CASE REPORT

Myoepithelial Carcinoma arising in a background of pleomorphic adenoma

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Abstract

Carcinoma ex pleomorphic adenoma is a neoplasm of the salivary gland that causes 3.6% of salivary gland tumours and 12% of salivary gland malignancies. It is a myoepithelial or epithelial neoplasm that arises from pleomorphic adenoma, whether primary or recurrent. Historically carcinoma ex pleomorphic adenoma is considered a high-grade malignancy. Salivary duct carcinoma and high-grade adenocarcinoma are the histologic types that most commonly arise in the background of Pleomorphic adenoma. However, 15% of tumours arising in Pleomorphic adenoma are considered low grade and have sluggish growth. Low-grade carcinoma ex pleomorphic adenoma can be difficult to differentiate from cellular pleomorphic adenoma.

The case of a 56-year-old female patient who had neck swelling is being presented. The biopsy showed spindle cell component with mild atypia, invasion into surrounding tissue, and increased mitotic activity on the basis of which a diagnosis of Low-grade carcinoma ex pleomorphic adenoma developing in a background of pleomorphic adenoma was made. The morphological and immunohistochemical features confirmed the carcinoma component to be myoepithelial.

Keywords: Pleomorphic Adenoma, Salivary gland, Carcinoma.

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Introduction

Carcinoma ex pleomorphic adenoma is a neoplasm of the salivary gland that causes 3.6 percent of salivary gland tumours and 12% of all salivary gland malignancies.[1] It is a myoepithelial or epithelial neoplasm that arises from pleomorphic adenoma, whether primary or recurrent. Literature suggests about 6.2% of pleomorphic adenoma harbour malignancy,[2] and most of these cases involve the parotid gland. Historically, Carcinoma ex pleomorphic adenoma is considered a high-grade malignancy with malignant features like increased mitosis, marked nuclear pleomorphism, necrosis and infiltrative growth. The most common histologic types that arise in the background of pleomorphic adenoma include salivary duct carcinoma and high-grade adenocarcinoma. However, 15% of tumours arising in Pleomorphic adenoma are considered low grade and have indolent growth.[3] Low-grade carcinoma ex pleomorphic adenoma can be of the following types: myoepithelial Carcinoma, epithelial-myoepithelial Carcinoma, basal cell adenocarcinoma, etc.

Low-grade carcinoma ex pleomorphic adenoma can be difficult to differentiate from cellular pleomorphic adenoma as it does not show obvious cytologic atypia. The case of a low-grade carcinoma, ex-pleomorphic adenoma arising in a background of pleomorphic adenoma in submandibular gland with morphological and immunohistochemical features compatible with myoepithelial carcinoma is reported here.

Myoepithelial Carcinoma is associated with a benign tumour in approximately 50-70% of cases.[4] Myoepithelial carcinoma developing in a background of pleomorphic adenoma accounts for 35% of the cases and is reported infrequently in the literature.[5,6]

Case Report

A 56-year-old female patient with neck swelling for 15-years, presented with complaints of shortness of breath on lying down. The patient was first seen in December 2019. Previous history was significant for thyroidectomy ten years back. The patient's previous record of thyroidectomy was not available for review. There was no significant past history of any malignancies and the patient was not taking any medications. Examination showed a huge cystic mass on the left side of the neck. The mass was non-tender on palpation and there were no overlying skin changes. No other significant findings were noted on general physical and systemic examination. Computed Tomography scan showed a large multi-loculated enhancing solid cum cystic mass involving the left side of the neck in the submandibular region measuring 10.0 x 10.0 x 6.0 cm extending to the anterior triangle of the neck. Bilateral cervical lymphadenopathy was noted.

