ABSTRACT

Spindle cell lesions are lesions that consist of spindle-shaped cells in the histopathology. Due to complex nature of the oral cavity, presence of neural tissue, and varied type of lesions occurring in oral cavity, Spindle cell lesions are seen the oral cavity. Even though the spindle cell lesions of oral cavity are rare finding. In the oral cavity, the spindle cell lesions are diverse and diagnostically challenging. The origin of the spindle cell lesions may be due to epithelial, mesenchymal and odontogenic components. This article aims to review the spindle cell lesions of the oral cavity with emphasis on histopathology and immunohistochemical findings.

KEYWORDS: Epithelial, mesenchymal and odontogenic components.

INTRODUCTION

Spindle cell lesions rarely but can encounter in the oral cavity. It is often very difficult for the oral pathologists to differentiate it from other similar microscopic simulates. Some spindle cell lesions are highly malignant while others are benign or just reactive lesion. In the oral cavity, the origin of the spindle cell lesion may be epithelial, mesenchymal and odontogenic components. The simple working type classification of the spindle cell neoplasm was proposed. This classification was based on the predominance of spindle cells in the histopathology of the lesions of the oral cavity. Such classification contain almost all the spindle cell lesions occurring in the oral and maxillofacial areas.

Neural tumors
- Neurofibroma
- Neurilemmoma (schwannoma)
- Palisaded encapsulated neuroma
- Traumatic neuroma (amputation neuroma)
- Malignant peripheral nerve sheath tumor

Myofibroblastic tumors
- Myofibroma
- Inflammatory myofibroblastic tumor
- Low-grade myofibrosarcoma

Muscle tumors
- Leiomyoma
- Vascular leiomyoma
- Leiomyosarcoma

Rhabdomyoma
- Rhabdomyosarcoma

Fibroblastic tumors
- Solitary fibrous tumor
- Fibromatosis
- Nodular fasciitis
- Fibrosarcoma
- Desmoplastic fibroma

Vascular tumors
- Hemangiopericytoma
- Kaposi sarcoma
- Spindle cell hemangioma

Epithelial tumors
- Spindle cell carcinoma
- Malignant melanoma
- Pleomorphic adenoma

Odontogenic tumors
- Ameloblastic fibroma
- Ameloblastic fibrosarcoma
- Central odontogenic fibroma
- Desmoplastic ameloblastoma

Miscellaneous tumors
- Benign fibrous histiocytoma
- Malignant fibrous histiocytoma
- Synovial sarcoma
- Ossifying fibromyxoid tumor
Giant cell angiofibroma
Blue nevus

Neural Lesions
Tumors arising from neural tissue are encountered the oral cavity. Majority of the times 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 tumor composed of Schwann cells, perineurial cells and endoneurial fibroblasts.

Histopathologically, the tumor is composed of interlacing bundles of spindle cells with wavy nuclei. Depending upon the ground substance, tumors can be categorized into myxoid and plexiform varieties.[3]

Immunohistochemically, the tumor cells show a scattered positive reaction for S-100 protein, signifying that they originate from neural crest derived tissue.[4]

Traumatic Neuroma
Traumatic neuroma involves simultaneous nerve repair and defensive mechanisms. That is reactive proliferation of perineurial cells following a trauma episode.[6]

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.[6] Immunohistochemically, axon filaments will take silver stains.[7]

Neurilemmoma
Neurilemmoma is a circumscribed encapsulated slow growing benign tumor composed of schwann cells.[8] 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.[9]

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.[10]

Histopathologically, the tumors are characterized by a moderately cellular, fascicular proliferation of spindle cells showing areas of nuclear palisading and whorling of cells.[11]

Immunohistochemical stains will reveal S-100 protein-positive Schwann cells and peripheral nerve axons will take positive neurofilament staining. The fibrous capsule of the lesions will show positive staining for epithelial membrane antigen, indicative of perineurium.[11]

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.[12]

Histopathologically, the tumor is composed of hyperchromatic spindle cells growing in a fascicular pattern with alternating hypocellular and hypercellular areas with increased mitotic activity. Immunohistochemically, neuron specific enolase is confirmatory for the neurogenic origin of this tumor.[13]

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.[14] 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.[15]

Immunohistochemically, the tumor cells will be positive for vimentin and α actin smooth muscle antibodies and negative for keratin, S-100, EMA (Epithelial Membrane Antigen) antibodies.[16]

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.[17] 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. Immunohistochemically, the tumor cells will be positive for vimentin, desmin, muscle-specific actin, smooth-muscle-actin and activin receptor-like kinase 1 (ALK-1).[18]

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
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.\(\text{[21]}\)

According to WHO, leiomyomas are classified into three histological groups:
(a) vascular (angioleiomyoma),
(b) solid,
(c) epithelioid (leiomyoblastomas).

