

Review Article

The Spindle Cell Neoplasms of the Oral Cavity

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ABSTRACT

Spindle cell neoplasms are defined as neoplasms that consist of spindle-shaped cells in the histopathology. Spindle cell neoplasms can affect the oral cavity. In the oral cavity, the origin of the spindle cell neoplasms may be traced to epithelial, mesenchymal and odontogenic components. This article aims to review the spindle cell neoplasms of the oral cavity with emphasis on histopathology.

Key words: Spindle Cell, Neoplasms; Oral Cavity

Introduction

Spindle cell neoplasms can affect the oral cavity and it is often very difficult for the oral pathologists to differentiate it from other similar microscopic simulates (1). In the oral cavity, the origin of the spindle cell neoplasms may be traced to epithelial, mesenchymal and odontogenic components. More recently, a simple working type classification was proposed by the author for the spindle cell neoplasms of the oral cavity (2). This classification was based on the predominance of spindle cells in the histopathology of the lesions of the oral cavity. This article aims to review the spindle cell neoplasms of the oral cavity with emphasis on histopathology. It includes neural, myofibroblastic, muscle, fibroblastic, vascular, epithelial, odontogenic and miscellaneous tumors.

Neural Tumors

Neural tumors include tumors of neural tissue origin. In the oral cavity, neural tumors are usually arising from nerve sheath. This category includes neurofibroma, neurilemmoma (schwannoma), palisaded encapsulated neuroma, traumatic neuroma (amputation neuroma) and malignant peripheral nerve sheath tumor.

Neurofibroma

Neurofibroma is a circumscribed non-encapsulated tumor composed of Schwann cells, perineurial cells and endoneurial fibroblasts (3). Histopathologically, the tumor is composed of interlacing bundles of spindle cells with wavy nuclei (3). Depending upon the ground substance, tumors can be categorised into myxoid and plexiform varieties (4). Immunohistochemically, the

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tumor cells show a scattered positive reaction for S-100 protein, signifying that they originate from neural crest derived tissue (5).

Neurilemmoma

Neurilemmoma is a circumscribed encapsulated slow growing benign tumor composed of schwann cells (6). Histopathologic identification of Antoni A and B areas, nuclear palisading, whorling of cells, and Verocay bodies along with strong and diffuse staining with S-100 stain will pathologically confirm the diagnosis of schwannoma (7).

Palisaded Encapsulated Neuroma

Palisaded encapsulated neuroma is a benign neural tumor, which occurs primarily on the facial skin of middle-aged adults, and in the oral cavity, it is more prevalent in the masticatory mucosa (8). Histopathologically, the tumors are characterized by a moderately cellular, fascicular proliferation of spindle cells showing areas of nuclear palisading and whorling of cells (9). Immunohistochemical stains will reveal S-100 protein-positive Schwann cells and peripheral nerve axons will take positive neurofilament staining (9). The fibrous capsule of the lesions will show positive staining for epithelial membrane antigen, indicative of perineurium (9).

Traumatic Neuroma

Traumatic neuroma is a rare disorder that involves simultaneous nerve repair and defensive mechanisms (i.e., reactive proliferation of perineurial cells) following a trauma episode (10). Histopathologically, it consists of a haphazard proliferation of nerve fascicles, including axons, schwann cells and fibroblasts embedded in the background of collagen and sometimes associated with chronic inflammation (10). Immunohistochemically, axon filaments will take silver stains (3).

Malignant Peripheral Nerve Sheath Tumor

The term “malignant peripheral nerve sheath tumor” refers to all the spindle cell sarcomas arising from the peripheral nerve or neurofibroma or showing nerve sheath differentiation (11). Histopathologically, the tumor is composed of hyperchromatic spindle cells growing in a fascicular pattern with alternating hypocellular and hypercellular areas with increased mitotic activity (12). Immunohistochemically, neuron-specific enolase is confirmatory for the neurogenic origin of this tumor (12).

Myofibroblastic Tumors

Myofibroblastic tumors include tumors of myofibroblasts (i.e., cells with both smooth muscle and fibroblastic features). This category includes myofibroma, inflammatory myofibroblastic tumor and low-grade myofibrosarcoma.

