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DIAGNOSTIC DILEMMA IN RARE SALIVARY GLAND TUMOURS: A CASE SERIES

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ABSTRACT
Salivary gland neoplasms are uncommon and pose diagnostic challenges due to their diverse morphology. Accurate diagnosis depends on meticulous histopathology supported by immunohistochemistry, making documentation of rare variants clinically relevant. The author presents a series of five rare salivary gland tumors, identified through histopathological evaluation and further confirmed by immunohistochemical analysis.
This case series includes five patients with salivary gland tumors. A 32-year-old male with a three-year history of right parotid swelling underwent parotidectomy and was diagnosed with carcinoma ex pleomorphic adenoma—minimally invasive secretory carcinoma type—with clear surgical margins. A 40-year-old female presented with secretory carcinoma of the left parotid gland, also showing negative margins. Two female patients, aged 74 and 60 years, were diagnosed with salivary duct carcinoma of the left and right submandibular glands, respectively, both demonstrating lymphovascular and perineural invasion. The series also includes a 21-year-old male with a benign pleomorphic adenoma exhibiting squamous metaplasia.Surgical excision remains the primary modality of treatment for these tumors. Postoperative radiotherapy is typically considered when adverse features such as positive margins, extraparotid extension, lymphovascular or perineural invasion, and lymph node metastasis are present.

Keywords: Benign, Carcinoma, Histological features, Diagnosis.

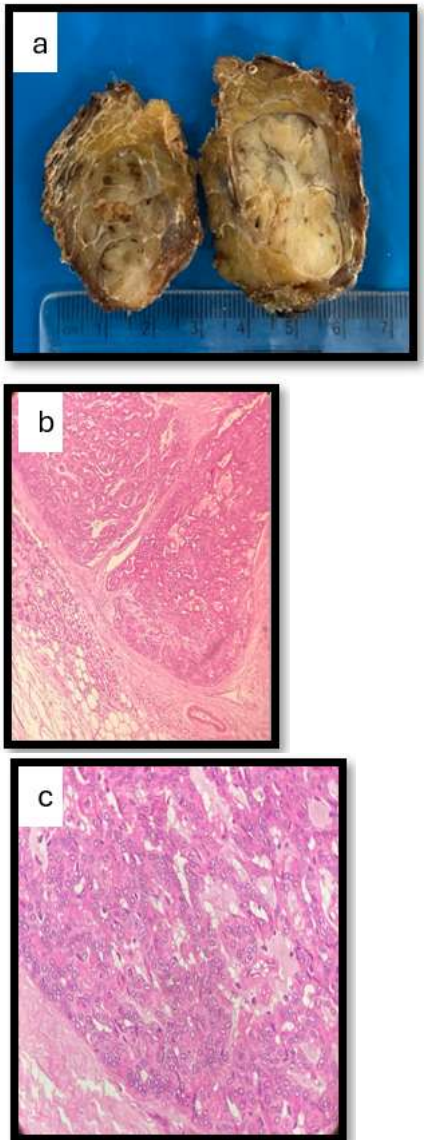
INTRODUCTION

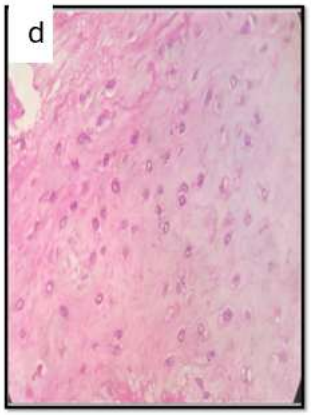
Salivary gland neoplasms represent an uncommon subset of head and neck pathology. The 5th edition of the World Health Organisation classification of H&N tumours lists more than 20 malignant and 15 benign entities, reflecting the wide heterogeneity of these lesions. Their rarity and diversity make both diagnosis and management challenging for clinicians.(1) Carcinoma ex pleomorphic adenoma is an unusual malignant tumour that develops from a pre-existing Pleomorphic adenoma and is known for its aggressive biology. Secretory carcinoma is a low-grade malignancy that mimics mammary secretory carcinoma and is defined by the ETV6-NTRK3 gene fusion.(2)
Initially identified by Skálova et al. [6] in 2010 during studies of acinic cell carcinoma, secretory carcinoma shows a distinct immunohistochemical profile and typically affects adults, though reported cases span ages 10–86 years with no sex predominance.(2) It arises most frequently in the parotid gland but can also appear in minor intraoral salivary glands. While usually indolent, rare instances exhibit high-grade transformation (dedifferentiation) associated with more aggressive features.(5) The emergence of secretory carcinoma as the malignant component within carcinoma ex pleomorphic adenoma is exceptionally uncommon and highlights the need for additional research into its biological behaviour.
Salivary duct carcinoma is a high-grade epithelial malignancy that closely resembles mammary ductal carcinoma. It may present de novo or arise as the malignant component in carcinoma ex pleomorphic adenoma, where SDC is the most frequently encountered carcinoma. It typically affects older males and is most often located in the parotid gland, though it also occurs in the submandibular gland.Salivary duct papilloma is another rare ductal lesion that usually originates in minor salivary glands but has been occasionally reported in the parotid.(3) Pleomorphic adenoma (PA), the most common benign salivary gland tumour, may show squamous metaplasia; however, extensive squamous change significant enough to mimic malignant processes is rarely observed.(7)

