Stromal Salivary Gland Neoplasms – A Review

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Abstract

Salivary gland mesenchymal tumors are rare and account for less than 5% of all salivary gland tumors. Stromal salivary gland tumors can be benign or sarcomatous .These can be further classified into tumors arising from blood and lymphatic vessels, nerves, fibrous tissue, adipose tissue, muscle and others. More than 90% of mesenchymal tumors arise in parotid gland and less than 10% involves submandibular or sublingual glands. These neoplasms of mesenchymal origin that involve or encroach on the major salivary glands are often difficult to diagnose. Since sarcomas are more aggressive or have poor prognosis, early diagnosis and treatment plan is mandatory for patient survival. This article hightlights the key features of the stromal salivary gland neoplasms.

Introduction

A salivary gland is composed of glandular secretory tissue and stroma. The supporting stroma/ connective tissue of salivary gland consists of fibroblasts, macrophages, and mast cells occasionally leukocytes, adipocytes, plasma cells embedded in ground substances. Capsule of the salivary gland is derived from connective tissue; connective tissue septa from capsule divide the glands into lobes and lobules and carry the blood vessels and nerves that supply the glandular components.

Salivary gland mesenchymal tumors are rare and account for less than 5% of all salivary gland tumors. More than 90% of mesenchymal tumors arise in parotid gland and less than 10% involves submandibular or sublingual glands. The striking predominance of mesenchymal tumors in the parotid gland when compared to other salivary glands is attributed to anatomic differences; the parotid gland lacks a well-defined capsule and contains neurovascular structures.[1] Mesenchymal tumors of salivary gland can be: Benign (>90%) or Malignant mesenchymal neoplasms.

Histogenesis

The stromal salivary gland tumors focuses on two diametrically opposed hypothesis[2]: The First hypothesis states that sarcomas of salivary glands are derived from myoepithelial cells that are capable of multidirectional differentiation. The second hypothesis states that the sarcomas arise from pluripotential or uncommitted mesenchymal cells.

CLASSIFICATION OF STROMAL SALIVARY GLAND NEOPLASMS[2]

Benign Mesenchymal Neoplasm of Salivary Gland

1. Tumors of blood and lymphatic vessels:
   - Hemangioma
   - Lymphangioma
2. Tumors of peripheral nerves:
   - Neurilemoma/schwannoma
   - Neurofibroma
   - Extracranial meningioma
3. Neoplasms of fibrous tissue:
   - Nodular fasciitis
   - Fibrous histiocytoma
   - Fibromatosis
   - Myxoma
4. Neoplasms of adipose tissue:
   - Lipoma
5. Neoplasms of smooth muscle origin:
   - Angiomyoma / vascular leiomyoma
6. Other benign mesenchymal lesions:
   - Granular cell tumor
   - Giant cell neoplasm of major salivary glands
   - Glomangioma

Malignant Mesenchymal Neoplasms of Salivary Gland

Commonest primary sarcomas

- Malignant haemangiopericytoma
- Angiosarcoma
- Malignant schwannoma
- Fibrosarcoma
- Malignant fibrous histiocytoma
- Rhabdomyosarcoma

Hemangioma

Of the various non-epithelial tumors affecting major glands, Hemangioma is one of the most common[3]. The vast majority of Hemangiomas arise in the parotid gland (85.1 %), and the remainder involves the submandibular gland. The diffuse distribution of minor salivary glands and the lack of distinct anatomic boundaries preclude unequivocal evidence of origin in the minor salivary gland connective tissue stroma.[3] The important types are capillary (including juvenile type) and cavernous type.[2] Diagnostic aid includes - Special stains, Electron microscopy, and Immunohistochemical techniques. USG, MRI Study, Colour Doppler study & Dynamic CT scan are reported to give an accurate picture of the degree of vascularity.[2,4] Though Hemangioma are rare, they can simulate other benign conditions like submandibular sialadenitis and should be kept as a differential diagnosis.[5] Treatment options include - Compression therapy, steroid therapy, and surgical approach.

Lymphangioma

Lymphangiomas are thought to develop from sequestered remnants of lymphatic tissue that may proliferate and accumulate large amounts of fluid. Majority of them clinically manifest during childhood; with about 50% of them present at birth Symptomatic inflammatory reactions in lymphangiomas are very common. . When compared with Hemangiomas, lymphangiomas are usually softer and more compressible and may transilluminate. It can also be diagnosed using CT, sonography, MRI and Sialography, salivary gland scintigraphy or tumor aspiration/ contrast injection. The treatment of choice is complete excision. Sclerotherapy is an alternative treatment option when surgical management is not possible[6].

