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Secretory Carcinoma Of Parotid Gland_: A Case Series From A Tertiary Care Centre In Western Uttar Pradesh

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SECRETORY CARCINOMA OF PAROTID GLAND

ABSTRACT
Secretory carcinoma (formerly "mammary analogue secretory carcinoma") is a rare, low-grade salivary gland malignancy, most often arising in the parotid gland. It resembles secretory carcinoma of the breast at both histological and molecular levels. It presents as a slow-growing, painless parotid mass.
Here we discuss 3 cases of secretory carcinoma of parotid gland with different presentations and how each case was managed with surgical approach. 3 patients diagnosed with Secretory carcinoma of parotid gland tumors between October 2023 and October 2024 were managed in Saraswathi institute of Medical Sciences , Hapur.

KEYWORDS – Secretory carcinoma parotid, Superficial Parotidectomy , Facial nerve , MASC

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INTRODUCTION

The parotid gland is the largest of the major salivary glands, located in the preauricular and retromandibular region, divided into superficial and deep lobes by the facial nerve, with the Stensen's duct as its main excretory duct[1]. Its principal function, like that of all salivary glands, is the production of serous saliva that aids in digestion, oral lubrication, and protection of the oral cavity[3].

Neoplasms of the parotid gland are relatively uncommon overall but comprise the majority (roughly 70-80%) of tumours arising within the major salivary glands[7]. While most parotid tumours are benign (e.g. pleomorphic adenoma, Warthin tumour), a significant subset are malignant and present diagnostic, therapeutic, and prognostic challenges[8].
Among malignant salivary gland tumours, **Secretory Carcinoma** (formerly known as **Mammary Analogue Secretory Carcinoma,** or MASC) has emerged as a distinct entity in the last decade[9]. First described in 2010, this tumor resembles secretory carcinoma of the breast in morphology, immunophenotype, and in many cases, genetic alterations - most notably the ETV6-NTRK3 fusion gene[9].

Until its recognition, many of these lesions had been misclassified as acinic cell carcinoma or adenocarcinoma, NOS (not otherwise specified)[11].
This article aims to review the current knowledge on secretory carcinoma of the parotid gland: its anatomy relevant to disease and surgery; its pathology (morphology, immunohistochemistry, genetics); clinical presentation; diagnostic approaches; therapeutic options; and prognostic factors, based on both classic texts and recent case series and systemic studies.

SUBJECTS AND METHODS

This case series included 3 patients with parotid gland swellings managed in the Department of Otorhinolaryngology, Saraswathi Institute of Medical Sciences, Hapur, between October 2023 and October 2024.

Clinical evaluation
All patients underwent detailed clinical history, physical examination, and radiological investigations (USG, CT, and MRI where indicated). Fine-needle aspiration cytology (FNAC) was performed preoperatively.

Surgical management
Superficial parotidectomy was performed depending on tumor extent and facial nerve involvement. Neck dissection and adjuvant therapy (radiotherapy/chemotherapy) were considered for advanced disease or high-risk histology.

Follow-up
Patients were followed at 2 weeks and 1 month postoperatively. Complications such as facial nerve paresis, wound infection, and hematoma were recorded.

STATISTICAL ANALYSIS
Data was analyzed using SPSS version 29 (SPSS Inc., Chicago, IL). Chi-square and Fisher exact tests were performed to test for differences in proportions of categorical variables between two or more groups. The level $P < 0.05$ was considered as the cutoff value or significance.

Ethical considerations
All treatments were part of routine clinical care. Patient data were anonymized, and informed consent was obtained for the use of clinical details and images for academic and publication purposes. As this is a descriptive case series without experimental intervention, formal ethical committee approval was not required under institutional guidelines.

CASE SERIES
CASE 1
A 34-years-old female presented to ENT OPD with swelling over the left side of her face for the past 8 months, which was insidious in onset and progressive in size, not associated with pain, facial weakness, ulceration or discharge, no difficulty in mastication, deglutition or speech. She had a sense of facial fullness.
On examination a swelling noted on left preauricular region approx. 3×3 cm in size, rounded, non-tender, firm, slightly moveable, no pulsation or fluctuation. Ear and mouth appear normal**(IMAGE 1).**
NCCT NECK revealed well-defined soft tissue lesion measuring 2.8×3.2 cm within superficial lobe of left parotid; no cystic areas or calcification**(IMAGE 2).**
FNAC revealed moderately cellular smear showing uniform epithelial cells with eosinophilic vacuolated cytoplasm. Suggestive of Pleomorphic Adenoma parotid or low-grade salivary gland neoplasm.

