CASE OF THE MONTH
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HISTORY

- 51 yr old male presented with swelling on right side of face since 7 months
- No history of pain/ fever/ weight loss/ night sweats/ radiation exposure
- No H/O any past surgery/ past therapy/ chronic illness
- Family history: not significant

CLINICAL EXAMINATION

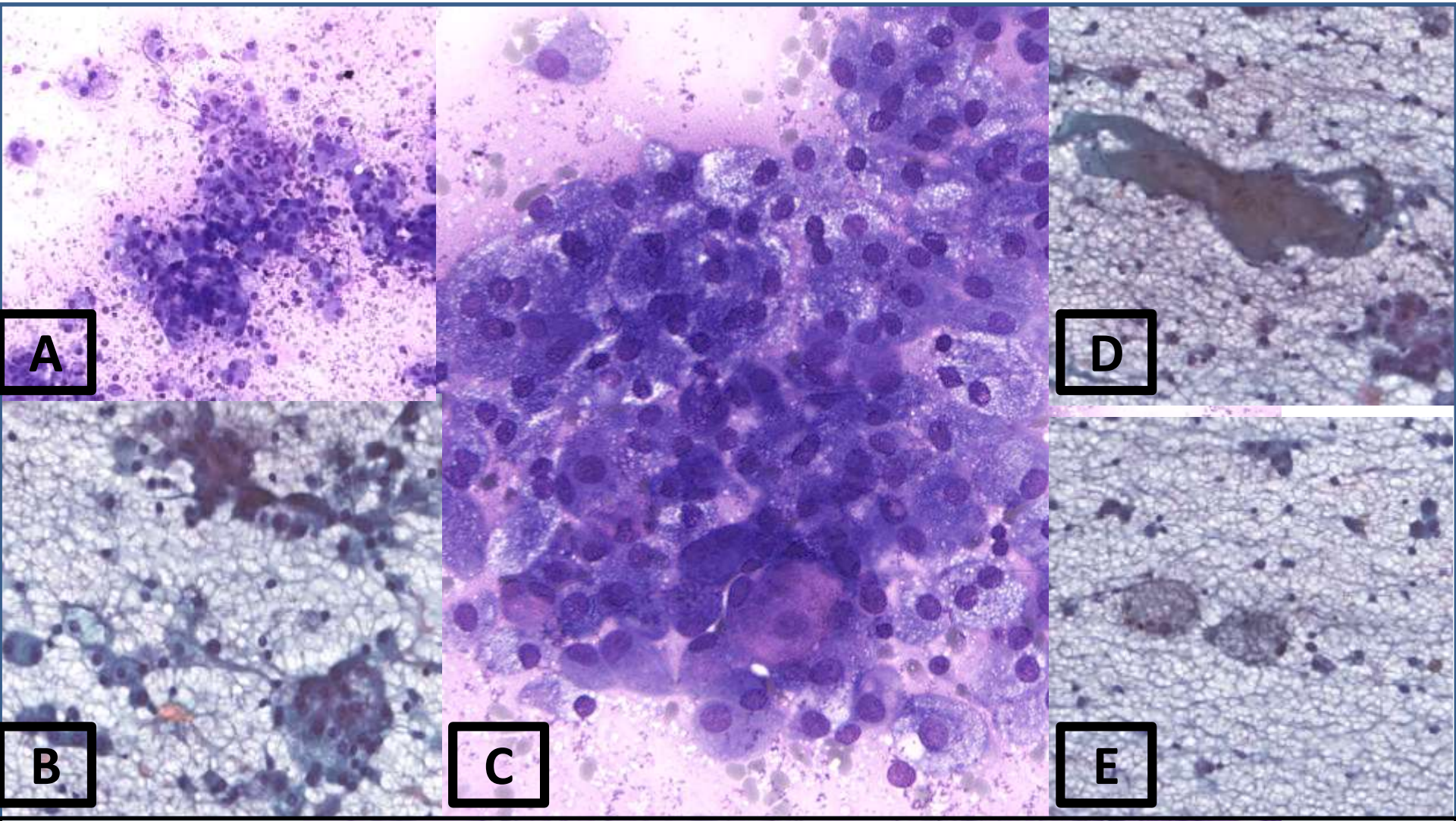
- 1.5 X 1cm swelling over right parotid area
- Mobile, superficial
- Cystic
- Non tender

INVESTIGATIONS

- CT Scan neck with face
  - well defined oval hypodense
  - mildly enhancing soft tissue mass
  - in superficial lobe of right parotid

