

Histomorphological Variants of Squamous Cell Carcinoma in Upper Aero-digestive Tract

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Abstract

Background: To determine the site wise frequency of squamous cell carcinoma variants in upper aero-digestive tract.

Methods: In this observational study all the cases of diagnosed squamous cell carcinoma of upper aero digestive tract were included. All the cases were formalin fixed and processed routinely to form paraffin blocks. Slides were made and stained with H&E.

Results: Out of 41 cases, 33 cases showed the classic pattern of squamous cell carcinoma, which arose from Oral cavity, alveolar ridge, tongue, oesophagus, palate, pharynx, nose, larynx and bronchus. Most of the classic squamous cell carcinomas were of keratinizing type.

Conclusions: Majority of cases of squamous cell carcinomas in upper aero-digestive tract revealed classical pattern.

Key Words: Histomorphological Variants, Squamous cell carcinoma, Upper aero-digestive tract

Introduction

Squamous cell carcinoma is the commonest malignancy seen in the upper aero-digestive tract. Several factors contribute to the causation of this malignancy, mainly including alcohol, smoking, snuff, radiations and genetic factors. There are different variants of squamous cell carcinoma, most of which do not pose diagnostic dilemma to the pathologist. Certain types, however, mimic benign and other malignant diseases on a morphological ground and therefore require correct diagnosis for prognostic and therapeutic reasons. Squamous cell carcinoma constitutes a major bulk of malignancies in the upper aero digestive tract.¹⁻³ Upper part of aero digestive tract is prone to injuries due to several environmental factors like alcohol, tobacco and snuff etc.⁴ which are proven risk factors for the development of malignancy. Nutritional deficiencies also have been found to increase the risk. Clinical

observation and epidemiologic studies have also identified ionizing radiation as an unequivocal risk factor, although of lesser importance from the public health point of view. Overall, epidemiologic evidence shows that occupational exposures also play a minor, though definite, role in the development of head and neck cancers.⁵ These along with the genetic predispositions cause development of squamous cell carcinoma by the classically described dysplasia to carcinoma sequence.⁶

There are different morphological variants of squamous cell carcinoma, most of which do not pose diagnostic dilemma to the pathologist. Certain types, however, mimic benign and other malignant diseases on a morphological ground & therefore require correct diagnosis for prognostic and therapeutic reasons.¹ The commonest of these variants is the classic type, constituting sheets and nests of atypical squamous cells, keratinizing or non-keratinizing.⁷ Different variants are seen in different areas, with the frequency of one being predominant at one place and other at some other place.

Variants, other than the classic pattern, that are seen in respiratory tract include lymphoepithelioma, spindle cell type and verrucous carcinomas.⁸ Papillary, clear cell and basaloid patterns have occasionally been described in lung. Similarly in digestive tract, verrucous, sarcomatoid, papillary, adenosquamous and basaloid patterns have been described.⁹ Usually majority of these patterns are identifiable if an adequate histopathology specimen is available, revealing squamous cell differentiation in at least few foci. However these patterns might be difficult to categorize as being histomorphological variants of Squamous cell carcinoma if biopsy material is small or not representing squamous differentiation.

Patients and Methods

This descriptive study was performed in Pathology department of Pakistan Institute of Islamabad from January to September 2016. Study included all the cases of diagnosed squamous cell carcinoma of upper aero digestive tract, during these nine (09) months,

retrieved from Laboratory management information system. All the cases were formalin fixed and processed routinely to form paraffin blocks. Slides were made and stained with H&E.

Results

Out of 41 patients, 19 were males and 22 were females. Thirty three cases showed the classic pattern of squamous cell carcinoma (Table 1;Figure 1-5). The tumour cases which showed classic squamous cell carcinoma pattern arose from oral cavity, alveolar ridge, tongue, oesophagus, palate, pharynx, nose, larynx & bronchus . Most of the classic squamous cell carcinomas cases showed keratinization in the form of keratin pearls and were placed in the well differentiated group. 11 cases were moderately differentiated and 5 were poorly differentiated (Table 2).

Table 1. Frequency of SCC variants at different sites

Type	Number	Site
Classic	33	Oral cavity, alveolar ridge, tongue, oesophagus, palate, pharynx, nose, larynx, bronchus
Spindle cell type	1	Alveolar ridge
Verrucous CA	3	Tongue
Adenosquamous type	1	Oesophagus
Basaloid squamous type	2	Oesophagus
Lymphoepithelioma type	1	Nasopharynx
Papillary type	0	-
Clear cell type	0	-
Total number of cases	41	-

Table 2. Differentiation of classic squamous cell carcinomas

Differentiation	Number
Well differentiated	17
Moderately differentiated	11
Poorly differentiated	5

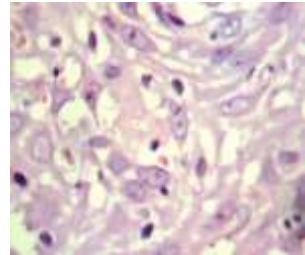


Figure 1. Spindle cell carcinoma(40X): Atypical spindle cells are seen. CA in situ was seen in the overlying epithelium



Figure 2. Verrucous carcinoma (10X): Blunt, pushing papillae with minimally atypical squamous cells.