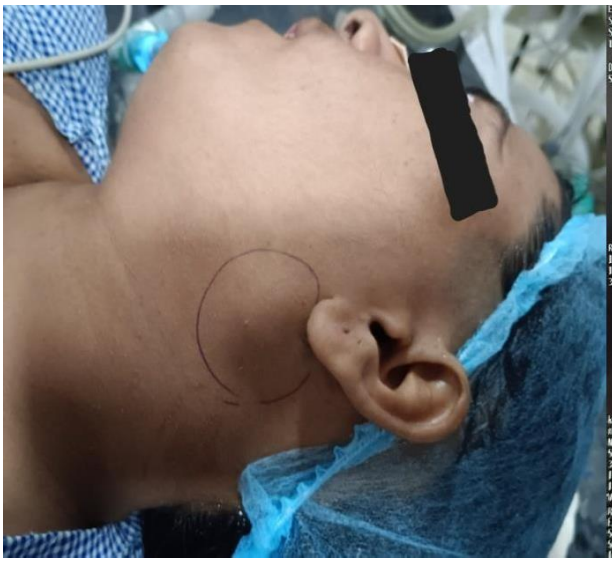

IMAGE 1

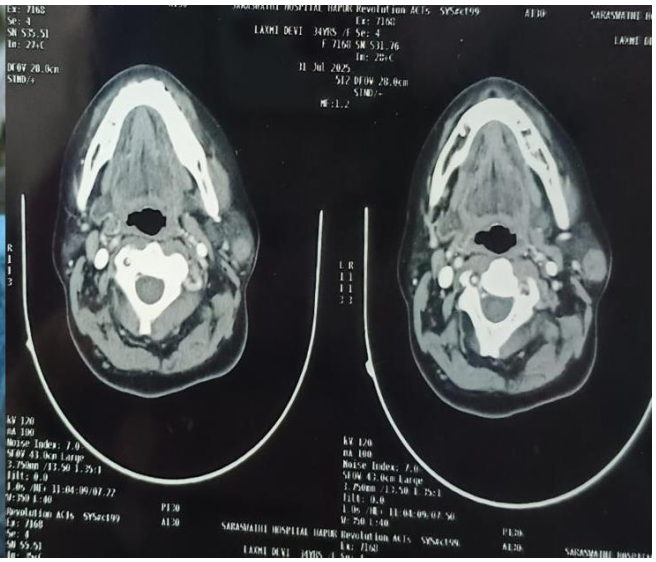

IMAGE 2

IMAGE 1 – LEFT PREAURICULAR SWELLING
IMAGE 2 – NCCT SCAN SHOWING SOFT TISSUE DENSITY IN LEFT PAROTID REGION

The patient was planned for Superficial Parotidectomy under General anaesthesia. All the branches of facial nerve were preserved and sample was sent for histopathological examination **(IMAGE 3&4).**

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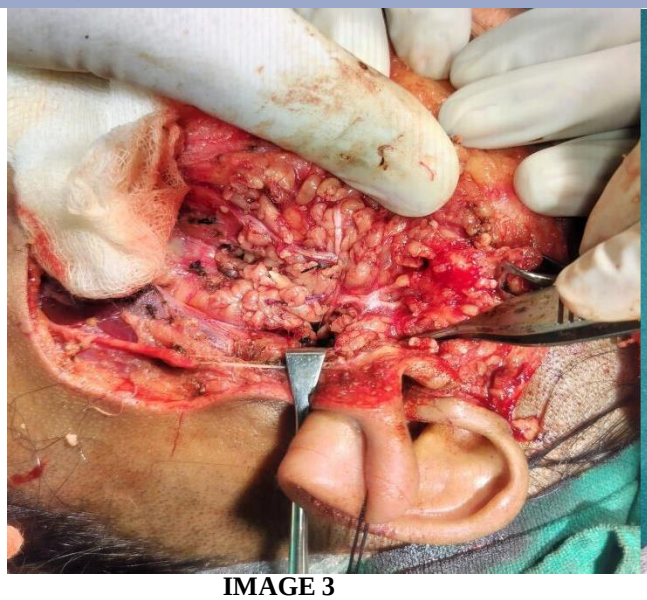


