Neuroendocrine Tumors of the Oral Cavity: A Summarized Overview

Sona Baburathinam[1], Devi.M[2], Therraddi Muthu R.M[3], Chitra N[4]

[1]Senior Lecturer, [2] Head of the Department,[3] Reader, [4]Senior Lecturer, Department of Oral Pathology and Microbiology, Asan Memorial Dental College and Hospital

Abstract

The neuroendocrine system is made up of neuroendocrine cells that are distributed throughout several organs, including digestive system and lungs. The neuroendocrine cells have characteristics of both nerve and endocrine cells. The neuroendocrine cells are locally aggregated constituting certain endocrine organs, such as adrenal medulla or are scattered throughout all organs with an epithelial lining (disseminated/diffuse neuroendocrine system- DNES). This article provides an overview of the neuroendocrine tumors that arise in the oral cavity.

Keywords: *Malignant Peripheral Nerve Sheath Tumor, Olfactory Neuroblastoma, Paraganglioma, Schwannoma*

Introduction

The neuroendocrine system is made up of neuroendocrine cells that are distributed throughout several organs, including digestive system and lungs. The neuroendocrine cells have characteristics of both nerve and endocrine cells. The neuroendocrine cells are locally aggregated constituting certain endocrine organs, such as adrenal medulla or are scattered throughout all organs with an epithelial lining (disseminated/diffuse neuroendocrine system- DNES). Tumors that arise from DNES, commonly involve the gastrointestinal tract, followed by the lung[1] . In the head and neck region, most tumors involve the larynx followed by salivary glands [2] .

Neuroendocrine cells of the oral mucosa:

Merkel cell, which is a member of the DNES, is the neuroendocrine cell of the oral mucosa. They are distributed in the basal layer of keratinized mucosa of gingiva and hard palate. They appear as scattered clear cells, occurring singly or in clusters[3] . They are not readily identifiable at light microscopic level. Immunohistochemically, they are positive for cytokeratins (CK 8, 18,19, 20)[3], villin, chromogranin A, synaptophysin, neuron specific enolase, vasoactive intestinal polypeptide, pancreastatin, substance P, epithelial and neural cell adhesion molecules and S-100 [4]. Dual expression of both epithelial antigens and neurosecretory substances are characteristic of both normal and neoplastic Merkel cells. But they show variability in expression of the various markers[5] . Merkel cells function as mechanoreceptors and mediate the sense of touch [6]. Ultrastuctural studies reveal the presence of a nuclear rodlet [7] .

Classification of neuroendocrine tumors:

Neuroendocrine tumors at any anatomic site, are classified into two groups [8] :

Group I: Tumors showing epithelial differentiation

Group II: Tumors showing neural features.

Group I

Well-differentiated neuroendocrine carcinoma (carcinoid tumor)

Moderately differentiated neuroendocrine carcinoma (atypical

Corresponding author:
Dr. Sona Baburathinam
Department of Oral Pathology and Microbiology,
Asan Memorial Dental College and Hospital
Chengalpatu, Tamil Nadu, India

carcinoid tumor)

Poorly differentiated neuroendocrine carcinoma, small cell type

Poorly differentiated neuroendocrine carcinoma, large cell type

Pituitary adenoma/carcinoma

Group II

Granular cell tumor

Heterotopic glial tissue

MPNST - Malignant peripheral nerve sheath tumor

Malignant melanoma

Neurofibroma

Olfactory neuroblastoma

Paraganglioma

PNET/Ewing's sarcoma

Schwannoma

(PNET- peripheral neuroectodermal tumor.)

Group I neoplasms:

Majority of lesions in the head and neck region arise from the larynx, while the second most common site is the salivary gland. Majority of lesions in the larynx are moderately differentiated, but those arising in the salivary gland are of poorly differentiated, small cell type. The well-differentiated neuroendocrine carcinoma or the "typical carcinoid tumor" grows in nests and cords, composed of uniform cells having 'salt and pepper' chromatin distribution [9] .