Histologically, solid leiomyoma consists of interlacing bundles of spindle-shaped or stellate smooth muscle cells with elongated, blunt-ended, palestaining nuclei. Immunohistochemically, the tumor cells will be positive for alpha smooth muscle actin and vimentin and negative for S-100 protein and desmin.\(\text{[22]}\)

Leiomyosarcoma
Leiomyosarcoma is a malignant lesion that exhibits smooth muscle differentiation and arises from undifferentiated pluripotential undifferentiated mesenchymal cells. 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.\(\text{[23]}\) 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.\(\text{[24]}\)

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).\(\text{[25]}\) Fetal category will demonstrate spindle shaped muscle cells with marked cellularity and mild pleomorphism in a myxoid stroma.\(\text{[26]}\)

Immunohistochemically, the tumor cells will be positive for desmin, myoglobin and alpha-smooth muscle actin and negative for vimentin.\(\text{[27]}\)

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. Immunohistochemically, the tumor cells will be positive for myo D1, desmin and actin.\(\text{[28]}\)

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. Histopathologically, round to ovoid or bland spindle cells with vesicular nuclei and sparse cytoplasm with thick hyalinated collagen interspersed between tumour cells showing patternless pattern with alternating hypo and hypercellular areas. Immunohistochemically, the tumor cells will be positive for S-100 protein, CD34 and CD21.\(\text{[29]}\)

Fibromatosis
Fibromatosis are proliferations of highly differentiated fibrous tissue. In the oral cavity, fibromatosis is presenting as aggressive type. Histopathologically, the lesion is characterized by cellular proliferation of streaming fascicles of spindle shaped cells showing moderate anisonucleosis with variable amount of collagen.\(\text{[30]}\)

Nodular fasciitis
Nodular fasciitis is a benign reactive proliferation of fibroblasts that is thought to be a response of tissue to injury.\(\text{[31]}\) Microscopically, the lesion will display a well-delineated but not encapsulated proliferation of spindle cells with a nodular growth pattern. Immunohistochemical analysis will reveal positivity of the spindle cells for the antibodies against smooth muscle actin and muscle-specific actin (HHF-35).\(\text{[32]}\)

Desmoplastic Fibroma
Desmoplastic fibroblastoma is a distinctive uncommon fibrous soft tissue tumor. Microscopically, the tumor is composed of stellate or spindle-shaped cells embedded in hypovascular fibrous stroma with focal entrapment of fat. The cells do not exhibit mitotic figures and tumor necrosis. Immunohistochemically, the tumor cells are immunopositive for vimentin, and alpha-smooth muscle actin.\(\text{[33]}\)

Fibrosarcoma
Fibrosarcoma is a malignant mesenchymal neoplasm of the fibroblasts. Microscopically, the tumor can be graded
as low and high grade of malignancy. Low-grade fibrosarcoma shows spindle cells arranged in fascicles with low to moderate cellularity and a herringbone appearance. There is a mild degree of nuclear pleomorphism and rare mitosis, with a collagenous stroma. High-grade lesions show an intense nuclear pleomorphism, greater cellularity and atypical mitosis. The nuclei can be spindle shaped, oval or round. The positive immunostaining for vimentin, along with negativity for muscular immunomarkers, helps in diagnosing the fibrosarcoma. [13]

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). The tumor usually exhibits tightly packed spindle, round to ovoid cells that surround endothelium lined vascular channels. Histologically, the tumor 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. [15]

Kaposi Sarcoma
Kaposi’s sarcoma is an angioproliferative tumour rarely found in the oral cavity. Microscopically the tumor shows spindle cells and poorly defined vascular slits with scattered hemosiderin and extravasation of red blood cells. [16]

Spindle Cell Hemangioma
Spindle cell hemangioma is an uncommon benign vascular tumor of the oral cavity. Microscopically, the tumor shows well-circumscribed vascular proliferation of spindle to epithelioid endothelial cells with intracytoplasmic vascular lumens. Immunohistochemically, the tumor is positive for CD31 and CD34. [17]

Due to extensive content related to various lesions it is not possible to cover lesion in the single review article. Hence further lesions related with spindle cell lesions are explained in the consequent article with same topic name.

REFERENCE
1. Lewis JS. Spindle cell lesions--neoplastic or nonneoplastic?: spindle cell carcinoma and other atypical spindle cell lesions of the head and neck. Head Neck Pathol, 2008; 2(2): 103-10.