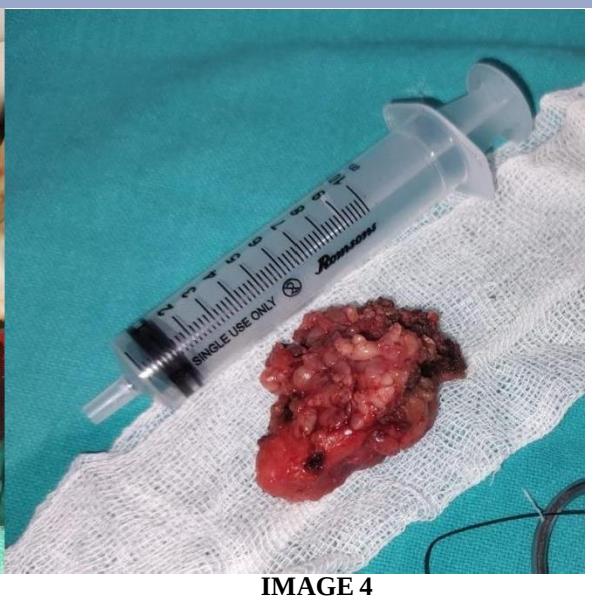
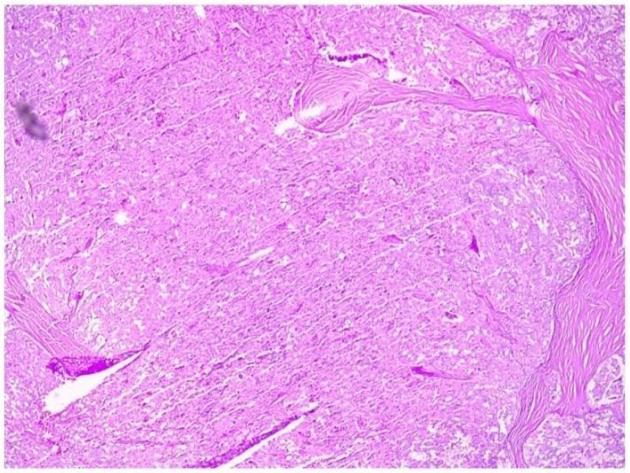


IMAGE 3 **IMAGE 4**

IMAGE 3 – INTRAOPERATIVE PICTURE SHOWING BRANCHES OF FACIAL NERVE
IMAGE 4 – EXCISED SPECIMEN

HISTOPATHOLOGICAL EXAMINATION of the specimen showed round to polygonal cells with round to oval nucleus eosinophilic to vacuolated and clear cell cytoplasm present in nests, cords , trabeculae **(IMAGE 5)**

IHC showed positive CK7 **(IMAGE 6)** , mammaglobin, S100 confirming diagnosis of secretory carcinoma of parotid gland.



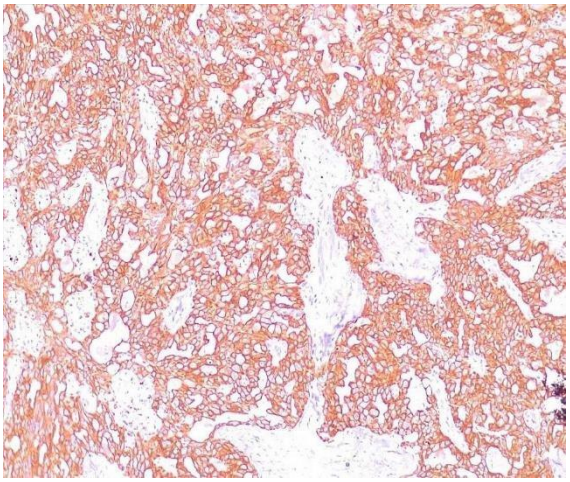


IMAGE 5 **IMAGE 6**

IMAGE 5 - HPE SHOWING ROUND TO POLYGONAL CELLS WITH ROUND TO OVAL NUCLEUS EOSINOPHILIC TO VACUOLATED AND CLEAR CELL CYTOPLASM PRESENT IN NESTS, CORDS , TRABECULAE.
IMAGE 6 – IMMUNOHISTOCHEMISTRY SHOWING CK7 POSITIVITY

Patient was followed up every month for 6 months with no signs of recurrence.