CASE SERIES

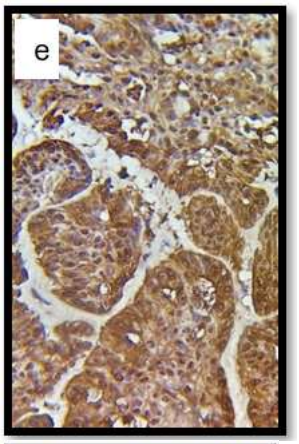
CASE 1

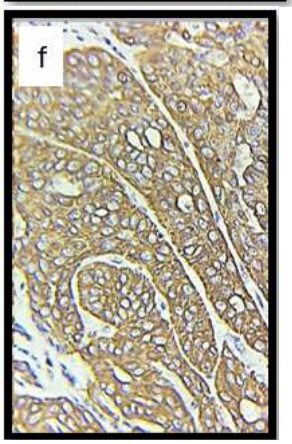
A 35-year-old woman presented with a painless, firm 3 × 3 cm swelling in the right parotid region for 3 years. MRI showed a well-defined, capsulated 29 × 27 × 27 mm superficial parotid nodule with T2 hyperintensity, heterogeneous enhancement, and internal papillary projections, suggestive of pleomorphic adenoma. She underwent a right superficial parotidectomy with preservation of all facial nerve branches. Grossly, the specimen measured 4.5 × 4 × 1.6 cm with a 3 × 2.6 cm well-circumscribed grey-white/yellow tumour containing small cystic areas [Table/Fig-1a]; the closest margin was 0.5 cm. Microscopically, [Table/Fig-1c]the tumour showed solid, cystic, and follicular patterns with eosinophilic intraluminal secretions, mild–moderate pleomorphism, scattered myoepithelial cells, and focal chondromyxoid stroma [Table/Fig-1d], with no necrosis, increased mitosis, lymphovascular or perineural invasion; minimal invasion into adjacent salivary tissue was noted. Three lymph nodes were reactive, and all margins were negative. The final diagnosis was Carcinoma ex pleomorphic adenoma- minimally invasive malignant component- secretory carcinoma, pT2 N0 Mx. Immunohistochemistry supported MASC, with tumour cells positive for S100, CK7, and GATA3 [Table/Fig-1e,f,g].

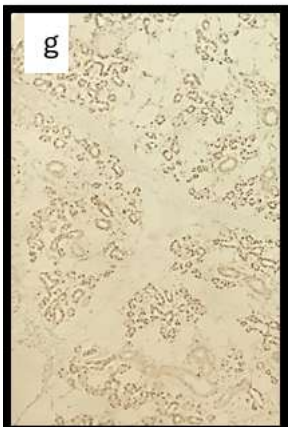




[Table/Fig-1]:(a): Cut surface of the parotidectomy specimen is solid with focal cystic area; b) Shows tumour lobules separated by irregular fibrocollagenous septae (H&E stain, 10X); c) Shows mild to moderate pleomorphism and are round to oval with vesicular nuclei, inconspicuous nucleoli, scant to vacuolated cytoplasm. Eosinophilic colloid like intraluminal secretions (H&E stain, 10X).d) Chondromyxoid stroma(H&E stain, 40X).