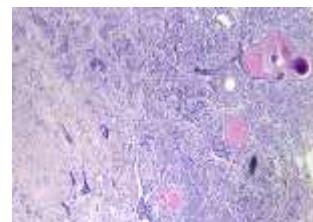


Figure 3. Basaloid squamous cell carcinoma (10X): Pleomorphic basaloid cells with squamous differentiation

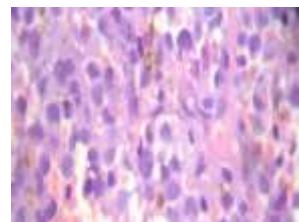


Figure4. Lymphoepithelioma (40X): Malignant squamous cells with lymphocytic infiltration

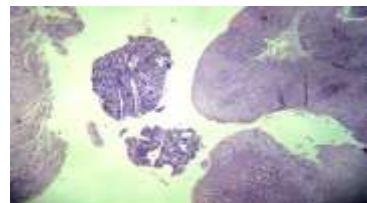


Figure 5. Adenosquamous carcinoma (10X): Components of malignant squamous cells and malignant glandular elements

Discussion

Squamous cell carcinoma of the head and neck region is an aggressive epithelial malignancy that constitutes 6th most common neoplasm in the world today.³ At the current rate, approximately 40,000 cases in the USA and > 5, 00,000 cases will be diagnosed each year worldwide.¹⁰ Despite the advancements made in treatment protocols, long term survival has remained <50% .^{11,12}

In the oral cavity, favoured sites for squamous cell carcinoma include ventral surface of tongue, floor of mouth, lower lip, soft palate and gingival.¹³ Intraoral squamous cell carcinomas vary widely in their degree of differentiation.¹⁴ Those located at the base of tongue or in tonsils are particularly undifferentiated.¹³ In this region, following the classic type of squamous cell carcinoma, verrucous carcinomas, are seen commonly.

Far less in frequency of occurrence are adenosquamous, basaloid squamous, spindle cell, small cell and lymphoepithelioma type carcinomas. In the upper respiratory tract, commonest squamous cell carcinoma types in sinonasal and nasopharyngeal areas include classic type followed in frequency by transitional, verrucous, basaloid squamous, sarcomatoid, small cell and undifferentiated types.¹⁴ Spindle cell variant of squamous cell carcinoma is a rare type of squamous cell carcinoma, with aggressive behaviour, which is predominantly found in the upper aero-digestive tract.^{15,16} This tumour is characterized by biphasic pattern composed of malignant spindle cells along with malignant squamous carcinoma/carcinoma in situ or dysplasia. Since it leads to obstructive features, quite early in the disease progression, therefore its detection rate is relatively high during the earlier part of natural history of disease.¹⁷

Verrucous carcinoma of upper aero-digestive tract is associated with a favourable prognosis compared to classic squamous cell carcinoma.¹⁸ Histologically, it is characterized by exophytic growth, minimal cytological atypia and broad, blunt papillae which are pushing in nature.¹⁹ Basaloid squamous cell carcinoma is a rare high grade type arising particularly from upper aero digestive tract.²⁰ Its preferred site of origin is base of tongue, tonsils and larynx.²⁰ Histologically, the tumours are invasive composed of pleomorphic, basaloid-appearing cells with hyperchromatic nuclei (Figure 3). Mitotic figures, including atypical forms, are identified along with foci of squamous differentiation.²¹

Lymphoepitheliomas are malignant epithelial tumours with infiltrate of non-neoplastic lymphocytes. This tumour is associated with EBV infection, and not infrequently located throughout the upper aero-digestive tract.²² It is an aggressive tumour with high metastatic rates.²³ Adenosquamous carcinoma is a rare aggressive neoplasm that has a worse prognosis than either squamous or adenocarcinomas.²⁴ It is characterized by a malignant squamous and malignant glandular components. It is also associated with frequent recurrences along with metastasis.²⁵