CASE 2
A 13-years-old female presented to ENT OPD with swelling over the right side of her face for past 1 year, which was gradually progressive in size, not associated with pain, redness or warmth over the swelling. No facial weakness, numbness or deviation of mouth while smiling or talking.
On examination swelling was noted on the right preauricular region of size ~3×2.5 cm, ovoid, non-tender, slightly elastic, moves slightly over deeper structures. Intraoral examination normal **(IMAGE 1**).
NCCT SCAN NECK revealed well-defined soft tissue lesion in the superficial lobe of right parotid gland, measuring 3.1 x 2.4 cm, with mild internal vascularity. No calcification or cystic degeneration**(IMAGE 2).**

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FNAC showed **m**oderately cellular smear with epithelial cells in microcystic and papillary patterns, containing eosinophilic vacuolated cytoplasm.

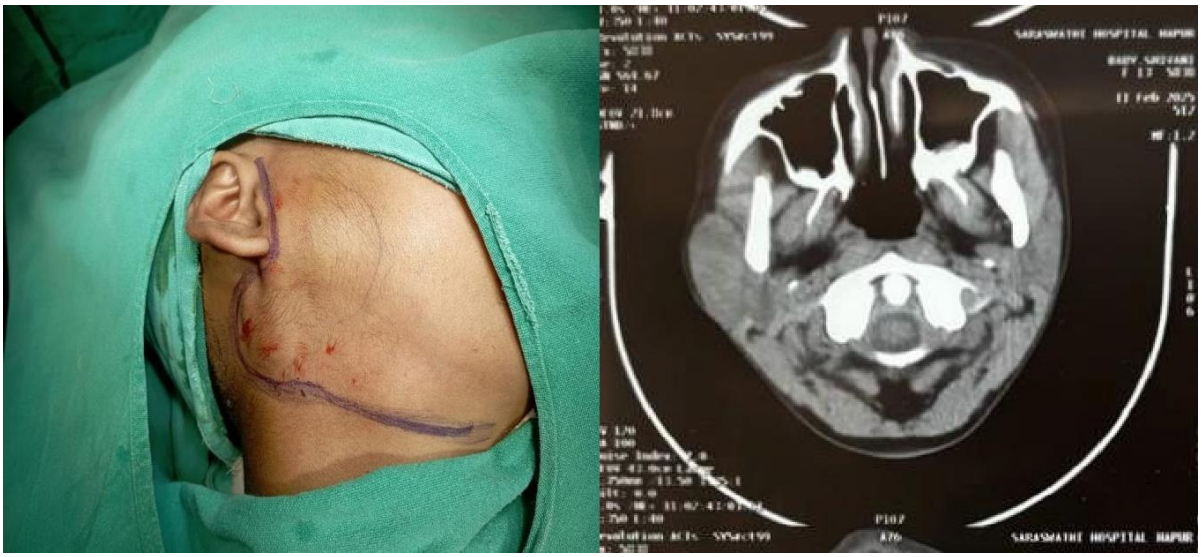

IMAGE 1 **IMAGE 2**

IMAGE 1 – RIGHT PREAURICULAR SWELLING
IMAGE 2 - NCCT SCAN SHOWING SOFT TISSUE DENSITY IN RIGHT PAROTID REGION

The patient was planned for Superficial Parotidectomy under General anaesthesia. All the branches of facial nerve were preserved and sample was sent for histopathological examination **(IMAGE 3).**