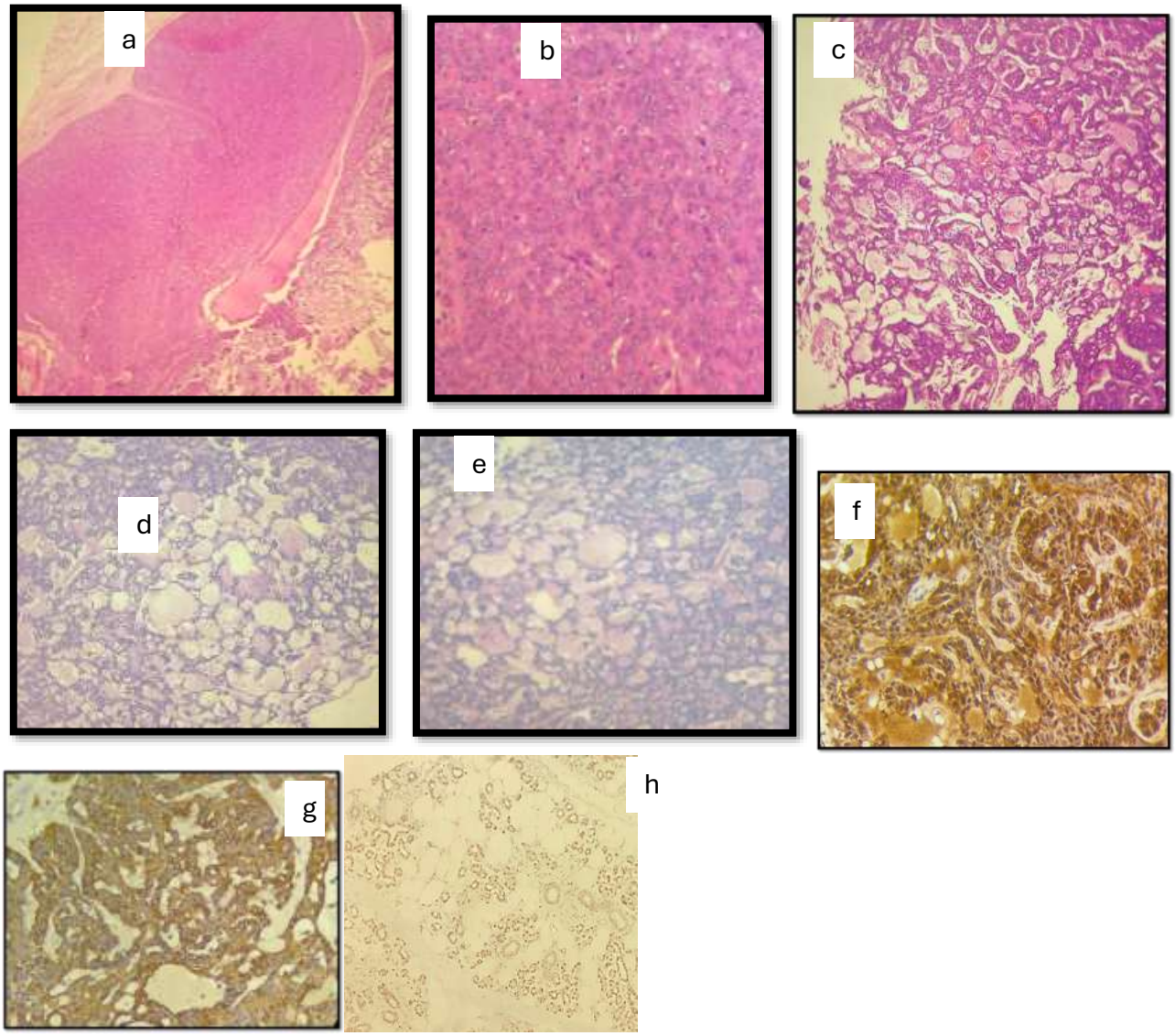




(e) S100 showed positive expression for the nuclear and membrane proteins.(f)CK 7 showed positive expression for membrane and cytoplasm (g)GATA 3 showed nuclear expression.

