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Analysis of Histological and Immunohistochemical Follow-Up for Salivary Gland Neoplasm of Uncertain Malignant Potential Proposed By the Milan System for Reporting Salivary Gland Cytopathology: A Case Report

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Abstract

The Milan System for Reporting Salivary Gland Cytopathology is a tiered classification scheme that includes 6 diagnostic categories. Here we are reporting a case with swelling on the upper palate in minor salivary glands, with short clinical history and increasing size qualified as NUMP with possibility of cellular pleomorphic adenoma on the basis of histopathological diagnosis of surgical resection was kept as Pleomorphic adenoma with solid component of Oncocytoma. On Immunohistochemistry came out to be pleomorphic adenoma with myoepithelioma. Case representing the importance of exact categorization by Milan system of reporting the salivary gland tumour. This case of Pleomorphic Adenoma arising in minor salivary glands highlights a potential diagnostic pitfall, essentially in FNA biopsy but also in histology, in the diagnosis of salivary gland tumors.

Keywords: Milan System for Reporting Salivary Gland Cytopathology, Myoepithelioma, Neoplasm of Uncertain Malignant Potential, Pleomorphic Adenoma.

INTRODUCTION

Fine-needle aspiration (FNA) biopsy is a well-established diagnostic tool for evaluating lesions in the salivary gland. In general, FNA has high accuracy in distinguishing non-neoplastic from neoplastic salivary gland lesions and low-grade from high-grade malignant salivary gland tumors.[1-3] However, given the wide diversity of salivary gland tumors, false-negative and false-positive results do occur.[4]

Recently, the Milan System for Reporting Salivary Gland Cytopathology (MSRSGC) has proposed a 6- category diagnostic classification scheme: nondiagnostic; non-neoplastic; atypia of undetermined significance; neoplasm, including benign neoplasm and neoplasm of

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uncertain malignant potential (NUMP); suspicious for malignancy; and malignant.[5,6] NUMP usually applies to salivary gland neoplasms without clear distinction between benign and malignant. This category is problematic in terms of cytology interpretation and subsequent clinical management and thus was the focus of the current study.

Most (64–80%) salivary glands tumors arise from the parotid gland. Tumors arising from the various smaller salivary glands minor represent 9–23% of all tumors, which makes them the second most common sites of salivary neoplasia. The palate is the most frequent site for minor salivary gland tumor (42–54%). As observed in the major glands, pleomorphic adenoma is the most common minor gland tumor and accounts for 40% of cases. However, a relatively high proportion of tumors arising from minor salivary glands are malignant (almost 50%). It is stated that the smaller the gland, the greater the likelihood of malignancy for a salivary gland tumor.[7] In smears from typical pleomorphic adenomas, three cellular components are present in varying degrees: the epithelial/ductal cells that are small and cuboidal arranged in flat sheets or trabeculae that can undergo squamous, oncocytic, or sebaceous metaplasia. Myoepithelial cells are usually present and can be spindled, stellate, or plasmacytoid and are found in clusters, singly, or within the chondromyxoid matrix. Finally, the presence of chondromyxoid matrix material is the most specific feature for making the correct diagnosis. However, in cellular pleomorphic adenomas, there is an abundance of the epithelial or myoepithelial cells with minimal stroma present.[8]

Myoepitheliomas of the salivary glands were first described by Sheldon WH et al., in 1943 and they were considered as a variant of pleomorphic adenoma.[9]

The World Health Organisation'sdefinition in 1991 distinguished a myoepithelioma from a pleomorphic adenoma,[10] classifying it as an independent entity. These tumours exhibit an admixture of four cellular morphologies, but the salivary gland tumours in which the ducts comprise less than 5% of the sections are classified as myoepitheliomas.[11] Also, in contrast to a pleomorphic adenoma, a myoepithelioma does not present a chondroid or an osteoid formation.

Myoepitheliomas represent less than 1% of all the salivary gland tumours.[12] Approximately, 50% of the salivary gland myoepitheliomas involve the parotid gland, 33% arise from the sublingual glands, and 13% affect the submandibular gland.[13] They present as asymptomatic, slowly growing masses in the patients with an average age of 40 years.[14]

CASE REPORT

A 48-year-old nonalcoholic, nonsmoker female presented with progressive palatal growth for three months. History of dental infection present in right upper jaw followed by the loss of tooth spontaneously. There was no

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history of dysphagia, odynophagia, sleep apnea, voice change, weight loss, loss of appetite, and fever.