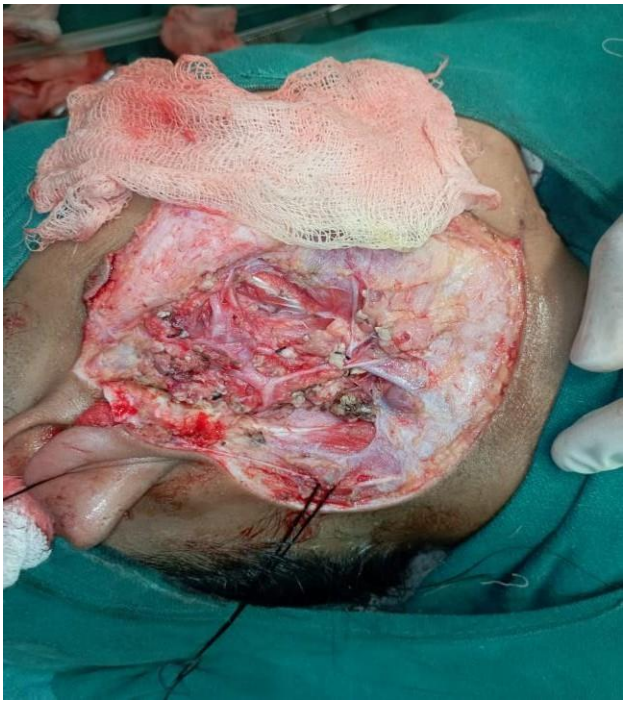

IMAGE 3 – INTRAOPERATIVE PICTURE SHOWING BRANCHES OF FACIAL NERVE

HISTOPATHOLOGICAL EXAMINATION shows papillae lined by monomorphic cells with round vesicular nuclei, and abundant eosinophilic cytoplasm showing hobnailing. (h&e 40x10) **(IMAGE 4).**

IHC revealed positive S100 **(IMAGE 5)** , mammaglobin, cytokeratin 7 confirming the diagnosis as Secretory Carcinoma of Parotid.

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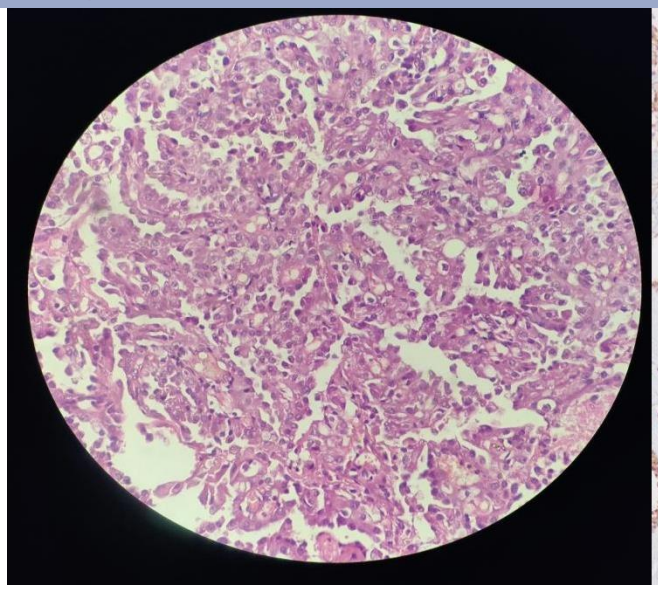
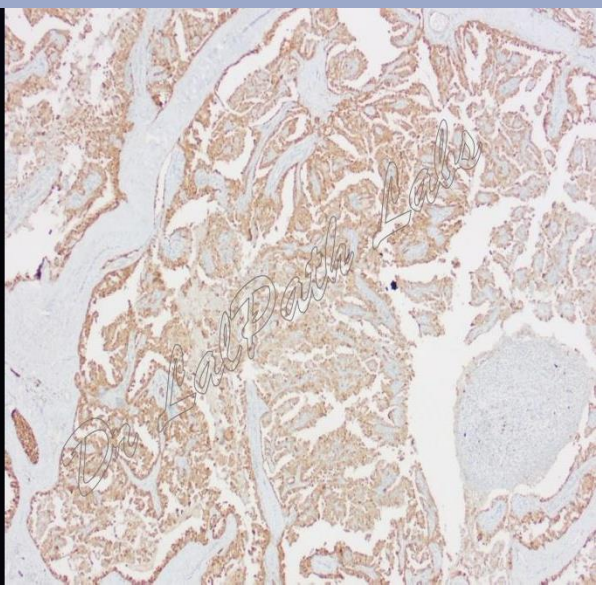

