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Commentary

Hempen and Ensnarled-Sclerosing Microcystic Adenocarcinoma

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Sclerosing microcystic adenocarcinoma is an exceedingly exceptional, unique, primary salivary gland neoplasm. Additionally designated as microcystic adnexal carcinoma, sclerosing sweat duct carcinoma of intraoral minor salivary glands or syringomatous adenocarcinoma not otherwise specified (NOS), sclerosing microcystic adenocarcinoma presumably arises from minor salivary glands confined to head and neck region. The infrequent, low grade tumefaction exemplifies significant morphological concurrence with cutaneous microcystic adnexal carcinoma.

Commonly incriminating minor salivary glands, immunosuppression may be implicated in disease pathogenesis. Tumefaction is confined to mucosal sites within head and neck region.

Sclerosing microcystic adenocarcinoma is constituted of bland ducts, tubules, cords and cellular nests of variable magnitude. Neoplasm is constituted of biphasic population of intrinsic cuboidal epithelial cells and extraneous myoepithelial cells circumscribed by an abundant, dense, sclerotic or collagenous stroma. Tumefaction appears intensely infiltrative into circumscribing soft tissues. Perineural invasion and infiltration into abutting skeletal muscle is preponderant.

Frequently, myoepithelial cells appear attenuated with few the emergence of clear cells. Cuboidal epithelium appears monomorphic wherein tumour cells are imbued with eosinophilic cytoplasm, spherical nuclei, uniform nuclear chromatin and occasional nucleoli. Mitotic activity is unremarkable.

Neoplasm is devoid of localized or regional tumour reoccurrence or distant metastases. Lesions with tumour cells confined to surgical margins may be optimally subjected to adjuvant radiation therapy. Generally, prognostic outcomes are favourable.

Average age of disease discernment is 52.6 years wherein tumefaction may arise within 41 years to 73 years. Tumefaction depicts a female predominance with female to male proportion of ~4:1 [1,2].

The contemporary modality of whole exome sequencing demonstrates moderate burden of genetic mutations within sclerosing microcystic adenocarcinoma. Besides, putative loss of function genetic mutation within CDK11B may be observed.

Additionally, molecular concurrence within genomic mutations discernible within microcystic adnexal carcinoma appear absent. Nevertheless, molecular spectrum of sclerosing microcystic adenocarcinoma is preponderantly undefined [2,3].

Majority of neoplasms incriminate minor salivary glands confined within intraoral cavity, especially glands situated upon the tongue, mucosa of lip, floor of mouth or buccal mucosa. Additionally, parotid gland or nasopharynx may be implicated.

Of obscure pathophysiology, sclerosing microcystic adenocarcinoma of salivary gland exhibits morphological concurrence with cutaneous microcystic adnexal carcinoma (MAC) as normal intraoral minor salivary glands demonstrate histological and functional concordance with normal eccrine sweat glands [2,3].

Whole exome sequencing of the neoplasm enunciates moderate tumour mutational burden, presumptive loss of function mutation within CDK11B gene and an absence of molecular concordance with genetic mutations discernible within cutaneous microcystic adnexal carcinoma.

Akin to microcystic adnexal carcinoma, immunosuppression may contribute to emergence of sclerosing microcystic adenocarcinoma, as exemplified with immunosuppressive therapy adopted for autoimmune disorders, chemotherapy or radiation therapy [2,3].

Typically, tumefaction represents as a painless, gradually progressive mass or submucosal lump. Sclerosing microcystic adenocarcinoma enunciates an infiltrative pattern of tumour evolution. The significantly aggressive neoplasm is associated with localized infiltration and perineural invasion with consequent emergence of numbness.

Extensive perineural invasion may be accompanied by accumulation of neoplastic cells within surgical perimeter of excised tissue. Therefore, obtaining tumour free surgical margin may be challenging [2,3].

Cytological examination exemplifies a distinct population of basaloid epithelial cells configuring sheets, clusters and branching cellular aggregates. Nuclear pleomorphism is minimal. Cytological smears are biphasic.

Few cellular clusters are circumscribed by a layer of flattened epithelial cells pervaded with bland, ovoid nuclei. Intra-nuclear inclusions are occasional.

Smears are devoid of circumscribing hyaline globular matrix, fibrillary metachromatic stroma or mucin. Mitotic figures, significant nuclear atypia and tumour necrosis are absent [2,3].

Grossly, an inadequately defined, firm, grey/white or tan tumour mass is observed. Tumefaction may exhibit macroscopic extension into adjacent skeletal muscle or mature adipose tissue.

Upon frozen section, intraoperative evaluation of surgical margins of the low grade, paucicellular tumefaction is extremely challenging.

Upon low power examination, sclerosing microcystic adenocarcinoma enunciates as a paucicellular neoplasm [3,4].

Upon microscopy, tumour is composed of ducts, tubules, cords and cellular nests of variable magnitude. Neoplastic cells are enmeshed within a densely sclerotic or desmoplastic stroma. Tumour perimeter appears infiltrative.

Invasive tumour component is constituted of biphasic cellular population comprised of intrinsic layer of cuboidal epithelium and an extraneous myoepithelial cell layer. Frequently, myoepithelial cells appear attenuated and flattened. However, prominent myoepithelial cell layer with clear cells may be observed [3,4].

Monomorphic cuboidal epithelial cells are pervaded with eosinophilic cytoplasm, spherical nuclei, uniform nuclear chromatin and occasional nucleoli. Nuclear atypia is insignificant.

Tumour configuring ducts and tubules are frequently pervaded with eosinophilic secretions which may be highlighted by mucicarmine stain.

