

Varying Causes Of Lymph Node Enlargement In Oral Squamous Cell Carcinoma- A Pilot Study



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Introduction:

Malignant tumors are significant contributors to death by their local invasion and distant metastases. The most common intraoral malignancy is squamous cell carcinoma. Most significant route for its metastasis is through lymphatics. An important indicator of patient's prognosis is the presence of regional lymph node involvement as designated in the Tumor-Node-Metastasis (TNM) staging system*. The majority of nodal macro metastasis can be accurately detected with the combination of preoperative clinical evaluation and computed tomography (CT) or magnetic resonance imaging (MRI). On the other hand, detection of micro metastasis requires serial sections, immunohistochemistry, and/or molecular analysis¹.

Although lymph node enlargement in the drainage area of a squamous cell carcinoma is a common phenomenon, it is not always an indicator of metastasis. Infective and inflammatory conditions in the nodal drainage area arising out of the neoplastic activity or changes secondary to it (such as infection following surface ulceration or severe immune response to the tumor cells or their products) can cause nonmetastatic lymph node enlargements. The absence of metastatic deposits in these nodes can only be ruled out by histopathological examination. Currently histopathological assessment is only used for the diagnosis of carcinoma, leading to the inclusion of all nonmetastatically enlarged nodes in the TNM staging. This may affect the patient prognosis and treatment plan which are wholly dependent on the TNM staging, negatively. It is necessary to identify the occurrence of such non-metastatically enlarged nodes in relation to oral squamous cell carcinoma (OSCC) to evaluate the possible impact of their diagnosis as positive and inclusion in working out the TNM stage.

This pilot study was, therefore, aimed at establishing the presence of nonmetastatic lymph node enlargements in oral squamous cell carcinoma patients.

Materials and Methods

Radical neck dissection specimens of three patients treated for OSCC in our institution were retrieved from the archives of the department of oral & maxillofacial pathology. Seven enlarged nodes (one cm or greater) that were reported as negative for metastasis in the records were identified, and corresponding blocks retrieved from the

archives. Each block was serially sectioned at 6 μ intervals using semiautomatic soft tissue microtome. Every 10th section was stained using Hematoxylin and Eosin and examined. The nodes were examined for histological nodal changes ranging from follicular hyperplasia to metastatic involvement based on following histologic criteria:

Normal – Lymph nodes with an intact capsule, distinct presence of the three compartments cortex, paracortex and medulla; presence of primary or secondary follicles only in the cortex with normal components of cells within the follicles, normal appearance of sinuses and medullary cords.

Follicular hyperplasia - Lymph node with an intact capsule, indistinguishable nodal compartments due to both increase in the number of follicles and presence of follicles in the cortex and paracortex. Secondary follicles with a mantle zone, germinal centers containing normal mixture of cells present.

Diffuse pattern – Intact capsule, indistinguishable nodal compartments, lymphocytes arranged in sheets with no distinct pattern of arrangement².

Metastatic – Capsule of the lymph node may or may not be intact, presence of squamous cells in sheets, islands or small nests within the node, with or without the presence of dysplastic features and keratin pearl formation. The architecture of the lymph node may be effaced.

Results

Lymph Nodes	Histologic Features	Follicular Hyperplasia	Metastasis
3	Normal	Absent	Absent
3	Follicular Hyperplasia	Present	Present (Single Node in Deeper Sections)
1	Diffuse Pattern	Present (in Deeper Sections)	Absent
Total - 7			

Foot note *- TNM classification

Tumor - T1-T4, T1 < 2cm, T2-2-4cm, T3 > 4cm, T4 > 4cm and into adjacent structures

Lymph node - N1-N3, N1 \leq 3cm Single ipsilateral node, N2 - 3-6cm ipsilateral, contralateral or bilateral nodes, N3 > 6cm

Metastasis - M0-M1, M0-no metastases, M1 - distant metastases.

The TNM data collected is collated and a corresponding stage (I-IV) assigned. Higher stage corresponds with poorer prognosis and reduced disease free survival/ life expectancy.

Discussion

This study was conducted on seven serially sectioned enlarged lymph nodes reported as negative for metastasis of three OSCC patients.

Three of the enlarged nodes examined were found to have follicular hyperplasia, with no metastatic deposits. A node draining the region of a tumor basin might be enlarged because of excessive drainage of lymph carrying antigens, immune cells and their products. The number, location and composition of follicles within a node can change when challenged by antigens in this manner. Reactive follicular hyperplasia of the node is a common outcome of such immune challenges which often cause hyperplasia of either the B or T cell zone. These enlargements are a healthy response and do not indicate a pathology of the node itself.