IMAGE 4 **IMAGE 5**

IMAGE 4 – THE HIGH-POWER VIEW SHOWS PAPILLAE LINED BY MONOMORPHIC CELLS WITH ROUND VESICULAR NUCLEI, AND ABUNDANT EOSINOPHILIC CYTOPLASM SHOWING HOBNAILING. (H&E 40X10)

IMAGE 5 – IMMUNOHISTOCHEMISTRY SHOWING S100 POSITIVITY

The patient was followed up on a monthly basis with proper wound healing and no signs of recurrence.

CASE 3

A 17-year-old male patient presented to ENT OPD with chief complaint of neck swelling over the right side of the face in the preauricular region from last 6 months, which was gradually progressive in size, not associated with pain, facial weakness, deviation of angle of mouth, drooling of saliva.

On examination swelling noted in right parotid region, approx. 3×2 cm in size solitary, firm, non-tender, mobile. Overlying skin free, ear lobule not lifted, facial nerve intact, no intraoral extension, no cervical lymphadenopathy **(IMAGE 1).**

NCCT SCAN NECK showed well-defined soft tissue lesion in superficial lobe of right parotid measuring 2.8×2.2 cm, no cystic change, no cervical lymphadenopathy.

FNAC showed cells arranged in microcystic pattern with vacuolated cytoplasm, features suggestive of Pleomorphic Adenoma parotid or low-grade salivary gland carcinoma.

The patient was planned for Superficial Parotidectomy under General anaesthesia. All the branches of facial nerve were preserved and sample was sent for histopathological examination **(IMAGE 2).**

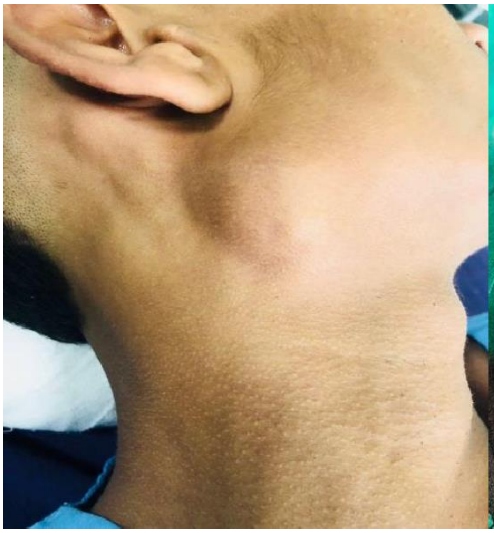
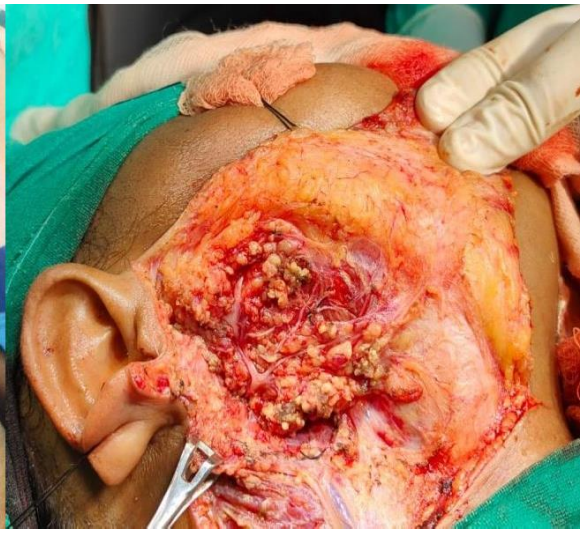

IMAGE 1 **IMAGE 2**

IMAGE 1 – RIGHT PREAURICULAR SWELLING

IMAGE 2 – INTRAOPERATIVE PICTURE SHOWING BRANCHES OF FACIAL NERVE

HISTOPATHOLOGICAL EXAMINATION showed variable-sized cystic spaces showing papillary projections, some with eosinophilic material and others with freely floating tumor cells **(IMAGE 3).**

IHC revealed tumor cells positive for SOX 7 **(IMAGE 4),** mammaglobin, S100, CK7 consistent with secretory carcinoma of Parotid gland.