The clinical examination revealed a flesh coloured mass on the right side of hard palate measuring 3x2 cm, soft, nontender, nonpulsatile, round with no ulceration or erosion of overlying mucosa. No significant cervical lymphadenopathy was noted.

Aspiration cytology of the mass showed epithelial cells lying in loosely cohesive clusters, aggregates, and few scattered singly. Individual cells were hyperchromatic with granular chromatin, mild nuclear atypia, nuclear overlapping in some with variable amount of cytoplasm. At few places in focal areas these epithelial cells were seen entrapped in fibrillary myxoid stroma. FNA was suggestive of salivary gland neoplasm of uncertain malignant potential with basaloid morphology. Keeping in view the morphological features of fibrillary stroma and cellularity the possibility of cellular Pleomorphic Adenoma was considered and resection was adviced to look for any capsular breach.

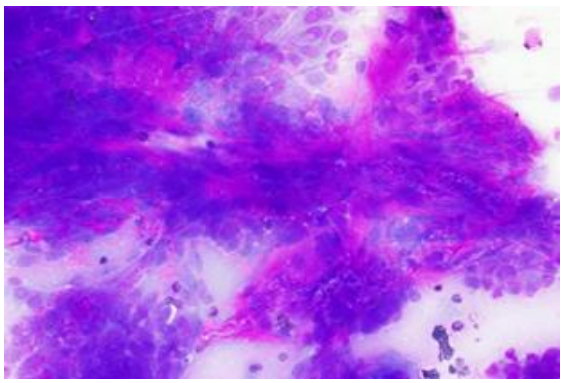

Figure 1: Epithelial cells entrapped in the fibrillary myxoid stroma.

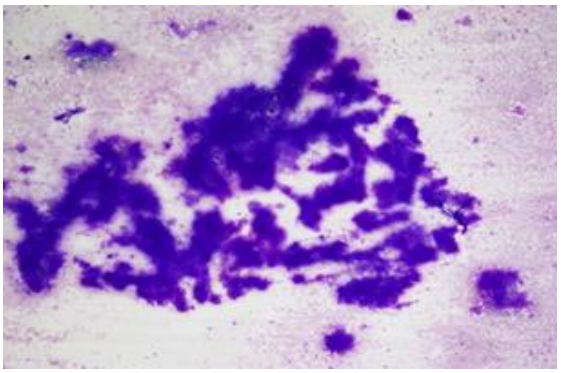

Figure 2: Epithelial cells in cohesive clusters were hyperchromatic with nuclear overlapping in some and variable amount of cytoplasm.

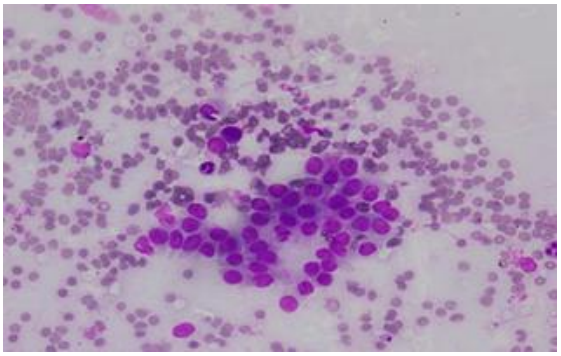

Figure 3: Epithelial cells lying in loosely cohesive clusters with mild nuclear atypia.

The CECT neckscan showed well-defined heterogeneous enhancing soft tissue mass involving right side of hard palate crossing midline to left side (measuring 5.4 × 4.4 × 4.2 cm). There was seen scalloping of overlying bone without any cortical dehiscence. There was no calcification, cystic component, or fat within the mass. The mass was closely abutting the base of the tongue and posterior pharyngeal wall with maintained fat plane between them. No significant cervical lymphadenopathy noted.

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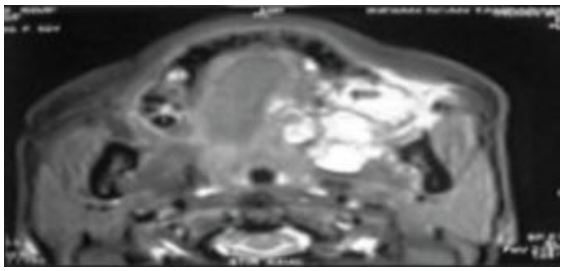

Figure 4: CT scan showing ill-defined heterogeneous expansile soft tissue attenuation lesion.