Myofibroma

Myofibroma is an uncommon spindle cell neoplasm rarely found in oral cavity. Microscopically, a typical biphasic pattern is observed with elongated spindle cells with eosinophilic cytoplasm in the borders, polygonal cells arranged in a palisading pattern, with hyperchromatic nuclei in the central portions (13). With the special stain such as Masson trichrome stain, myofibromas shows more collagenous stroma intermixed with the spindle cells and thick fibrous bundles with random, irregularly intersecting angles (14). Immunohistochemically, the tumor cells will be positive for vimentin and α actine smooth muscle antibodies and negative for keratin, S-100, EMA (Epithelial Membrane Antigen) antibodies(15).

Inflammatory Myofibroblastic Tumor

Inflammatory myofibroblastic tumor is a rare tumor found in oral cavity composed of myofibroblastic cells accompanied by an inflammatory infiltration of plasma cells, lymphocytes, macrophages and

eosinophils intermingled within collagen fibers (16). Histologically three basic patterns can be recognized i.e., a) myxoid or vascular pattern with spindle or stellate myofibroblasts in an abundant myxoid stroma with an inflammatory component resembling granulation tissue or nodular fasciitis; b) compact spindle cells that may adopt a storiform pattern intermingled with inflammatory cells resembling fibrous histiocytoma and c) dense plate-like collagen with low cell density and rare inflammatory cell stroma, resembling a desmoids (17). Immunohistochemically, the tumor cells will be positive for vimentin, desmin, muscle-specific actin, smooth-muscle-actin and activin receptor-like kinase 1 (ALK-1) (17).

Low Grade Myofibrosarcoma

Low-grade myofibrosarcoma is a rare entity in the oral cavity composed of myofibroblasts with more predilections in tongue followed by mandible and gingival (18). Histologically, the lesion will show hypercellular areas of neoplastic cells, which are spindle, shaped showing elongated, atypical nuclei with prominent nucleoli and eosinophilic cytoplasm (19). Immunohistochemically, the tumor cells will be diffusely positive for vimentin, smooth muscle actin and desmin and negative for cytokeratin, CD34 and CD21 (19).

Muscle tumors

Muscle tumors include tumors of muscle tissue origin. This category includes leiomyoma, vascular leiomyoma, leiomyosarcoma, rhabdomyoma and rhabdomyosarcoma.

Leiomyoma

Leiomyoma is a benign smooth muscle tumour that is usually seen in the uterine myometrium, gastrointestinal tract, skin and lower extremities of middle-aged women (20). According to WHO, leiomyomas are classified into three histological

groups: (a) vascular (angioliomyoma), (b) solid and (c) epithelioid (leiomyoblastomas) (21). Histologically, solid leiomyoma consists of interlacing bundles of spindle-shaped or stellate smooth muscle cells with elongated, blunt-ended, pale-staining nuclei (21). Immunohistochemically, the tumor cells will be positive for alpha smooth muscle actin and vimentin and negative for S-100 protein and desmin (21).

Vascular Leiomyoma

Vascular leiomyoma (Angiomyoma) is a rare benign smooth muscle tumor composed of numerous blood vessels together with spindle-shaped smooth muscle cells (22). Histologically, the vascular leiomyoma is characterized by a well-defined proliferation of mesenchymal tapered cells with eosinophilic cytoplasm and elongated basophilic nuclei (cigar shaped nuclei) (23). Immunohistochemically, the tumor cells will be positive for actin and vimentin and negative for S-100 protein and CD34 (23).

Leiomyosarcoma

Leiomyosarcoma is a malignant lesion that exhibits smooth muscle differentiation and arises from undifferentiated pluripotential undifferentiated mesenchymal cells (24). Histopathologically, the tumor is characterized by sheets of sweeping, alternating bundles and fascicles of densely packed spindle cells with abundant fibrillar eosinophilic cytoplasm and indistinct cytoplasmic borders, aligned in a palisade pattern (24). The tumor cells will show marked cellular pleomorphism with irregular shaped large hyperchromatic bizarre nuclei. Immunohistochemically, the tumor cells will be positive for smooth muscle actin, muscle specific actin and vimentin and negative for S-100 protein, cytokeratin and desmin (25).