References

1. Stelow EB, Mills SE. Squamous cell carcinoma variants of the upper aerodigestive tract. American journal of clinical pathology 2005; 124(S1): 911-15
2. Landry D, Glastonbury CM. Squamous Cell Carcinoma of the Upper Aerodigestive Tract. Radiologic Clinics of North America. 2015; 53: 81-97.
3. Argiris A, Karamouzis M V, Raben D, Ferris RL. Head and neck cancer. Lancet 2008;371(9625):1695-709.
4. Webb JL, Burns RE, Brown HM, Leroy BE, Kosarek CE. Squamous cell carcinoma. Compend Contin Educ Vet 2009;31(3):133-42.
5. Cann CI, Fried MP, Rothman KJ. Epidemiology of squamous cell cancer of the head and neck. Otolaryngol Clin North Am 1985;18(3):367-88.
6. Lacko M, Braakhuis BJM, Sturgis EM. Genetic susceptibility to head and neck squamous cell carcinoma. International Journal of Radiation Oncology 2014;89: 38-48.
7. McMahon S, Chen AY. Head and neck cancer. Cancer Metastasis Rev 2003;22(1):21-24.
8. Shah AA, Jeffus SK, Stelow EB. Squamous cell carcinoma variants of the upper aerodigestive tract: A comprehensive review With a focus on genetic alterations. Arch Pathol Lab Med 2014;138(6):731-44.
9. Slootweg PJ, Richardson M. Squamous cell carcinoma of the upper aerodigestive system. In: Diagnostic Surgical Pathology of the Head and Neck. 2009; 45-110.
10. Jemal A, Tiwari R, Murray T, Ghafoor A, Samuels A. Cancer Statistics , 2004. CA Cancer J Clin. 2004;54(1):8-29.
11. Forastiere A, Koch W, Trotti A, Sidransky D. Head and neck cancer. N Engl J Med. 2001;345(26):1890-900.
12. Vokes EE, Weichselbaum RR, Lippman SM, Hong WK. Head and Neck Cancer. N Engl J Med. 1993;3(328):184-94.
13. Chidzonga MM, Mahomva L. Squamous cell carcinoma of the oral cavity, maxillary antrum and lip in a Zimbabwean population: A descriptive epidemiological study . Oral Oncology. 2006;42:184-89.
14. Feller L, Lemmer J. Oral Squamous Cell Carcinoma: Epidemiology, Clinical Presentation and Treatment. J Cancer Ther 2012;3(4):263-68.
15. Reyes M, Pennacchietti G, Valdes F, Montes R, Veloso M. Sarcomatoid (spindle cell) carcinoma of tongue.. Case Rep Dent. 2015; 780856. doi: 10.1155/2015/780856
16. Gerry D, Fritsch V a, Lentsch EJ. Spindle cell carcinoma of the upper aerodigestive tract: an analysis of 341 cases with comparison to conventional squamous cell carcinoma. Ann Otol Rhinol Laryngol 2014;123(8):576-83.
17. Navaneetham A, Dayananand Saraswathi MC, Santosh BS. Oral Verrucous Hyperplasia: A Case Report. J Maxillofac Oral Surg 2014;13(3):346-48.
18. Alonso JE, Kuan EC, Arshi A, St John MA. A population-based analysis of verrucous carcinoma of the oral cavity. Otolaryngol - Head Neck Surg 2016;155:76-78.
19. Pravda C, Srinivasan H, Koteeswaran D, Manohar LA. Verrucous carcinoma in association with oral submucous fibrosis. Indian J Dent Res. 2011;22(4):615.
20. Vasudev P, Boutross-Tadross O, Radhi J. Basaloid squamous cell carcinoma: Two case reports. Cases J. 2009;2(12): 9351-54
21. Wieneke JA, Thompson LDR, Wenig BM. Basaloid squamous cell carcinoma of the sinonasal tract. Cancer. 1999;85(4):841-54.
22. Frank DK, Cheron F, DiCostanzo D, Cho H. Nonnasopharyngeal lymphoepitheliomas (undifferentiated carcinomas) of the upper aerodigestive tract. Ann Otol Rhinol Laryngol. 1995;104(4):305-10.
23. Dubey P, Ha CS, Ang KK, El-Naggar AK, Knapp CL. Nonnasopharyngeal lymphoepithelioma of the head and neck. Cancer. 1998;82(8):1556-62.
24. Rawal YB, Anderson KM. Adenosquamous Carcinoma of the Tongue. Head Neck Pathol [Internet]. 2017;12105-017-0877
25. Keelawat S, Liu CZ, Roehm PC, Barnes L. Adenosquamous carcinoma of the upper aerodigestive tract: A clinicopathologic study of 12 cases and review of the literature. Am J Otolaryngol 2002;23(3):160-68.