The neck swelling was biopsied, and the specimen was received in the Department of Histopathology at The Indus Hospital, Karachi on January 09, 2019. The biopsy showed a neoplastic lesion predominantly seen in the subcutaneous tissue exhibiting nodular appearance separated by thick fibrous bands. The tumour nodules were invading the

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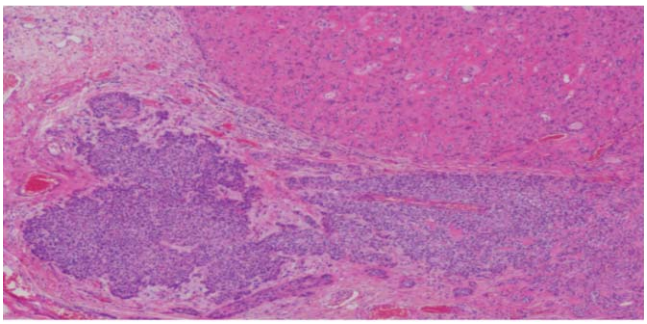

Figure-1: Low power magnification showing areas of pleomorphic adenoma with foci of myoepithelial Carcinoma. 20 X.

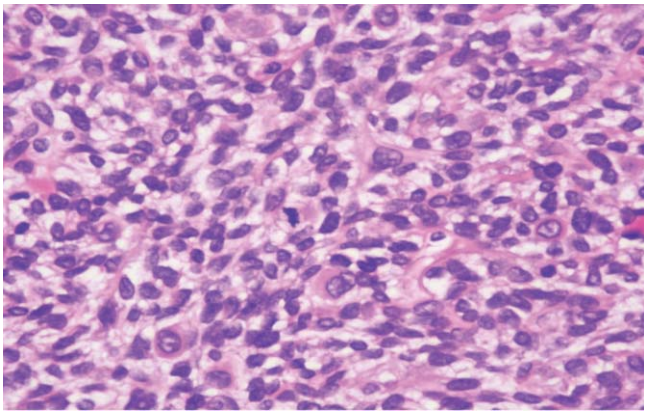

Figure-2: Note pleomorphic hyperchromatic nuclei with occasional prominent nucleoli and mitoses. 40 X.

adjacent stroma and capsule. The area of invasion measured less than 1.5 mm in the largest focus. The tumour cells exhibited a diffuse population of plump spindle cells exhibiting mild nuclear pleomorphism predominantly seen at the periphery of the nodules (Figure-1). The nuclei were elongated with inconspicuous nucleoli. The tumour cells showed moderate cytoplasm. Mitotic count was 7-8 mitosis / 10 high power field (HPF) (Figure-2). Focal areas of necrosis were noted. In adjacent areas, the tumour cells exhibited ductal differentiation within the markedly hyalinized stroma. Dilated ducts with eosinophilic secretions were also seen. Extensive areas of squamous metaplasia and calcification were noted. No salivary gland parenchyma was identified after meticulous sampling. The tumour was positive for immunohistochemical markers PLAG 1, Pan keratin, S-100, GFAP, Caldesmon, SMA, and desmin. EMA highlighted the ductal structures. HMGA2 was negative. The tumour was diagnosed as Myoepithelial Carcinoma, low grade developing in a background of pleomorphic adenoma. A written consent was obtained for reporting this case.

Discussion

Pleomorphic adenoma is a well-circumscribed neoplasm with variable architectural and cytomorphological features. Carcinoma ex pleomorphic adenoma presents as a solid, firm, rapidly growing mass that develops in a pre-existing long-standing mass in parotid gland. It may involve the minor salivary glands and submandibular gland. It exhibits a biphasic population of epithelial/myoepithelial and mesenchymal cells with tongue-like projections in surrounding salivary gland parenchyma. Pleomorphic adenoma can present similarly; however, malignancy should be considered when a slow-growing mass presents with a rapid increase in size. Pleomorphic adenoma histologically shows prominent zones of hyalinization and mitotic activity (mean, 1.5/10 HPF) with a 13.8% probability of malignant transformation.[7] Older age, mean 61 years, longer duration, and large tumour size, mean 4 cm, have a greater chance of malignant transformation. Histological features like marked and diffuse nuclear pleomorphism, infiltrative growth, increased mitoses, especially atypical mitoses, and necrosis indicate malignancy. Microscopically there is an obvious contrast between areas of pleomorphic adenoma and areas showing nuclear pleomorphism, increased mitoses, necrosis, and invasion in the stroma.