Rhabdomyoma

Rhabdomyoma is a benign tumor originating

from striated muscle cells. Rhabdomyoma can be classified into adult and fetal categories depending upon the age. Histopathologically in the adult category, the tumor is characterized by round and polygonal cells with abundant granular eosinophilic cytoplasm (spider web appearance) (26). Fetal category will demonstrate spindle shaped muscle cells with marked cellularity and mild pleomorphism in a myxoid stroma (27). Immunohistochemically, the tumor cells will be positive for desmin, myoglobin and alpha-smooth muscle actin and negative for vimentin (28).

Rhabdomyosarcoma

Rhabdomyosarcoma is a malignant tumor originating from striated muscle cells. Histopathologically, the tumor cells shows marked nuclear and cellular pleomorphism, nuclear hyperchromatism, prominent nucleoli, loss of cohesion between the cells, abundant abnormal mitotic figures and occasional spindle cell morphology (29). Immunohistochemically, the tumor cells will be positive for myo D1, desmin and actin (29).

IV. Fibroblastic tumors

Fibroblastic tumors include tumors of fibroblasts. This category includes solitary fibrous tumor, fibromatoses, nodular fasciitis, desmoplastic fibroma and fibrosarcoma.

Solitary fibrous tumor

“Solitary fibrous tumor is a rare spindle cell neoplasm that has been originally and most often documented in the pleura” (30). Histopathologically, round to ovoid or bland spindle cells with vesicular nuclei and sparse cytoplasm with thick hyalinised collagen interspersed between tumour cells showing patternless pattern with alternating hypo and hypercellular areas (31). Immunohistochemically, the tumor cells will be positive for CD34 (31).

Fibromatosis

Fibromatosis are proliferations of highly differentiated fibrous tissue (32). In the oral cavity, fibromatosis is presenting as aggressive type. Histopathologically, the lesion is characterised by cellular proliferation of streaming fascicles of spindle shaped cells showing moderate anisonucleosis with variable amount of collagen (32).

Nodular fasciitis

Nodular fasciitis is a benign reactive proliferation of fibroblasts that is thought to be a response of tissue to injury (33). Microscopically, the lesion will display a well-delineated but not encapsulated proliferation of spindle cells with a nodular growth pattern (34). Immunohistochemical analysis will reveal positivity of the spindle cells for the antibodies against smooth muscle actin and muscle-specific actin (HHF-35) (34).

Desmoplastic Fibroma

Desmoplastic fibroblastoma is a distinctive uncommon fibrous soft tissue tumor (35). Microscopically, the tumor is composed of stellate or spindle-shaped cells embedded in hypovascular fibrous stroma with focal entrapment of fat (35). The cells do not exhibit mitotic figures and tumor necrosis (35). Immunohistochemically, the tumor cells are immunopositive for vimentin, and alpha-smooth muscle actin (35).

Fibrosarcoma

Fibrosarcoma is a malignant mesenchymal neoplasm of the fibroblasts. Microscopically, the tumor can be graded as low and high grade of malignancy (36). Low-grade fibrosarcoma shows spindle cells arranged in fascicles with low to moderate cellularity and a herringbone appearance (36). There is a mild degree of nuclear pleomorphism and rare mitosis, with a collagenous stroma (36). High-grade lesions show an intense nuclear pleomorphism, greater cellularity and atypical mitosis (36). The nuclei

can be spindle shaped, oval or round (36). The positive immunostaining for vimentin, along with negativity for muscular immunomarkers, helps in diagnosing the fibrosarcoma (36).

V. Vascular Tumors

Vascular tumors include tumors of vascular tissue origin. This category includes hemangiopericytoma, Kaposi sarcoma and spindle cell hemangioma.