The moderately differentiated neuroendocrine carcinoma or the "atypical carcinoid tumor" grow in nests and cords with peripheral palisading of nuclei. There is mild-moderate nuclear pleomorphism seen [10].

The poorly differentiated neuroendocrine carcinoma, small cell type that occurs in the salivary glands is composed of sheets of spindled to oval cells with little cytoplasm and high mitotic rate. Areas of necrosis are common. Foci of glandular differentiation may be seen[11]. Poorly differentiated neuroendocrine carcinoma, large cell type is composed of intermediate to large cells. The sino-nasal undifferentiated carcinoma is a classic example [12]. The pituitary adenoma may arise in the nasopharynx as an ectopic mass[13].

Group II neoplasms:

Granular cell tumor:

It is a rare, benign, soft tissue tumor that arises from Schwann cells[14]. The lesion could be benign or malignant. Abrikosoff, in 1926 described a tumor of the tongue that was composed of granular cells. The granular cells are large, polygonal, oval or bipolar cells with abundant fine or coarsely granular cytoplasm and an eccentrically located vesicular, pale staining nucleus. The cells occur in ribbons separated by fibrous septa. Pseudoepitheliomatous hyperplasia is characteristic. Of the head and neck lesions, 70% occur intaorally in the tongue, buccal mucosa and hard palate[14]. Granular cells are positive for S 100, neuron specific enolase, laminin and myelin basic protein, confirming their neural origin[15].

Malignant peripheral nerve sheath tumor:

They are rare, highly aggressive soft tissue sarcomas of ectomesenchymal origin that may arise de novo or from a pre-existing neurofibroma. There is a higher incidence in patients with neurofibromatosis I and in those with radiation exposure[16]. Most tumors have spindle cells arranged in fascicles and resemble fibrosarcoma. Mitotic activity is high. Few tumors exhibit variable differentiation. A MPNST with rhabdomyoblastic differentiation exhibits both skeletal muscle and neural differentiation. Other tumors with differentiation include glandular malignant Schwannoma, epithelioid malignant Schwannoma and superficial epithelioid variant[17].

Malignant melanoma:

It is aggressive neoplasm composed of small round cells resembling small cell carcinoma or lymphoma. They may be composed of epithelioid cells, rhabdoid cells or spindle cells[18]. They thus mimick a variety of sarcomas. They exhibit diffuse positive staining for S 100 protein, HMB-45 and anti-tyrosinase [2].

Olfactory neuroblastoma:

Rare tumor that is found in the nasal cavity and nasopharynx. They may also arise from the maxillary sinus or invade it. Microscopically, they are composed

of densely packed masses of small darkly staining cells, with poorly defined eosinophilic cytoplasm and round, vesicular nucleus. Rosette formation with non-ciliated columnar cells and eosinophilic neurofibrils is commonly found. Stroma has a fibrillar neuroid pattern. Few mitotic figures are seen[19].

Paraganglioma:

The tumor is characterized by presence of round or polygonal epithelioid cells that are organized into nests or zellballen. The nests are composed of chief cells, with centrally located vesicular nucleus and a granular, eosinophilic cytoplasm. The tumor is vascular and is surrounded by a thin fibrous capsule [20].

Melanotic neuroectodermal tumor of infancy:

This tumor has a striking predilection for head and neck, frequently involving anterior maxilla. They have a biphasic population of small and large cells forming alveolar or tubular patterns. The small cells resemble neurofibroblasts, while the large cell shave prominent cytoplasmic melanin pigment. The larger cells are positive for cytokeratin, vimentin and HMB-45. Both cell types are positive for neuron specific enolase and may also exhibit positivity for Leu-7 or muscle markers. They may also stain for synaptophysin and GFAP[21].

Conclusion

The basis of classification of neuroendocrine tumors is largely determined by their histologic differentiation. Though they reveal biologic heterogeneity, there should be an awareness of the occurrence of such lesions in the oral cavity to enable them to be detected and treated early.

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Conflicts of Interest : Nil .

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