Case 2

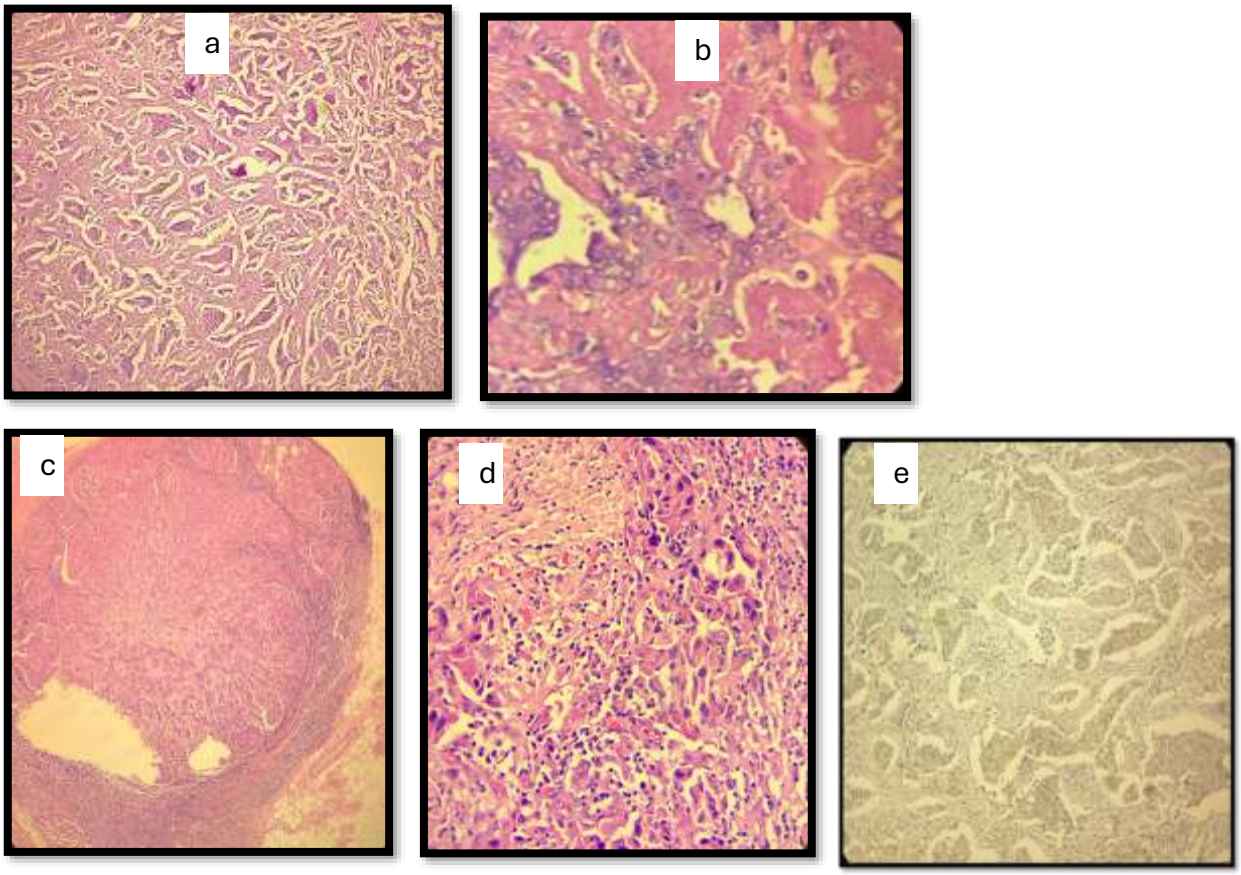
A 38-year-old woman presented with a painless, firm 2.5 × 2 cm swelling in the right parotid region for 2 years. MRI demonstrated a well-marginated superficial lobe parotid mass measuring 24 × 22 × 20 mm**,** showing T2 hyperintensity with mixed solid–cystic areas and mild internal septations, along with moderate post-contrast enhancement—features suggestive of a low-grade salivary gland tumour. A right superficial parotidectomy was performed with complete preservation of all facial nerve branches. Grossly, the specimen measured 4.2 × 3.8 × 1.5 cm, containing a 2.4 × 2.1 cm well-demarcated grey-white to yellow lesion with small cystic foci. Microscopy revealed [Table/Fig-2a]a lobulated neoplasm arranged in solid, microcystic, and follicular patterns with tumour cells showing vesicular nuclei, fine chromatin, and vacuolated cytoplasm, [Table/Fig-2b] accompanied by eosinophilic colloid-like luminal secretions [Table/Fig-2c]that were PAS-positive and PAS-diastase–resistant [Table/Fig-2d,e], consistent with secretory differentiation. There was no necrosis, mitotic activity, lymphovascular invasion, or perineural invasion, and all margins were negative, with the closest margin at 0.7 cm. Two sampled lymph nodes showed no metastasis**.** The final diagnosis was **Secretory Carcinoma (MASC) of the parotid gland**, staged as pT1 N0 Mx, supported by immunohistochemical positivity for S100, CK7, and GATA3 [Table/Fig-2f,g,h].



[Table/Fig-2]: a) Shows tumour lobules separated by irregular fibrocollagenous septae (H&E stain, 10X); b) Shows mild to moderate pleomorphism and are round to oval with vesicular nuclei, inconspicuous nucleoli, and scant to vacuolated cytoplasm. (H&E stain, 40X). c)Eosinophilic colloid-like intraluminal secretions (H&E stain, 10X).d,e) Intraluminal secretions are PAS positive and diastase resistant. (PAS stain,10x) (f) S100 showed positive expression for the nuclear and membrane proteins.(g)CK 7 showed positive expression for the membrane and cytoplasm. (h)GATA 3 showed nuclear expression.