Hemangiopericytoma

Hemangiopericytoma is a rare tumor that is presumably derived from Zimmerman's pericytes (small pericapillary spindle-shaped cells) (37). The tumor usually exhibits tightly packed spindle, round to ovoid cells that surround endothelium lined vascular channels (37). Histologically, the tumour will demonstrate staghorn-like vasculature and immunohistochemically the tumor cells will be positive for CD34 and negative for calponin, CD68 KP1, AE1-AE3, smooth muscle actin, P63 and S-100(37).

Kaposi Sarcoma

Kaposi's sarcoma is an angioproliferative tumour rarely found in the oral cavity (38). Microscopically the tumor shows spindle cells and poorly defined vascular slits with scattered hemosiderin and extravasation of red blood cells (38).

Spindle Cell Hemangioma

Spindle cell hemangioma is an uncommon benign vascular tumor of the oral cavity (39). Microscopically, the tumor shows well-circumscribed vascular proliferation of spindled to epithelioid endothelial cells with intracytoplasmic vascular lumens (39). Immunohistochemically, the tumor is positive for CD31 and CD34 (39).

VI. Epithelial Tumors

Epithelial tumors include tumors of epithelial tissue origin. This category includes spindle cell

carcinoma, pleomorphic adenoma and malignant melanoma.

Spindle Cell Carcinoma

Spindle cell carcinoma is considered a rare variant of squamous cell carcinoma (40). Microscopically, the streaming fascicles of pleomorphic spindle cells will represent anaplastic epithelial cells (40). The diagnosis is supported by immunohistochemical demonstration of cytokeratins within the tumor cells (40).

Pleomorphic adenoma

Pleomorphic adenoma is the most frequently encountered salivary gland neoplasm derived from ductal and myoepithelial elements (41). Microscopically, myoepithelial cells form the major share and shows spindle shaped cells and plasmacytoid appearance in a myxomatous background (42).

Malignant Melanoma

Oral malignant melanoma is a rare aggressive neoplasm of melanocytic origin representing 0.2-8% of all melanomas (43). Microscopically, the presence of atypical melanocytes showing varying degrees of nuclear pleomorphism, hyperchromatism, prominent nucleoli and abundant cytoplasm with brown pigment in the epithelial and connective tissue junction confirm the diagnosis of oral malignant melanoma (43). Immunohistochemically, the tumor cells stain positively with antibodies against HMB-45, S-100 protein and vimentin (43).

VII. Odontogenic tumors

Odontogenic tumors include tumors of odontogenic origin. This category includes ameloblastic fibroma, ameloblastic fibrosarcoma, central odontogenic fibroma and desmoplastic ameloblastoma.

Ameloblastic fibroma

Ameloblastic fibroma is a rare odontogenic tumor constituting neoplastic epithelial and mesenchymal tissues (44). Microscopically, the tumor is composed of islands and strands of odontogenic epithelial cells in a loose connective tissue stroma resembling primitive dental papilla (44). The peripheral epithelial cells lining the islands and strands are low columnar, similar to the cells found in the peripheral layer of the follicle in ameloblastoma (44).

Ameloblastic Fibrosarcoma

Ameloblastic fibrosarcoma is a rare malignant odontogenic tumour characterized by a benign epithelial component within a malignant fibrous stroma (45). Histologically, the mesenchymal portion of the tumor is highly cellular and shows hyperchromatism, pleomorphism and prominent mitoses (45). The sarcomatous mesenchymal component of ameloblastic fibrosarcoma is positive to Ki67, PCNA and p53, in front of the negativity of ameloblastic fibroma (45).

Central Odontogenic Fibroma

The central odontogenic fibroma (COF) is a benign odontogenic tumour derived from the dental mesenchymal tissues (46). Gardner defined two histological variants: a) hyperplastic dental follicle with a connective fibrous tissue and small amounts of odontogenic epithelium and b) WHO type with a prominent epithelial component and the presence of variable quantities of dentine or cement-like tissue (46).

Desmoplastic Ameloblastoma

Desmoplastic ameloblastoma is a rare variant of ameloblastoma (47). Histologically, the tumor shows scattered epithelial odontogenic nests and extensive desmoplasia with hypercellular central area composed of spindle-shaped or polygonal epithelial cells (47). Immunohistochemically, the

tumor cells show variable expression of S-100 protein and desmin and connective tissue stroma will exhibit strong positive reaction for collagen type VI (47).