Mitotic activity is minimal. Tumour necrosis is absent. Superimposed mucosa is devoid of epithelial dysplasia. Tumefaction may infiltrate adjoining skeletal muscle. Perineural invasion is commonly discerned [3,4].

Low grade	Intermediate grade	High grade	Variable grade
Acinic cell carcinoma	Myoepithelial carcinoma	Salivary duct carcinoma	Mucoepidermoid carcinoma
Basal cell adenocarcinoma	Sebaceous adenocarcinoma	Squamous cell carcinoma	Adenoid cystic carcinoma
Epithelial-myoepithelial carcinoma	Lymphoepithelial carcinoma	Small cell carcinoma	Salivary carcinoma NOS
Secretory carcinoma		Large cell neuroendocrine carcinoma	Intraductal carcinoma
Polymorphous adenocarcinoma		Large cell undifferentiated carcinoma	Carcinoma ex pleomorphic adenoma
Hyalinising clear cell carcinoma		Carcinosarcoma	
Mucinous adenocarcinoma		Salivary gland carcinomas with high grade transformation	
Micro-secretory adenocarcinoma			
Sclerosing microcystic adenocarcinoma			
Sialoblastoma			
Metastasizing pleomorphic adenoma			

Table: *Histopathological stratification of salivary gland malignancies [2].*
NOS: Not Otherwise Specified.

Epithelial cells of sclerosing microcystic adenocarcinoma appear immune reactive to CK7, carcinoembryonic antigen (CEA), epithelial membrane antigen (EMA), AE1/AE3, CAM5.2 or CK5/6. Myoepithelial cells characteristically demonstrate immune reactivity to myoepithelial markers as p40, p63, S100 protein or smooth muscle actin (SMA).

Intra-luminal secretions can be highlighted with mucicarmine [4,5].

Ki67 proliferation index is beneath < 5%. Generally, tumour cells recapitulate immune reactive pattern exhibited by cutaneous microcystic adnexal carcinoma (MAC).

Tumour cells appear immune non reactive to CD117, SOX10, MYB, oestrogen receptor (ER), progesterone receptor (PR) or androgen receptor (AR) [4,5].

Sclerosing microcystic adenocarcinoma requires segregation from neoplasms such as squamous cell carcinoma, tubular variant of adenoid cystic carcinoma, epithelial myoepithelial carcinoma, cribriform adenocarcinoma of the tongue and minor salivary glands, polymorphous adenocarcinoma, low grade mucoepidermoid carcinoma, mammary analogue secretory carcinoma, low grade adenocarcinoma, chronic sclerosing sialadenitis or sclerosing sialometaplasia [4,5].

Tumefaction may be visualized or appears palpable upon physical examination.

Radiographic modalities as computerized tomography (CT) and magnetic resonance imaging (MRI) may be beneficially adopted to assess extent of disease.

Upon fluorodeoxyglucose positron emission tomography (FDG PET), tumefaction appears as an irregular, amorphous, fluorodeoxyglucose (FDG) avid lesion exemplifying an infiltrative tumour pattern which may obliterate adjacent adipose tissue planes.

Cogent surgical tissue sampling or excisional biopsy is necessitated for obtaining a definitive diagnosis [4,5].

Sclerosing microcystic adenocarcinoma can be appropriately treated with localized surgical extermination of the neoplasm with resection of broad perimeter of uninvolved circumscribing tissue and selective dissection of regional cervical lymph nodes. Generally, regional lymph node metastasis is absent.

Adjuvant radiation therapy may be adopted for treating neoplasms with tumour cells confined to surgical margins or demonstrating perineural invasion.

Extended monitoring is recommended as long term prognostic outcomes remain undefined [4,5].

Sclerosing microcystic adenocarcinoma is accompanied by an indolent clinical course. Regional lymph node involvement or distant metastasis remains undocumented, in spite of infiltrative morphological countenance. Generally, prognostic outcomes are uniformly superior. Tumefaction is devoid of localized or regional tumour reoccurrence or distant metastases, as currently assessed with monitoring for up to 5 years [4,5].

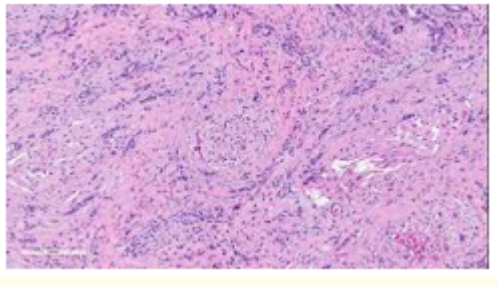

Figure 1: *Sclerosing microcystic adenocarcinoma demonstrating cords, nests, aggregates and tubules lined by neoplastic cuboidal epithelial cells and an extraneous layer of myoepithelial cells embedded within a desmoplastic stroma [6].*

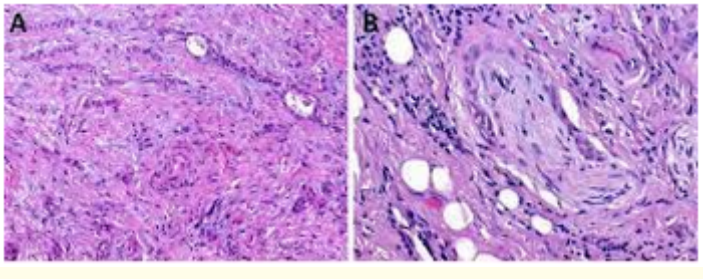

Figure 2: *Sclerosing microcystic adenocarcinoma delineating cords, nests, glands and tubules lined by cuboidal epithelial cells and an external layer of myoepithelial cells enmeshed within a densely sclerotic stroma(t).*

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6. Image 1 Courtesy: Pathology outlines.
7. Image 2 Courtesy: Research gate.

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