Low-grade carcinoma ex pleomorphic adenoma can be very difficult to differentiate from cellular pleomorphic adenoma as it does not have obvious cytologic atypia. Necrosis is not usually seen and Ki-67 labelling index is generally below 5 percent. The current case showed the presence of mildly atypical spindle cells, which made the diagnosis more challenging for pathologists. Invasive growth pattern and extension of the lesion outside the capsule into the adjacent non-neoplastic tissue is one of the hallmarks of low-grade carcinoma ex pleomorphic adenoma and as many as 64% of cases are infiltrative. However, the pleomorphic adenoma can show pseudopodia extending into the surrounding tissue, which can raise problems in assessing the true invasion. Several authors have shown that the extent of infiltration beyond the capsule predicts behaviour and outcome of carcinoma ex pleomorphic adenoma.[8,9] By degree of invasion, they are subdivided into the following sub-types: non-invasive (intracapsular, in-situ), minimally invasive ($\leq$ 1.5 mm), and invasive carcinomas ($\geq$15 mm).[10] Our case is an example of minimally invasive carcinoma ex pleomorphic adenoma. Recent studies suggest that intracapsular and minimally invasive carcinoma ex pleomorphic adenoma are indolent types and should not be considered the same as typical carcinoma ex pleomorphic adenoma.[8]

Although pleomorphic adenoma can show vascular invasion, multinodular pattern and protrusion of neoplastic cells into the capsule, the tumour extension through the capsule into the adjacent benign salivary gland parenchyma or surrounding soft tissue is recognized as an invasive growth pattern and is considered diagnostic of

malignancy.[11] These findings should raise concern for malignancy in a conventional Pleomorphic adenoma. Lewis et al[3] correlated prognosis to the degree of invasion in 66 cases and found no recurrences and metastases for patients with extracapsular invasion of less than 5 mm. However, extracapsular invasion of 15 mm significantly decreased survival. Therefore, it is mandatory to report the type of tumour and differentiation along with the extent of invasion as it greatly impacts prognosis.

The carcinoma component in low grade carcinoma ex pleomorphic adenoma can be of any malignant salivary gland neoplasm. These include myoepithelial Carcinoma, low grade adenocarcinoma NOS, epithelial-myoepithelial Carcinoma, acinic cell adenocarcinoma etc. In our case, the carcinoma component was myoepithelial.

In 70% of pleomorphic adenomas, translocations or intrachromosomal re-arrangements with sporadic non-clonal changes, that cause fusion of genes involving the transcription factor genes PLAG1 on 8q12 and HMGA2 on 12q14-15, are seen. PLAG1 and HMGA2 fusions have only been encountered in carcinoma ex pleomorphic adenoma and are not found in other salivary gland tumours.[12]

This case was sent for international consultation and was positive for PLAG1 immunohistochemical stain and negative for HMGA2, further confirming the evidence of a pleomorphic adenoma harbouring a malignancy. The final diagnosis concurred with our diagnosis.

Literature suggests that it is not enough to report Carcinoma ex pleomorphic adenoma only. Accurate identification of high-grade carcinoma ex pleomorphic adenoma, low-grade carcinoma ex pleomorphic adenoma, and pleomorphic adenoma is mandatory for assessment of prognosis and treatment options. Low-grade carcinoma ex pleomorphic adenoma is an under-recognized category among salivary gland tumours. It is not a well-defined entity in the WHO classification of Head and Neck Tumours. Intra capsular / minimally invasive tumours or tumours with low-grade histology are considered low risk. In contrast, widely invasive tumours with high-grade histology are considered high risk as per WHO risk stratification. Histologic grade, histologic type, percentage of carcinoma, and degree of invasion of the carcinomatous component are mandatory to report as per current recommendations.

Conclusion

In the current case, the diagnosis of low-grade carcinoma ex pleomorphic adenoma was challenging for the pathologists since nuclear atypia was mild and infiltration into the surrounding tissue can be difficult to discern. However, increased mitotic rate, increased cellularity, mild atypia in spindle cell component, and presence of invasive growth pattern into the surrounding fibro adipose tissue were helpful in reaching the correct diagnosis in this case.

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Consent: Consent for publication of the case, was obtained from the patient.

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