Neurilemoma (Schwannoma)

Schwannoma (neurilemmoma) is a slow growing encapsulated tumor of neuroectodermal derivation that originates from the Schwann cells of the neural sheath. Approximately, 25-30% of all reported schwannomas occur in the head and neck and most of these in the eighth nerve[7]. Schwannoma of the parotid gland is rare and may be mistaken as pleomorphic adenoma. Cytological features such as small fascicles of cells and wavy spindle-shaped nuclei are helpful features to distinguish this tumor from pleomorphic adenoma.[8] Distinctive pathologic features of schwannoma include a dimorphic growth pattern comprising of cellular (Antoni A) and loose-textured (Antoni B) areas, Verocay bodies and hyaline blood vessels.[9] With early diagnosis of parotid schwannoma by FNAC, management of patient can be planned and ultimately, facial nerve function can be optimized.[8]

Neurofibroma

Neurofibromas are benign nerve sheath tumours, which present in three forms; local discrete, generalized neurofibromatosis and plexiform neurofibromas. Neurofibromas constitute only 0.4% of all salivary neoplasms.[10] The neurofibroma is not encapsulated, is more likely to be diffuse or multiple, and may be associated with Von Recklinghausen's disease.[2] Neurofibromas represent 14 % of all benign mesenchymal tumors affecting the salivary gland. It is present as a solitary lesion, it occurs as a slow growing, painless nodule that is firm to palpation. The histologic appearance of the neurofibroma is quite variable, depending on the nature of its stroma and degree of cellularity. Conservative excision is the treatment of choice.

Extracranial Meningioma

Meningiomas are the second most common group of brain tumors, accounting for 13 to 18% of all primary intracranial neoplasms. In rare instances, meningiomas also occur in extracranial locations, such as the nasal cavity, paranasal sinuses, parapharyngeal space, cervical region or parotid gland. Meningiomas involving the major salivary gland are exceedingly rare.[11] Four mechanisms of the formation of ectopic meningioma have been suggested: (1) direct extension of an intra-cranial lesion, (2) distant metastasis from an intra-cranial meningioma, (3) origination from arachnoid cells within the sheaths of cranial nerves and (4) origination from embryonic nests of arachnoid cells. The treatment of choice for extra-cranial meningiomas is surgical excision and it has good prognosis.[12]

Nodular Fasciitis

It is a benign, probably reactive, fibroblastic growth with pseudosarcomatous features. It most commonly involves the parotid gland. A 4:1 predominance of occurrence is seen in male patients. Usually affects individuals in the 3rd decade of life. The most disturbing clinical feature is rapid growth. When it arises from the parotid sheath, the lesion appears well circumscribed but unencapsulated and may infiltrate the parenchyma of the gland. It is difficult to distinguish nodular fasciitis from pleomorphic adenoma by FNAC. The aspirate material shows cohesive parts composed of cells that had oval or spindle nuclei and relatively abundant cytoplasm and some cells with plasmacytoid features. The background substance is fibromyxoid. IHC stains positive for SMA and CD-68. Nodular fasciitis behaves in a benign fashion with rare recurrence after local excision. Spontaneous regression has been known to occur. [2,13]

Fibrous Histiocytoma

Fibrous histiocytoma is considered to be a true neoplasm and is composed of an admixture of fibroblasts and histiocyte -like cells that are often arranged in a cartwheel configuration with varying numbers of inflammatory cells, xanthoma cells, and hemosiderin-laden macrophages.

Fibrous histiocytoma in the major salivary glands are rare- seven cases reported in parotid gland and two in submandibular gland. Benign fibrous histiocytoma exhibits fairly frequent reactivity to leucocyte common antigen. Electron microscope studies have reveals the presence of myofibroblasts and rounded cells resembling histiocytes. Surgical excision is the treatment of choice.[14]

Fibromatosis

It is a deceptively benign-appearing tumor with the tendency to progressively enlarge, infiltrate adjacent tissues and recur.[2] The Tumor occurs as a painless, sessile mass that may be partially fixed to adjacent and underlying tissues. The rate of growth is slow and steady. Most commonly involves the parotid gland when compared to submandibular gland. Males and females are equally affected. It is characterized by a

poorly circumscribed mass of collagenous fibrous connective tissue that infiltrates surrounding tissue. The most widely accepted treatment is a wide en bloc excision of the tumor. Radiation therapy can also be used.[15]

Myxoma

The myxoma is a benign mesenchymal tumor composed of stringy, gelatinous tissue that microscopically resembles the core of the umbilical cord.[2] Several theories concerning the pathogenesis of this tumor include - fibroblasts or myofibroblasts could produce an excess of mucopolysaccharides and were commonly incapable of forming mature collagen even if some cells could retain their capacity. Another theory attributed the origin of these tumors to mesenchymal elements derived from dental papilla, dental follicle or periodontal membrane.[16]

The tumor commonly affecting the parotid region usually associated with pain and facial paralysis. The myxoma is composed of an abundant mucoid stroma, sparse cells with small hyperchromatic nuclei and indistinct cytoplasm, and a meshwork of delicate reticular fibers. Superficial parotidectomy is the initial treatment of choice.