Case 3

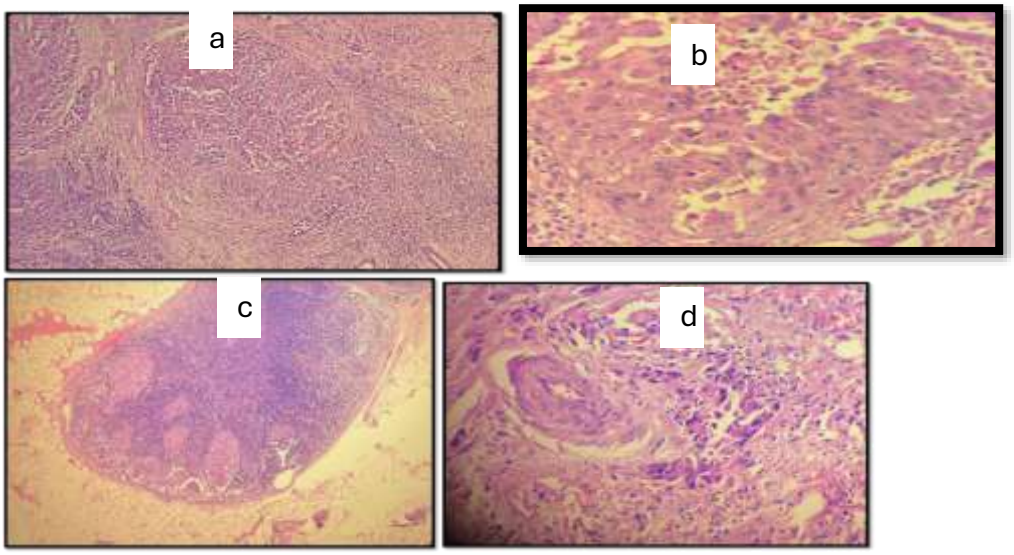
T a atient presented with a 4 × 3 cm left submandibular swelling. FNAC showed highly pleomorphic atypical epithelial c picious for malignancy. CT neck revealed a heterogeneously enhancing left submandibular lesion with loss of fat plan d enlarged level II lymph nodes. Submandibular gland excision with level II dissection was performed. Grossly, the soft tissue mass was 5x3x2.5cm ,firm and grey-white with two lymph nodes. Histology showed an invasive high-grade malignant epithelial tumor arranged in nests and micropapillary structures [Table/Fig-3a] with marked pleomorphism, prominent nucleoli, necrosis, high mitoses [Table/Fig-3b], lymphovascular and perineural invasion, [Table/Fig-3d] and infiltration into adjacent skeletal muscle and fat. Three level II lymph nodes showed metastasis without extracapsular spread [Table/Fig-3c]. HER2neu showed moderate membranous positivity in 50–60% of tumor cells [Table/Fig-3e], confirming **salivary duct carcinoma, micropapillary variant**.



[Table/Fig-3]: (a) shows malignant cells arranged in micropapillary pattern. (H&E stain, 10X); b) shows large vesicular nuclei with coarse chromatin, prominent nucleoli, irregular nuclear membranes, marked pleomorphism, and abundant eosinophilic cytoplasm; many bizarre nuclei. (H&E stain, 40X c) Lymph node with metastatic deposit with no extra capsular spread.d) Lymphovascular emboli e)HER2/neu shows intermediate intensity of membranous positivity(50-60%)of tumour cells.

