, hard palate, and upper alveolar ridge. These nodes are not included in the standard supraomohyoid neck dissection, and a better method is needed to define the inclusion of such structures. [16] To not further confuse this issue, it was determined by the committee that exclusion of these "named" neck dissections would facilitate the standardization and referencing of these procedures. Therefore, further in this text, we will no longer refer to these "named" selective

neck dissections except in the description of specific levels.[17]

Selective Neck Dissection (SND) for Oral Cavity Cancer

In the treatment of oral cavity cancer, the procedure of choice is SND (I-III). This refers to the removal of lymph nodes contained in the submental and submandibular triangles (level I), the upper jugular lymph nodes (level II), and the middle jugular lymph nodes (level III). The cutaneous branches of the cervical plexus and the posterior border of the SCM mark the posterior limit of the dissection. The inferior limit is the junction between the superior belly of the omohyoid muscle and the internal jugular vein. One of the justifications to eliminate naming of dissections for oral cavity cancer comes from the observations regarding invasive oral tongue carcinomas. In the case of oral tongue cancer, there is evidence indicating level IV is also at risk. Thus, some authorities recommend the selective neck dissection procedure for this subsite within the oral cavity to be SND (I-IV). For cancers involving the midline structures including the floor of mouth and ventral tongue, the lymph nodes on both sides of the neck are at risk and the procedure of choice is a bilateral SND (I-III).[18]

Anneroth et al (1987)

They also use Jakobsson et al. system for application to squamous cell carcinoma in the tongue and floor of mouth. One of the parameters, “vascular invasion” was omitted. Statistical analysis revealed that the reproducibility of the system was good for all morphologic variables. Mean total malignancy, tumor population and tumor-host relationship scores showed statistically significant correlation with mean rating for all the different morphologic parameters with certain specified exceptions. The clinical validity of this system was tested in a comprehensive study was tested in 89 patient of squamous cell carcinoma in the floor of mouth.

A statically significant correlation was found between mean total malignancy scores and clinical staging, frequency of recurrence, and death from first oral primary carcinoma.[19]

Bryne’s (1989, 1992) (ITF) Invasive Tumor Front Grading System

Bryne M. (1998) presented a hypothesis suggesting that molecular and morphological characteristics at the invasive front area of various squamous cell carcinomas may reflect tumor prognosis better than other parts of the tumor. He further states that several molecular events of importance for tumor spread like gains and losses of adhesion molecules, secretion of proteolytic enzymes, increased cell proliferation and initiation of angiogenesis occur at the tumor host interface; consequently, they have developed a simple morphological malignancy grading system that restricts the evaluation to the deep invasive front of the tumor. Several studies have shown that this system is a significantly better predictor of prognosis. All studies performed so far show that invasive front grading is a valuable supplement to clinical staging, suggesting that it should be introduced into the clinic.[20]

Current

The submandibular gland, which, unlike the parotid, does not contain lymph nodes, is rarely involved in early stage (stages I–II) oral cavity cancers. Any involvement would be by direct invasion; thus, the gland can be preserved in selective neck dissections in its absence. [21]However, it is important to remove all the submandibular lymph nodes, which are the first echelon lymph nodes of oral cavity, when preserving the submandibular gland to avoid a neck recurrence. This is sometimes difficult to perform without

removal of the gland, especially when nodal disease is located medial to the mylohyoid muscle or subjacent to the jaw in the posterior aspect of the sub-mandibular triangle.[22]

Projection

Among the OCSCC series, only one case of bilateral SMG involvement was seen. [23] There was no bilateral SMG involvement in other study. It is not rational to excise both glands for an OCSCC. The authors other study strongly recommended preserving at least one SMG in light of this data. There is no data about the prognostic significance of SMG involvement in OCSCC. Clark investigated sublingual gland invasion in oral cavity cancers and did not find any differences in disease-specific survival (DSS), loco regional control or distant metastasis rates. [24] Decisions regarding the excision of SMGs must be entirely based on the proximity of the primary tumour to the gland. [25] As seen in other study, in early stages and except for FOM tumours, involvement of the SMG in oral cavity tumours is very rare. [26] Because the gland has a unique structure and because its capsule displays resistance against tumour invasion, oncologically, it is enough to dissect only the capsule of the gland with the surrounding lymph nodes. It is better to strive to preserve the glands unless there are adherent pathologic lymph nodes or very close metastatic or primary tumors. [27]Instead of preoperative planned gland resection, the decision to excise the SMG must be determined during the operation with the help of inspection and frozen sections. One must take into account that xerostomia is a very important complication that may decrease the quality of life and lead to cessation of treatment. Surgeons should try to modify and develop techniques to protect SMGs in the treatment of oral cavity tumours. More research is warranted to investigate the effects of SMG preservation on survival and loco regional control of disease.[28]

Future

Improved understanding of the biology of metastatic spread of head and neck cancer has allowed modifications in the surgical management of cervical lymph nodes to reduce morbidity without compromising regional control or survival. Concurrent with this growth in surgical options, we advocate, preservation of submandibular glands can be a good technique for reducing future complications in a patient undergoing Neck Dissection wherever feasible. Therefore, if there is no need to expose large oral cavity tumors through the submandibular triangle, or when there is no direct extension of the primary and/or regional lymph nodes into the submandibular gland, it may be safe to preserve the submandibular gland and although regular follow up is required so as to comment on the oncological safety of the procedure. This observation can be adopted as a routine step to help patient in better rehabilitation and preventing xerostomia related complications when giving radiation therapy in future.[29]

Future research direction

Advances in the management of submandibular gland carcinoma studies stress the need towards molecular targeted therapy of the unusual subpopulation of tumorigenic cancer cells which could arrest the recurrence and metastasis of the tumor. In this direction, the cancer stem cell research needs to be further explored in the submandibular gland carcinoma. [30]

Recently a non-invasive, academic prototype chair side cancer diagnostic kit (GC America Inc.) has been devised by Wong DT for the early detection of carcinoma.[31] Newer field like Proteomics helps in the analysis of the salivary proteins which is extensively used in identification of a specific protein biomarker in saliva for diseases including oral cancer, periodontal disease and mammary gland carcinoma. Using Point-of-care salivary

diagnostic screening tests kit.It is possible to detect viruses in viral infectious diseases such as human papillomavirus (HPV), HCV and HIV.[32]

Further advancements are now being focused at “Omic technologies”, which include genomics, proteomics, transcriptomics, and metabolomics have already set their mark in life science research studies. [33] These emerging technologies have shown to offer highly sensitive, specific, quick and affordable diagnostic test kits in future. In cancer therapeutics, Nano particles, such as, semiconductor quantum dots, biodegradable micelles, iron oxide nano-crystals [34], are linked with bio targeting ligands, to aim at specific sites in malignant tumors, helpful in cancer therapeutics. Endothelin-1 is one of the probable salivary biomarkers for oral cancer has been reported for early cancer detection. Salivaomics, the future of saliva-based techniques for early diagnosis of dental diseases, is promising. However, further long-term studies are needed before these newer methods are adapted to routine clinical practice.[35]

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