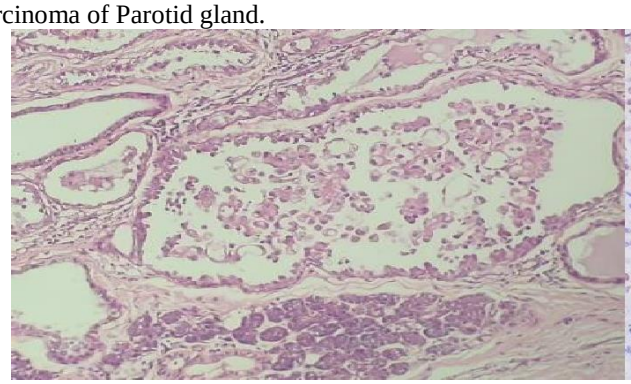

IMAGE 3

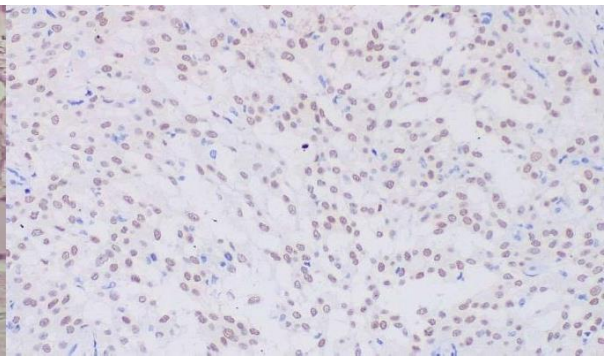

IMAGE 4 - SOX 7

IMAGE 3- HISTOPATHOLOGICAL EXAMINATION SHOWING VARIABLE-SIZED CYSTIC SPACES SHOWING PAPILLARY PROJECTIONS, SOME WITH EOSINOPHILIC MATERIAL AND OTHERS WITH FREELY FLOATING TUMOR CELLS

IMAGE 4 –IMMUNOHISTOCHEMISTRY SHOWING SOX7 POSITIVITY

HPE and IHC confirmed secretory carcinoma of the parotid gland. The patient was followed up monthly for 6 months with no signs of recurrence.

DISCUSSION

Secretory carcinoma (SC) of the salivary glands is a recently recognized, distinct malignant entity that was historically misclassified as acinic cell carcinoma or adenocarcinoma NOS. Its recognition as a separate clinicopathologic entity largely followed the demonstration of characteristic molecular alterations[7].

No consistent environmental, occupational or lifestyle exposures have been reproducibly linked to SC; like many salivary gland tumours, it appears sporadic and rare. Large-scale epidemiologic data are limited because the entity has only been clearly delineated in the past 10-15 years[5].

The hallmark molecular event in the majority of SC cases is a recurrent chromosomal translocation producing the ETV6-NTRK3 fusion gene (t(12;15) (p13;q25))[2,7]. This fusion encodes a constitutively active tyrosine kinase that can drive oncogenesis through MAPK/PI3K and related signaling pathways the same fusion originally described in secretory carcinoma of the breast and some pediatric mesenchymal tumors[8]. The presence of ETV6-NTRK3 is therefore both a defining molecular signature and a potential therapeutic target[7,8].

Although ETV6-NTRK3 is the commonest fusion, other fusions involving ETV6 (and occasional alternative partners such as RET or others) have been reported; molecular heterogeneity exists and molecular testing should not be assumed negative if pan-TRK IHC is equivocal. Recent case series and molecular studies document ETV6 heterogeneity in some specimens[2,7,8]. Clinically, SC of the parotid usually presents as a slow-growing, painless mass in adult patients; some series show mean age in the 40s to 50s, with occasional occurrence in children[2,3,7]. Imaging findings are non-specific: well defined margins, round or oval shape, often cystic mixed solid-cystic components[7,8].

Clinical assessment- Typical presentation: slow-growing, Painless, well-circumscribed parotid mass in adults (commonly 4th-6th decade but can occur in children). Facial nerve function is usually preserved at presentation; pain, rapid growth, fixation or facial nerve palsy are red flags suggesting more aggressive behavior[9].