One node in the study showed diffuse pattern in spite of being clinically enlarged. This is a reflection of the changes that take place in disease progression from normal to identifiable pathological conditions.

One node in our study showed the presence of metastasis along with follicular hyperplasia on assessment of serial sections. This is noteworthy since only nodes reported as negative were included in the study. The identification of any disease process through histological examination requires the actual inclusion of the damaged cells or in this case invading tumor cells in the sections. However, in micrometastatic involvement the numbers of tumor cells will be very few and the extent of involvement very small. In such cases, serial sectioning of the entire node is the only means of identification of all involved nodes. While identifying nodes involved by tumor metastasis is of prime importance, the required serial sectioning of all harvested nodes in a case of radical neck dissection is currently not possible in most laboratories. Establishing histological changes that identify high risk nodes for subsequent serial sectioning can be the answer to this dilemma. Current knowledge has shown that certain morphologic changes such as germinal center predominance in a node indicate a high risk of metastatic involvement³. The single positive node in this study also showed germinal center predominance.

This study was a pilot project and did not include a sufficient number of specimens to provide confirmed results. Nevertheless, it has highlighted the need for future studies to examine various causes of lymph node enlargement in the drainage area of a carcinoma and histopathological changes that identify high risk nodes in relation to the presence of micro metastasis.

Conclusion

Clinical Lymph node enlargement in oral squamous cell carcinoma is an essential element in formulating the TNM classification of the tumor, its staging and treatment

planning. From this pilot study, we conclude that lymph node enlargement seen in relation to these carcinomas can be histologically nonmetastatic. However to rule out metastatic involvement of an enlarged node, examination of the entire node by serial sections is mandatory.

References

1. Genden E.M, Ferlito A, Bradley P.J, Rinaldo A, Scully C. Neck disease and distant metastases. *Oral Oncology* 2003; 39: 207-12.
2. Benign White Cell Disorders: Reactive Lymphadenopathy [Internet]. 2010 June [cited 23/1/12]. Available from URL: <http://www.meded.virginia.edu/courses/path/innes/wcd/reactive.cfm>.
3. Di Giorgio A, Mingazzini P, Sammartino P, Canavese A, Arnone P, Scarpini M. Host defense and survival in patients with lung carcinoma. *Cancer* 2000; 89(10):2038-45.

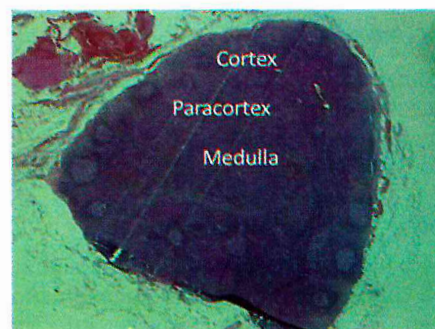


Fig 1 – Normal histological picture of a lymph node showing cortex, paracortex and medulla.

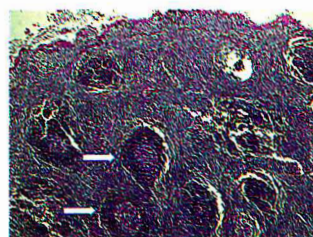


Fig 2 – Arrows indicating lymphoid follicles. Picture depicting increased number and changed position of lymphoid follicles within a lymph node - Follicular hyperplasia (4X).

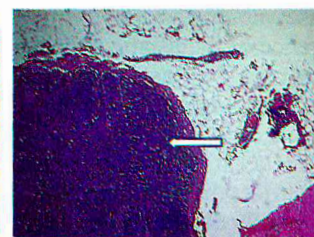


Fig 3 – Arrow indicating diffuse pattern of arrangement of lymphocytes within the lymph node (4X).

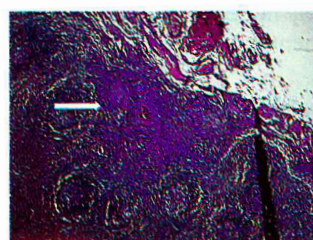


Fig 4 – Arrow depicting Squamous Cell Carcinoma metastasis into the lymph node (4X).

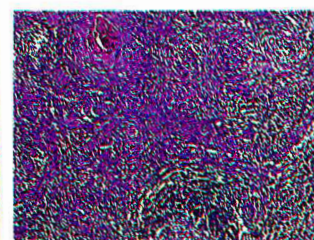


Fig 5 – Metastatic deposit within a lymph node (10X).