Lipoma

Lipoma is the most common mesenchymal neoplasm in the human body and may occur in the major salivary glands. Parotid gland Lipomas reported to constitute 1 to 4 % of all salivary gland tumors and 18.5 to 22.5 % of non-epithelial salivary gland tumors.[2] In a superficial location, the Lipoma usually present as an asymptomatic, round or ovoid nodule of a moderately firm, doughy consistency that is readily movable. The tumor shows a well-defined mass of mature adipose tissue that is usually separated from adjacent gland by a fibrous capsule.

On the basis of proportion and distribution of adipose tissue, the tumor could be categorized in to 3 main groups[17]: Ordinary Lipoma, Oncocytic lipoadenoma, Non Oncocytic sialolipoma. Sialolipoma is a new distinct variant, is characterized by proliferation of mature adipocytes with secondary entrapment of normal salivary gland element.[18] Usually, Superficial lobectomy with preservation of the facial nerve is aimed for treatment.

Angiomyoma

Angiomyoma is a common soft tissue tumour of the head and neck that sometimes presents to the otolaryngologist; however, it seldom occurs in the major salivary glands.[19] The Angiomyoma (vascular leiomyoma) is a solitary tumor of smooth muscle that presents as firm subcutaneous nodules than 2 cm in diameter. The characteristic appearance is that of an encapsulated nodule of smooth muscle that contains thick walled vessels and narrow lumina.[2] Special stains, such as masons trichrome or phosphotungstic acid-hematoxylin can be used to demonstrate myofibrils. Simple excision is the treatment of choice.

Malginant Hemangiopericytoma (HPC)

HPCs are uncommon vascular tumors arising from perivascular cells known as pericytes. The single most common type of sarcoma within the major salivary gland is haemangiopericytoma. HPCs present as painless slow growing tumors. Diagnostic work up includes CT and or/ MRI. Definitive diagnosis is made through histopathology, which allows the observation of a neoplasm composed of cells similar to fibroblasts, with little or no mitotic activity distributing in a fasciculate and storiform pattern along a stroma rich in collagen that resembles a cheloid. This tumor usually shows positivity for CD34, CD99, Vimentin, laminin and type IV collagen; it yields negative results with cytokeratin, EMA, S100, smooth muscle actin and desmin, The treatment of choice for HPCs from any location is surgical resection of the encapsulated tumor along with the gland.[20]

Angiosarcoma

An Angiosarcoma is an uncommon malignant neoplasms characterized by rapidly proliferating, extensively infiltrating anaplastic cells derived from blood vessels.[2] Oral and salivary gland Angiosarcomas are extremely rare, comprising only 25% of a series of all Angiosarcomas. The most common Angiosarcoma morphology in the oral and salivary gland location is spindled, vasoformative and solid. One third of oral and salivary gland Angiosarcomas in in the literatures are the unusual epithelioid Angiosarcoma variant.[21]

Malginant Schwannoma

It is a neural tumor that may arise from facial nerve and present as salivary gland tumor. The tumor is slow growing, usually asymptomatic, neurologic signs when associated with nerve compression. The tumor consist of cells with wavy nuclei and irregular nuclear contours that are arranged in densely cellular fascicles. Malignant epithelioid schwannomas unlike carcinoma but similar to melanomas may be immune reactive with LEU-7 and S-100 protein and unreactive for keratin.[2]

Malginant Fibrous Histiocytoma

Malignant fibrous histiocytoma is an uncommon, aggressive pleomorphic tumor that originates from the tissue histiocyte or "facultative fibroblast". Considerable controversy surrounds the histiogensis of fibrous histiocytoma – histiocytes and undifferentiated mesenchymal cells.[22] Only a few cases of primary MFH arising in salivary gland have been reported. The histologic sections revealed proliferation of spindle fibroblasts with large numbers of bizarre, multinucleated giant cells and mononuclear cells resemble histiocyte, arranged in short fascicles and loose

storiform patterns with large nucleus. Immunostaining of the tumor cells is negative for cytokeratin, epithelial membrane antigen, desmin, vimentin and S 100 protein. Weak focal staining for smooth muscle actin is seen in some cells.[23]

Rhabdomyosarcoma

Rhabdomyosarcoma is a cancerous (malignant) tumor of the skeletal muscles. It is a rare tumor that can be seen in the parotid gland (88% cases). The tumor cells are encapsulated, the tumor composed primarily of relatively uniform, intercalating bundles of plump spindle cells with vesicular nuclei. Occasionally rounded multinucleated giant cells with acidophilic granular cytoplasm can be seen; tadpole like cells also can be seen. Tumor can metastasize to lung and other sites, including brain; small bowel, heart and pancreas were often involved. Metastatic rate was higher for tumor located in the submandibular gland than that of parotid gland.[24]

Conclusion

All the swellings/growth occurring in the salivary glands may not be due to infections, hyperplasia, but may be due to benign or malignant neoplasm. Because of this all salivary gland enlargement should be viewed seriously. The neoplasms may be epithelial/stromal in origin. Stromal salivary gland can be benign or sarcomatous. Since sarcomas are common in younger age and is more aggressive or poor prognosis, early diagnosis and treatment plan is mandatory for patient survival. A thorough knowledge of these stromal tumors will aid in better identification and early diagnosis.

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