Imaging-Ultrasound is useful for initial assessment (solid vs cystic), but cross-sectional imaging with contrast- enhanced CT or MRI provides best preoperative definition of tumor extent, relation to the facial nerve, deep-lobe involvement, and nodal disease[14]. MRI better characterizes cystic/solid components and soft tissue planes. Imaging findings are nonspecific but often show well-defined, lobulated lesions, occasionally with cystic change[14].

Tissue diagnosis- *FNAC* (fine needle aspiration cytology) is commonly performed as an initial tissue test for parotid masses; however, cytology can be challenging because SC may be misinterpreted as acinic cell carcinoma or other low-grade salivary tumours. When FNAC is indeterminate or suggests malignancy, core biopsy or excision biopsy (in a planned surgical setting) may be required[7,9].

Histopathology: SC shows variable architecture - microcystic, tubular, papillary-cystic or solid patterns - with uniform cells that often have vacuolated/eosinophilic cytoplasm and bland nuclei. Periodic acid-Schiff (PAS)-positive secretions may be present. Morphology alone can overlap with other entities[7,8].

Immunohistochemistry (IHC) and molecular testing- IHC panel typically shows positivity for S-100, mammaglobin, and often GCDFP-15; these markers support the diagnosis but are not entirely specific. Pan-TRK IHC (detecting TRK A/B/C protein expression) is a practical screening immunostain because many SCs harbor NTRK fusions; positive pan-

TRK should prompt confirmatory molecular testing[15]. Several studies show pan-TRK IHC is a useful screening tool but requires careful interpretation (to avoid false positives from physiologic TRK expression or staining artefact)[15].

Differential diagnosis includes acinic cell carcinoma, low-grade mucoepidermoid carcinoma, adenocarcinoma NOS, and intraductal carcinomas[16].

Surgery (mainstay) -Surgical excision (*parotidectomy*) is the cornerstone for localized disease. The choice between superficial, total, or extended parotidectomy depends on tumour location (superficial vs deep lobe), size, proximity to or involvement of the facial nerve, and presence of regional nodes[4,16]. Preservation of the facial nerve is prioritized where oncologically safe; nerve sacrifice is considered only with direct tumor infiltration. Neck dissection is indicated for clinically or radiologically positive nodes[16].

Radiotherapy -Adjuvant external beam radiotherapy is considered for adverse pathological features - positive or close margins, perineural invasion, high T-stage, lymph node metastases, or high-grade transformation[9]. For most low-grade SC completely excised with negative margins, adjuvant radiotherapy is not routinely required[9]. Evidence is largely drawn from salivary gland management principles and case series rather than randomized trials[9,13].

Systemic therapy - targeted TRK inhibitors -Because many SCs harbors NTRK fusions, selective TRK inhibitors are an important option for advanced, unresectable, recurrent or metastatic disease: *Larotrectinib* and *entrectinib* are oral TRK inhibitors that have shown high response rates in NTRK fusion-positive tumors across histologies, including secretory carcinoma of the salivary gland -durable responses and occasional complete remissions have been reported in case series and pooled trials[10]. These agents are used when a tumor harbors an actionable NTRK fusion and systemic therapy is indicated[4,10].

Chemotherapy/Other systemic options- Conventional cytotoxic chemotherapy has limited and inconsistent activity in salivary gland carcinomas; its use is typically reserved for palliative intent when targeted therapy is not an option[10]. Enrollment in clinical trials is encouraged where possible. Harrison's and oncology reviews discuss systemic options in advanced head-and neck and salivary malignancies[10].

However, long-term follow up is essential due to risk of recurrence or, less commonly, lymph node/distant spread.

CONCLUSION

From a public health and preventive medicine perspective although secretory carcinoma is rare and accounts for a tiny fraction of salivary gland neoplasms, awareness of newer tumor entities, improved diagnostic pathology including molecular diagnostics, and early detection are important. Given that malignancies in salivary glands may be misdiagnosed, accurate classification assists in prognostication, guiding treatment modalities, and potentially improving outcomes. The rarity also implies challenges in generating large clinical series and in resource-limited settings the reliance on morphology and immunohistochemistry becomes more crucial.

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