Case 4

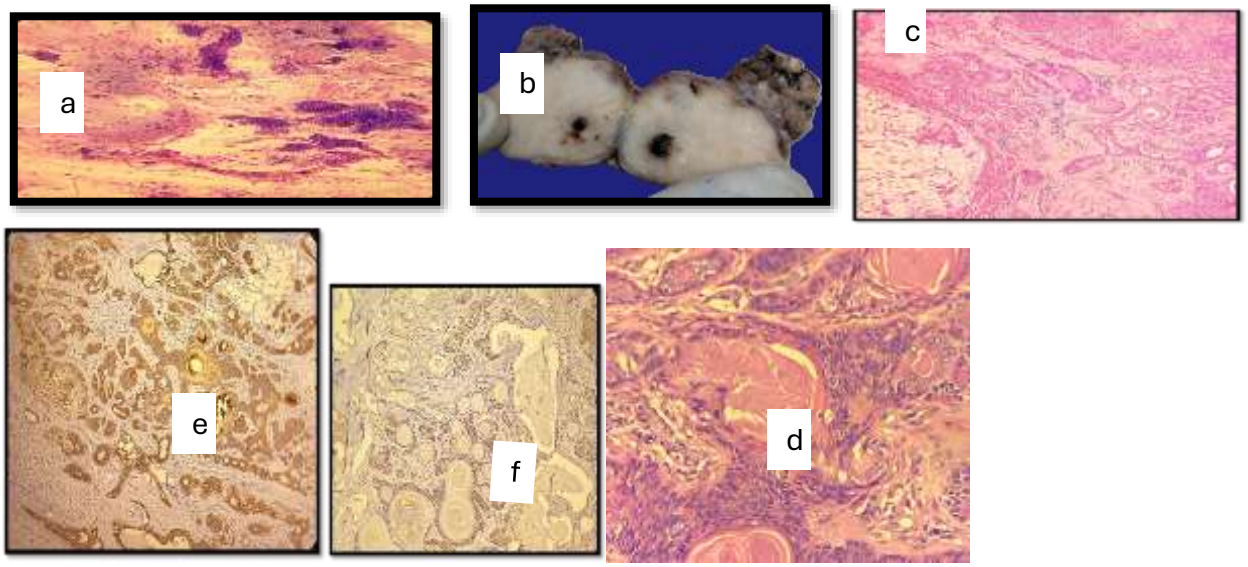
The patient presented with a firm, non-tender left submandibular swelling. Ultrasound and CT neck revealed a well-defined, heterogeneously enhancing lesion in the left submandibular gland with loss of fat planes and enlarged left level II lymph nodes, suggestive of malignancy. The patient underwent excision of the left submandibular gland with level II lymph node dissection. Grossly, the tumor measured 4 × 2.5 × 2 cm, firm and grey-white, with two lymph nodes measuring 1.2 × 1 × 0.5 cm and 1 × 0.8 × 0.5 cm. Histology showed an invasive malignant epithelial tumor [Table/Fig-4a] composed of ducts, nests, and solid sheets with marked pleomorphism, prominent nucleoli, abundant eosinophilic cytoplasm, and comedo-type necrosis, infiltrating adjacent skeletal muscle and fat [Table/Fig-4b]. Both level II lymph nodes contained metastatic deposits without extracapsular spread [Table/Fig-4c]. Also lymphovascular invasion was noted [Table/Fig-4d]. Features were consistent with salivary duct carcinoma**.**



[Table/Fig-4]: (a) shows malignant cells arranged in nest, sheets and a large ductular pattern. (H&E stain, 10X); b) shows large vesicular nuclei with coarse chromatin, prominent nucleoli, irregular nuclear membranes, marked pleomorphism, and abundant eosinophilic cytoplasm; many bizarre nuclei. (H&E stain, 40X c) Lymph node with metastatic deposit d) Lymphovascular emboli

Case 5

A patient presented with a painless swelling over the right mandibular-to-mastoid region for 2 years. Examination showed a mobile, soft-to-firm 3 × 2 cm preauricular mass with normal skin. Ultrasound revealed a well-defined 3.0 × 2.9 × 1.7 cm heteroechoic superficial parotid lesion with mild posterior enhancement, minimal peripheral vascularity, and internal calcifications. CECT neck showed a well-defined 3.1 × 3.1 × 2.4 cm heterogeneously enhancing lesion with tiny calcific foci in the superficial right parotid lobe, abutting the masseter but with preserved fat planes and only small reactive lymph nodes. USG-guided FNAC demonstrated epithelial clusters, myoepithelial cells, and abundant chondromyxoid stroma, favouring pleomorphic adenoma [Table/Fig-5a]. The patient underwent right total parotidectomy with facial nerve preservation, and a 4 × 3 × 2 cm encapsulated bosselated mass with additional 3 × 2 × 0.5 cm extended tissue was excised. Grossly, the tumour was grey-white and firm with focal grey-brown areas [Table/Fig-5b]. Microscopy [Table/Fig-1c]showed a partly circumscribed biphasic tumour composed of epithelial and myoepithelial elements in cystic and tubular patterns with eosinophilic/mucoid secretions, extensive squamous metaplasia with keratin pearls [Table/Fig-1d], chondromyxoid stroma, lipomatous foci, and dystrophic calcification, without atypia, necrosis, mitosis, capsular breach, lymphovascular or perineural invasion; adjacent parotid tissue was unremarkable. The extended tissue showed normal salivary gland. IHC revealed p63 positivity in myoepithelial cells and PanCK positivity in epithelial cells, [Table/Fig-5e,f] confirming pleomorphic adenoma with extensive squamous metaplasia.