The patient underwent excisional biopsy of the palatal mass. The histopathological examination revealed encapsulated tumor with capsule of variable thickness. Beneath the capsule was seen epithelial tumor tissue lying as lobules and nests which were separated by thin fibrovascular tissue as glands, trabeculae and papillae. Interspersed in this areas were seen areas of chondromyxoid tissue, fibrocollagenous stroma and areas of myxoid material. The epithelial cells in the lobules were large size with intercellular junction, hyperchromatic to vesicular nuclei and variable amount of pale to eosinophilic cytoplasm. The cells in the papillae are small with hyperchroamtic nuclei, high nuclear cytoplasmic ratio. Myxoid areas are interspersed. No evidence of increased mitotic figures. Capsule was seen breached at places by the tumor cells. Histopathological diagnosis of Pleomorphic adenoma with lobules of oncocytic component was made.

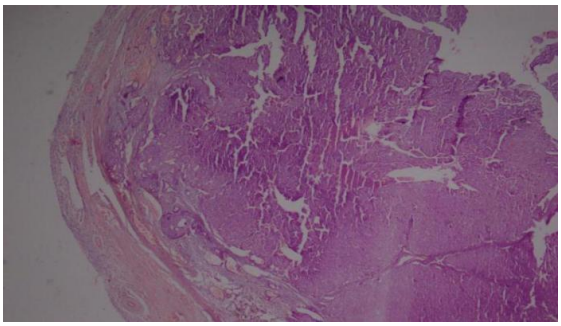

Figure 5: Encapsulated tumor with capsule of variable thickness. Beneath the capsule seen epithelial tumor tissue lying as lobules and nests separated by thin fibrovascular tissue.

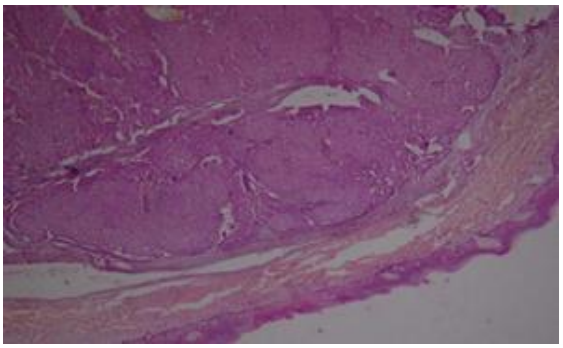

Figure 6: Encapsulated tumor with capsule of variable thickness. Beneath the capsule seen epithelial tumor tissue lying as lobules and nests separated by thin fibrovascular tissue.

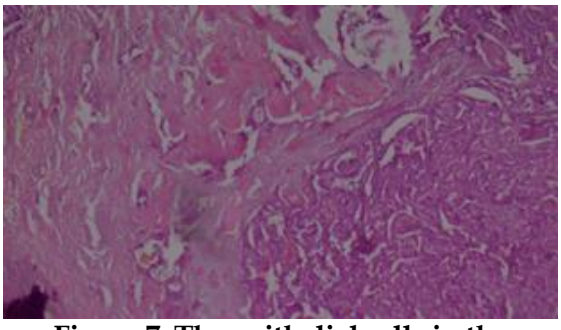

Figure 7: The epithelial cells in the lobules: large size with intercellular junction, hyperchromatic to vesicular nuclei and variable amount of pale to eosinophilic cytoplasm.

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Howerver, on Immunohistochemistry, the tumor cells were diffusely positive for CK7; focally positive for SMA, CK5/6 and S100P; while they were negative for p63. Features were of Myoepithelial cell rich lesion; Possibilties considered were

