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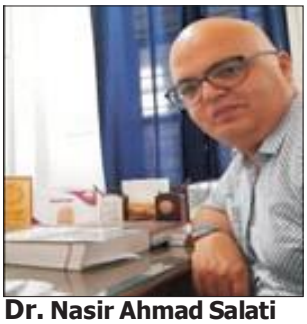
Role of Immuno-histochemistry in evaluation of Salivary Duct Carcinoma



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Introduction:

Salivary gland malignancies are clinically and histo-morphologically diverse group of lesions. These account for less than 1% of all malignancies and about 5% of head and neck cancers. [1] Minor salivary gland tumors are infrequent, accounting for about 10–15% of the salivary gland neoplasms. The varied histological types of minor salivary gland tumors account for its varied prognostic potential. Salivary duct carcinoma (SDC) is a high-grade adenocarcinoma of the ductal epithelium of salivary glands. It shows aggressive behavior along with early metastasis, local recurrence, and high mortality. [2] The primary tumors of various origin and histologic type may metastasize or invade into the salivary glands, posing a significant diagnostic challenge.

Histopathology:

SDC resembles histopathologically ductal carcinoma of the breast, along with intraductal and invasive components. The intraductal component consists of solid, papillary, cribriform, and comedo patterns. A lack of definite lobular arrangement with fenestration (Roman bridge) is seen. The invasive carcinoma consists of irregular glands and cords of cells, sometimes showing a desmoplastic reaction. [3] The different types of SDC histologically are: sarcomatoid, mucin-rich and invasive micropapillary. .

Immuno-histochemistry:

Most of the salivary gland malignancies including SDC are positive for CK-7. Thus, CK-7 may add valuable information for the differential diagnosis of the primary salivary gland carcinomas and metastatic tumors and also in the diagnosis of metastatic salivary gland malignancies.. SDC is positive for cytokeratins (CKs), carcinoembryonic antigen, and epithelial membrane antigen. [4]

The HER-2/neu gene, also known as c-erbB-2, encodes a transmembranous tyrosine kinase growth factor receptor, and its overexpression has been reported in various carcinomas, including breast and salivary gland tumors, mostly SDCs. However, unlike breast ductal carcinomas, the frequency of positivity for estrogen and progesterone receptors in SDC is considerably less. HER-2/neu gene amplification or overexpression is demonstrated in approximately 15–20% of breast cancers. Furthermore, this highly malignant tumor might respond to therapy with monoclonal antibody trastuzumab directed against the extracellular domain of the HER-2/neu protein.[5]. Prostate-specific antigen (PSA) and androgen receptor (AR) are also positive. The high AR expression in SDC has been found to be related to tumor progression. The androgen receptor (AR), along with other biomarkers, can be helpful in evaluating the long-term prognosis of these tumors. [4] The strong expression of AR and frequent demonstration of PSA are similar to prostatic carcinoma. In addition, anti-androgen therapy used in prostatic carcinoma might be beneficial in patients with metastatic SDC when other treatment modalities fail. [6]

An Overview of IHC in Salivary tumors:

Salivary gland tumors are a heterogeneous group of tumors, challenging researchers, pathologists and clinicians. Histo-pathologically, SDCs resemble various other tumors of the salivary glands and breast carcinomas.

Immunohistochemical markers are of value in diagnosing rare salivary gland malignancies, including SDCs. The long-term prognosis of these tumors can be evaluated by a combination of different biomarkers. The salivary gland cells show diffuse positivity to cytokeratins with low molecular weight, weak positivity for cytokeratins with high molecular weight, diffuse positivity to α-amylase and DOG1, and weak positivity for lactoferrin, lysozyme, carcinoembryonic antigen (CEA), and epithelial membrane antigen (EMA). [7] Myoepithelial cells show positivity for muscle proteins such as smooth muscle actin (SMA), muscle-specific actin (MSA), and calponin). Myoepithelial and basal cells are CK14 and p63-positive and negative for CEA and EMA. S-100 is not a specific marker for myoepithelial cells.[3,7] Glial fibrillary acidic protein (GFAP) is a myoepithelial marker (low sensitivity), but it is most advantageous in pleomorphic adenomas and myoepitheliomas, where it shows intense positivity. GFAP is useful for differentiating these from polymorphous adenocarcinoma or adenoid cystic carcinoma. [7]

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