[Table/Fig-5]: a) FNAC showing cohesive epithelial clusters with a honeycomb pattern, round-oval nuclei, and focal plasmacytoid/spindled cells, set in abundant chondromyxoid stroma—suggestive of pleomorphic adenoma.; b) Gross examination showed grey-white, homogenous with focal grey-brown areas. c) The cyst and tubules show prominent

intraluminal eosinophilic and focal mucoid secretions, also chondromyxoid stroma(H&E 10x) d) Squamous metaplasia and keratin pearl formation were noted(H&E 40x). e): PanCK: Positive in all tumour cells;f): P63 shows nuclear in myoepithelial cells lining the ducts and tubules;

case	Age(yrs)/gender	Site	Preoperative findings	Histological Diagnosis	Stage	IHC
1	35, Female	Right Parotid gland	MRI showed a well-defined, capsulated nodule with T2 hyperintensity, heterogeneous enhancement, internal papillary projections, firm consistency, lifting the earlobe, suggestive of pleomorphic adenoma.	Carcinoma ex pleomorphic adenoma-minimally invasive malignant component-secretory carcinoma	pT2 N0 M0	**S100, CK7, and GATA3 -positive**
2	38/ Female	Left Parotid gland	MRI showed well-marginated mass with T2 hyperintensity, mixed solid–cystic areas, moderate enhancement, and firm consistency, suggestive of a low-grade salivary gland tumor.	Secretory Carcinoma	pT2N0 M0	**S100, CK7,GATA3 -positive**
3	74/ Female	Left submandibular gland	Firm swelling with a heterogeneously enhancing lesion, loss of fat planes, and enlarged level II nodes, suggestive of metastasis.	Salivary duct carcinoma, micropapillary variant.	pT3 N2b M0	HER2neu-positive
4	60/ Female	Right submandibular gland	Firm swelling with well-defined, heterogeneously enhancing lesion, loss of fat planes, and enlarged level II nodes, suggestive of malignancy.	Salivary duct carcinoma	pT2N2b M0	Not done
5	21/ Male	Right parotid gland	Well-defined heteroechoic/heterogeneously enhancing lesion with internal calcifications, mild vascularity, abutting the masseter with preserved fat planes, FNAC suggestive of pleomorphic adenoma.	Pleomorphic adenoma with extensive squamous metaplasia	-	p63, PanCK-positive

[Table/Fig-6]: Brief overview of all five salivary gland tumor presentations.

DISCUSSION

This case series highlights the spectrum of salivary gland neoplasms, ranging from low-grade secretory carcinoma and pleomorphic adenoma (PA) with metaplasia to high-grade salivary duct carcinoma (SDC) and carcinoma ex pleomorphic adenoma (Ca ex PA). Secretory carcinoma (MASC) represents a low-grade malignancy, most commonly arising in the parotid gland, with indolent behavior, rare metastasis, and favourable prognosis (1,5). In our cases (Cases 1 and 2), imaging demonstrated well-circumscribed, cystic-solid lesions with T2 hyperintensity and mild heterogeneous enhancement, consistent with literature descriptions (7,8,9,10). Histologically, MASC shows microcystic, solid, tubular, and follicular patterns with eosinophilic luminal secretions, lacking zymogen granules, and is immunoreactive for S100, CK7, and GATA3, aiding differentiation from acinic cell carcinoma (1).

Carcinoma ex pleomorphic adenoma (Case 1) and high-grade SDC (Cases 3 and 4) represent aggressive salivary malignancies with infiltrative growth, marked cytologic atypia, necrosis, and frequent perineural and lymphovascular invasion (1,12,13). Imaging is less specific but suggests malignancy when loss of fat planes, heterogeneous enhancement, and lymphadenopathy are present (7,8,9). SDC exhibits ductal, nested, and micropapillary patterns with comedo-type

necrosis and may express HER2/neu, a potential therapeutic target (13). These cases underline the importance of correlating imaging, histology, and immunohistochemistry for accurate diagnosis and prognostication (1,5).
Pleomorphic adenoma with extensive squamous metaplasia (Case 5) represents a diagnostic pitfall, mimicking low-grade mucoepidermoid carcinoma or squamous cell carcinoma (8,10,11,12). Key differentiating features include absence of cytological atypia, necrosis, mitotic activity, and perineural invasion, along with characteristic immunostaining patterns (p63 in myoepithelial cells, PanCK in epithelial cells) (10,11). Recognition of these features is crucial to avoid overtreatment (8,10,11).
Overall, this series demonstrates the broad histopathologic and clinical spectrum of salivary gland tumors, emphasizing the necessity of integrating imaging, gross findings, histology, and immunohistochemistry for accurate classification and management planning (1,5,7,8).