1. Myoepithelioma
2. Myoepithelial cell rich Pleomorphic Adenoma.

DISCUSSION

Given the wide variety of tumors and the overlapping cytomorphologic features of many benign and low-grade malignant tumors of the salivary gland, descriptive diagnoses are common practice. Standardized terminology for reporting salivary gland FNA is lacking.[2,3] At the 2015 European Congress of Cytology held in Milan, Italy, a group of experienced cytopathologists initiated their efforts to create a unified salivary gland FNA reporting system. Later, the American Society of Cytopathology and the International Academy of Cytology organized an international panel of cytopathologists and surgical pathologists to establish a classification scheme for reporting salivary gland FNA. This classification scheme is under the title of the "Milan System for Reporting Salivary Gland Cytopathology (MSRSGC)." The MSRSGC has proposed the following 6-category diagnostic classifications: nondiagnostic; non-neoplastic; atypia of undetermined significance; neoplasm, including benign neoplasm and neoplasm of uncertain malignant potential (NUMP); suspicious for malignancy; and malignant.[5,6] In general, cases in the NUMP category are those confirmed as neoplasms by FNA, but cytology cannot exclude the possibility of low-grade malignant malignancies.[6] It is well known that many salivary gland benign and malignant tumors have at least partial myoepithelial differentiation, including, but not limited to, cellular PA, myoepithelioma, BCA, and BCAC, etc.[15]

This case of pleomorphic adenoma arising in minor salivary glands highlights a potential diagnostic pitfall, essentially in FNA biopsy but also in histology, in the diagnosis of salivary gland tumors . Pleomorphic adenoma is the most common salivary gland tumor. Neoplastic cells with myoepithelial differentiation are often present in both benign and malignant salivary glands neoplasms. In smears from typical pleomorphic adenomas, three cellular components are present in varying degrees: the epithelial/ductal cells that are small and cuboidal arranged in flat sheets or trabeculae that can undergo squamous, oncocytic, or sebaceous metaplasia. Myoepithelial cells are usually present and can be spindled, stellate, or plasmacytoid and are found in clusters, singly, or within the chondromyxoid matrix. Finally, the presence of chondromyxoid matrix material is the most specific feature for making the correct diagnosis. However, in cellular pleomorphic adenomas, there is an abundance of the epithelial or myoepithelial cells with minimal stroma present. Myoepithelioma,

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which is composed almost exclusively of myoepithelial cells, is distinguished from pleomorphic adenoma on the base of the relative lack of ducts and chondromyxoidstroma.[8]Myoepithelio ma is, however, an uncommon benign tumor, which accounts for only 1.5% of all tumors in the major and minor salivary glands. Its malignant counterpart, myoepithelial carcinoma or malignant myoepithelioma, is even rarer and is mainly distinguished from myoepithelioma on histological grounds based on the presence of necrosis and infiltrative growth.[8]

Myoepitheliomas show four different morphological patterns which include nonmyxoid (solid), myxoid (pleomorphic adenoma like), reticular (canalicular like), and mixed.[16] The cellular patterns of myoepitheliomas consists of plasmacytoid cells, spindle cells, epitheloid cells, and clear cell patterns which do not account for differences in recurrence rate, biological behavior, or the patient age. In oral cavity, plasmacytoid cell type is more commonly seen while spindle cell type is more frequently seen in parotid gland.[17] Myoepithelial cells are most commonly seen in salivary glands. It is also seen in extrasalivary gland tissues like breast, skin, lung, and larynx. Myoepitheliomas occurring in both salivary and extrasalivary tissues showed similar morphologicalandimmunohistological characteristics.

Pleomorphic adenoma is the most common minor salivary gland constituting 40% of total cases having epithelial and ductal cells in its tissue. Presence of chondromyxoid matrix is considered most specific for pleomorphic adenoma while it is absent in myoepithelioma along with absence of glanduloductal differentiation.[18]

Mochizuki Y et al presented the case report on Myoepithelioma of the Parotid Gland Presenting as a Retroauricular Cutaneous nodule with the similar findings as of ours and finally the diagnosis was made on Immunohistochemistry.[19]

Ali J et al reported a case on "Myoepithelial Carcinoma of the Floor of the Mouth: A Rare Salivary Gland Tumor in an Unusual Location" and discussed the role of early diagnosis and treatment of such rare tumor and their prognosis.[20]

CONCLUSION

Diagnosis of certain salivary gland lesions on FNA cytology as Neoplasm of uncertain malignant potential is challenging and histopathological examination is must for more affirmative diagnosis and for further management of patient. However, Immunohistochemistry remain the gold standard for the confirmatory diagnosis.

Thus early and correct diagnosis helps clinicians to plan proper treatment to suit individual patient.

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