VIII. Miscellaneous Tumors

Miscellaneous tumors comprise of unclassified category tumors. This category includes benign fibrous histiocytoma, malignant fibrous histiocytoma, synovial sarcoma, ossifying fibromyxoid tumor, giant cell angiofibroma and blue nevus.

Benign Fibrous Histiocytoma

Benign fibrous histiocytoma is one of the most common tumors of the superficial and deep soft tissues, made up of a mixture of fibroblastic and histiocytic cells (48). Histologically, the tumor is characterized by uniform spindle-shaped cells arranged in whorled or storiform pattern with scattered xanthomatous cells, multinucleated giants cells, lymphocytes and deposits of hemosiderin (48). Immunohistochemically, the tumor cells are positive for vimentin and CD68 and negative for S100, factor XIIIa and CD34 and SMA (49).

Malignant Fibrous Histiocytoma

Malignant fibrous histiocytoma is a tumor of mesenchymal origin, which rarely occurs in head and neck (50). Histopathologically, the tumor can be divided into 4 morphologic subtypes depending on the predominant cellular components: a) storiform or pleomorphic, b) myxoid, c) giant cell and d) inflammatory (50). Immunohistochemically, the tumor cells and giant cells are positive for vimentin.

Synovial Sarcoma

The head and neck synovial sarcomas account for 6.8% of all synovial sarcomas occurring in the body (51). Histopathologically synovial sarcoma can be sub classified into four types: (a) biphasic

type with distinct epithelial and spindle cell components present in various proportions and patterns, (b) monophasic spindle cell type with little or no evidence of epithelial differentiation, (c) monophasic epithelial type, and (d) poorly differentiated type (52). Immunohistochemically, both epithelial and spindle cells are positive for cytokeratin and epithelial membrane antigen, while only the spindle cells are positive for vimentin (52).

Ossifying Fibromyxoid Tumor

Ossifying fibromyxoid tumor is a rare tumor of mesenchymal origin with varied presentation at head and neck and only a few cases have been reported in the oral cavity with predilection on gingiva (53). Histopathologically the tumor is characterised by proliferation of round to spindle-shaped cells arranged in cords and nests embedded in a fibromyxoid matrix with incomplete shell of bone trabeculae located beneath the fibrous pseudocapsule at the periphery (54). Immunohistochemical analysis will show positivity for vimentin and S-100 protein and negativity for smooth muscle actin, muscle-specific action, and glial fibrillary acidic protein (54).

Giant Cell Angiofibroma

Giant cell angiofibroma (GCA) is a distinctive orbital tumor with only 3 cases reported as painless solitary nodule in buccal mucosa (55). Histopathologically, the tumor is characterized by a patternless spindle-cell proliferation within a generally myxoid stroma containing areas of perivascular sclerosis with numerous floret type multinucleated giant cells (56). Immunohistochemically, the tumor cells and multinucleated giant cells will show positivity for CD34 (56).

Blue Nevus

A blue nevus is a benign acquired melanocytic lesion that typically presents as an asymptomatic,

slate blue or blue-black smooth-surfaced macule or papule which measures less than 6 mm in diameter (57). Histopathologically, blue nevus can be classified into common and cellular subtypes. The common blue nevus is characterized by an intramucosal proliferation of elongated, bipolar, spindle-shaped melanocytes that are often grouped in short fascicles arranged parallel to the overlying epithelium (57). The cellular blue nevus is characterized by an intramucosal, nodular proliferation of dendritic spindle-shaped, pigmented melanocytes, tightly packed aggregates of larger oval-to-round melanocytes with pale cytoplasm and little or no melanin (57). Immunohistochemically, the spindle-shaped cells of blue nevi will express both S-100 and HMB-45 (58).

Conclusion

Spindle cell neoplasms of the oral cavity form a diverse group and it is very difficult to diagnose these neoplasms from routine haematoxyline and eosin sections of histopathology. Immunohistochemistry investigations have to be carried out to rule out individual neoplasms.

Conflict of interest

The authors declare that there is no conflict of interests.

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