CONCLUSION

This case series highlights the rarity and diverse spectrum of salivary gland neoplasms. Secretory carcinoma (MASC) is an uncommon low-grade malignancy, typically arising in the parotid gland, with distinctive microcystic, tubular, and papillary patterns, eosinophilic luminal secretions, and characteristic immunoprofile (S100, CK7, GATA3) (1,5,7,10). Pleomorphic adenoma with extensive squamous metaplasia is an unusual variant, representing a potential diagnostic pitfall that can mimic other epithelial malignancies, yet retains benign histologic features and immunostaining patterns (8,10,11,12). High-grade salivary duct carcinoma and carcinoma ex pleomorphic adenoma are rare but aggressive entities, often presenting with infiltrative growth, comedo-type necrosis, perineural and lymphovascular invasion, and possible HER2/neu expression, which influence prognosis and management (1,12,13).
Recognition of these rare variants and careful integration of imaging, histopathology, and immunohistochemistry are essential for accurate diagnosis, appropriate surgical planning, and prognostication in salivary gland tumors (1,5,7,8,10,12).

REFERENCE

1. Swid MA, Li L, Drahnak EM, Idom H, Quinones W. Updated salivary gland immunohistochemistry: A review. Arch Pathol Lab Med [Internet]. 2023;147(12):1383–9. Available from: http://dx.doi.org/10.5858/arpa.2022-0461-ra
2. Skálová A, Hyrcza MD, Leivo I. Update from the 5th edition of the world health organization classification of head and neck tumors: Salivary glands. Head Neck Pathol [Internet]. 2022;16(1):40–53. Available from: http://dx.doi.org/10.1007/s12105-022-01420-1
3. Ishikawa T, Imada S, Ijuhin N. Intraductal papilloma of the anterior lingual salivary gland. Case report and immunohistochemical study. Int J Oral Maxillofac Surg [Internet]. 1993;22(2):116–7. Available from: http://dx.doi.org/10.1016/s0901-5027(05)80816-1
4. Jaehne M, Roeser K, Jaekel T, Schepers JD, Albert N, Löning T. Clinical and immunohistologic typing of salivary duct carcinoma: a report of 50 cases: A report of 50 cases. Cancer [Internet]. 2005;103(12):2526–33. Available from: http://dx.doi.org/10.1002/cncr.21116
5. Chiosea SI, Griffith C, Assaad A, Seethala RR. Clinicopathological characterization of mammary analogue secretory carcinoma of salivary glands: Mammary analogue secretory carcinoma. Histopathology [Internet]. 2012;61(3):387–94. Available from: http://dx.doi.org/10.1111/j.1365-2559.2012.04232.x
6. Skalova A. Mammary Analogue Secretory Carcinoma of Salivary Gland Origin: An Update and Expanded Morphologic and Immunohistochemical Spectrum of Recently Described Entity. Head and Neck Pathology. 2013;7:30–6.
7. Neville BW. Update on current trends in oral and maxillofacial pathology. Head Neck Pathol [Internet]. 2007;1(1):75–80. Available from: http://dx.doi.org/10.1007/s12105-007-0007-4
8. Terada T, Kawata R, Noro K, Higashino M, Nishikawa S, Haginomori S-I, et al. Clinical characteristics of acinic cell carcinoma and secretory carcinoma of the parotid gland. Eur Arch Otorhinolaryngol [Internet]. 2019;276(12):3461–6. Available from: http://dx.doi.org/10.1007/s00405-019-05604-4
9. Mc G, Fara F, Goulart P, Deolivera GR, Roman AM, Sares CB. Pleomorphic adenoma with extensive squamous metaplasia and keratin metaplasia and keratin cyst formations in minor salivary gland: A case report. J Appl Oral Sci. 2011;19:182–8.
10. Lim S, Cho I, Park J-H, Lim S-C. Pleomorphic adenoma with exuberant squamous metaplasia and keratin cysts mimicking squamous cell carcinoma in minor salivary gland. Open J Pathol [Internet]. 2013;03(03):113–6. Available from: http://dx.doi.org/10.4236/ojpathology.2013.33020
11. Joshi SA, Halli R, Koranne V, Singh S. Necrotizing sialometaplasia: A diagnostic dilemma! J Oral Maxillofac Pathol [Internet]. 2014;18(3):420–2. Available from: http://dx.doi.org/10.4103/0973-029X.151336
12. Zohar Y, Shem-Tov Y, Gal R. Salivary duct carcinoma in major and minor salivary glands. J Craniomaxillofac Surg [Internet]. 1988;16:320–3. Available from: http://dx.doi.org/10.1016/s1010-5182(88)80071-4
13. Nagao T, Gaffey TA, Visscher DW, Kay PA, Minato H, Serizawa H, et al. Invasive micropapillary salivary duct carcinoma: a distinct histologic variant with biologic significance. Am J Surg Pathol [Internet]. 2004;28(3):319–26. Available from: http://dx.doi.org/10.1097/00000478-200403000-00004