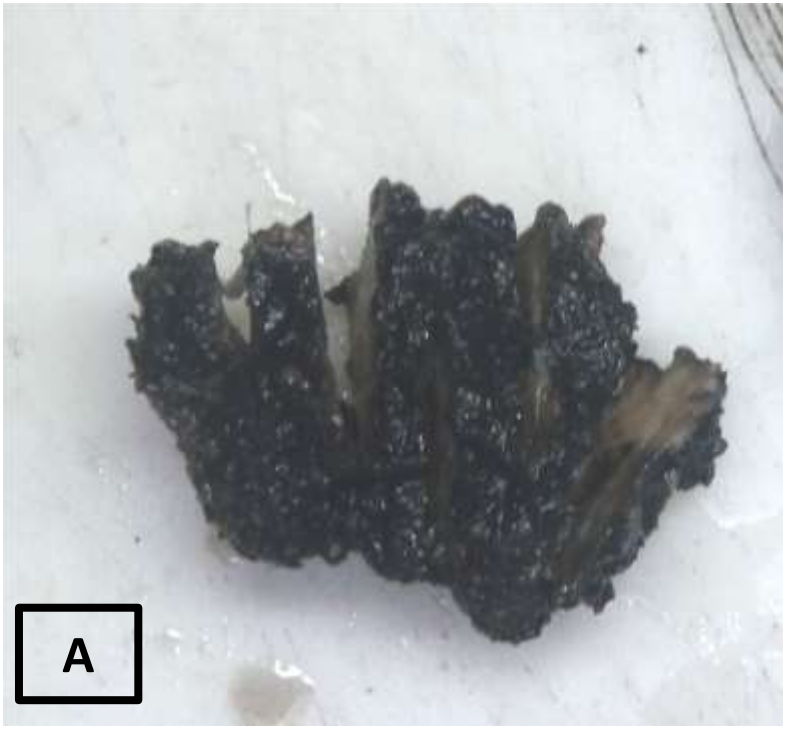
- USG Guided FNAC from right parotid

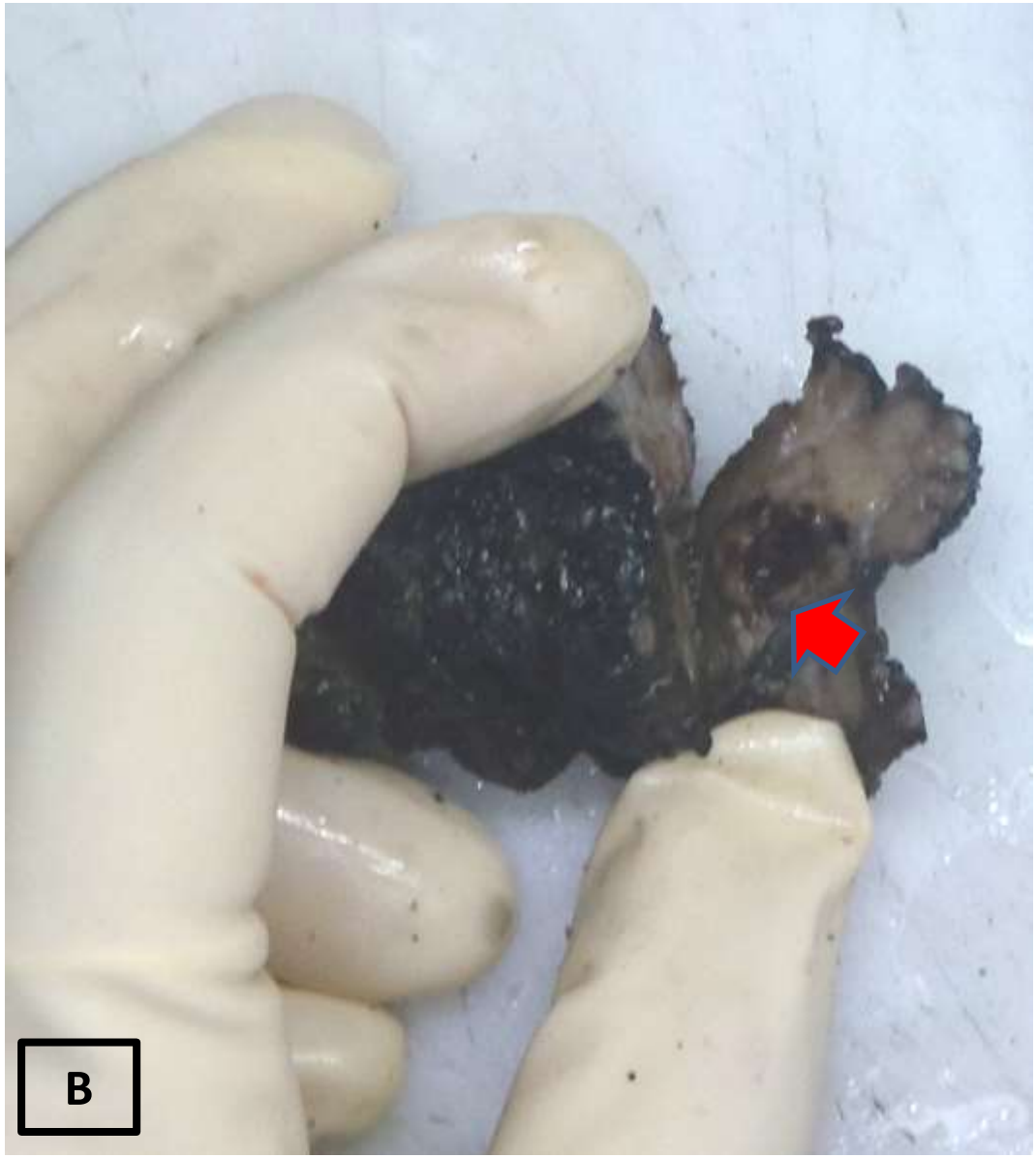
Suggestive of MUCOEPIDERMOID CARCINOMA



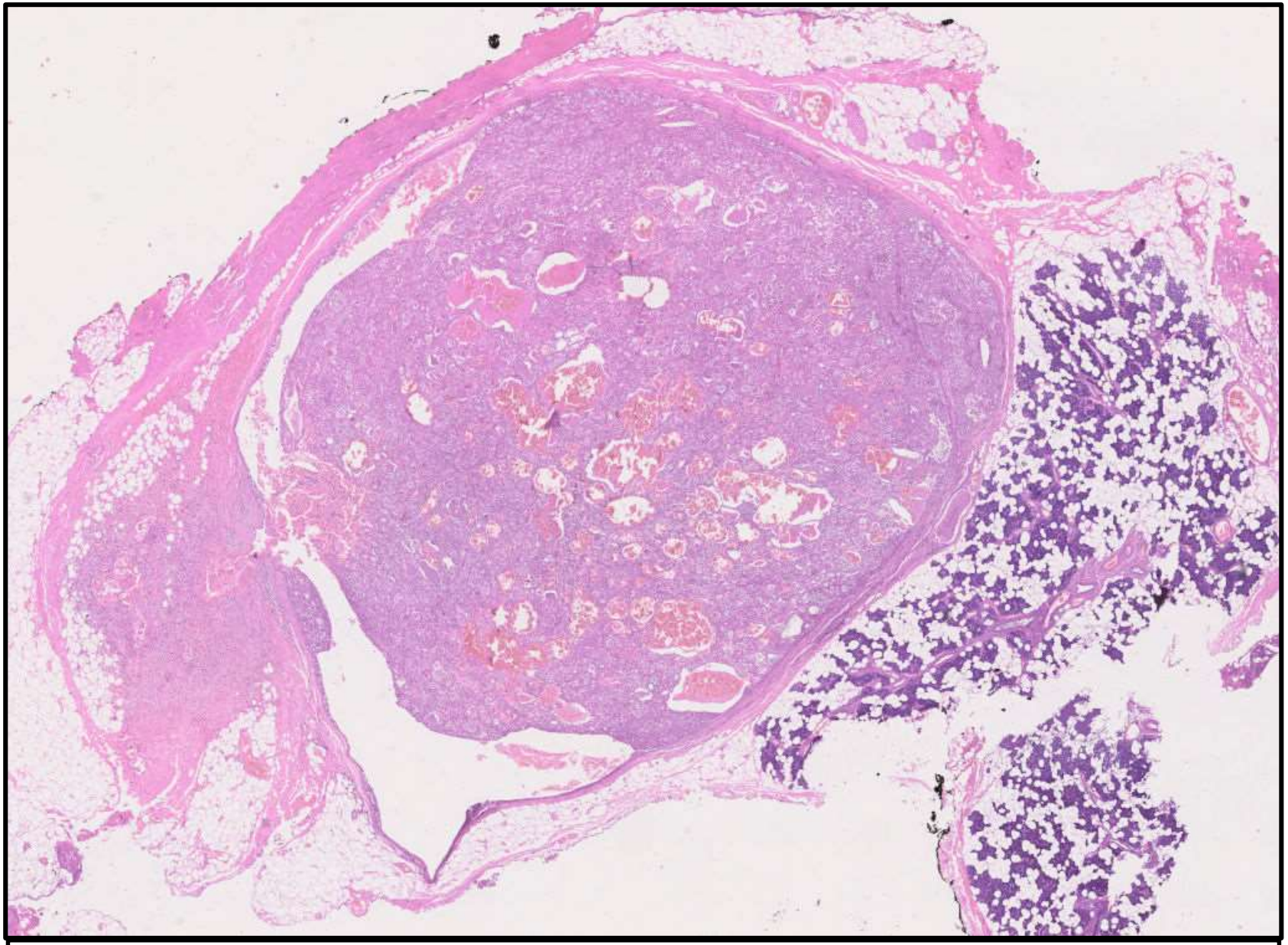
FNAC: A, B. Cellular smears with two population of cells arranged in clusters and singly scattered (MGGX10, PAPX10); C. One with dense cytoplasm and other with vacuolated cytoplasm at the periphery (MGGX20); D. Proteinaceous fluid in the background (PAPX4); E. Intracellular vacuoles (PAPX10)

HISTOPATHOLOGY

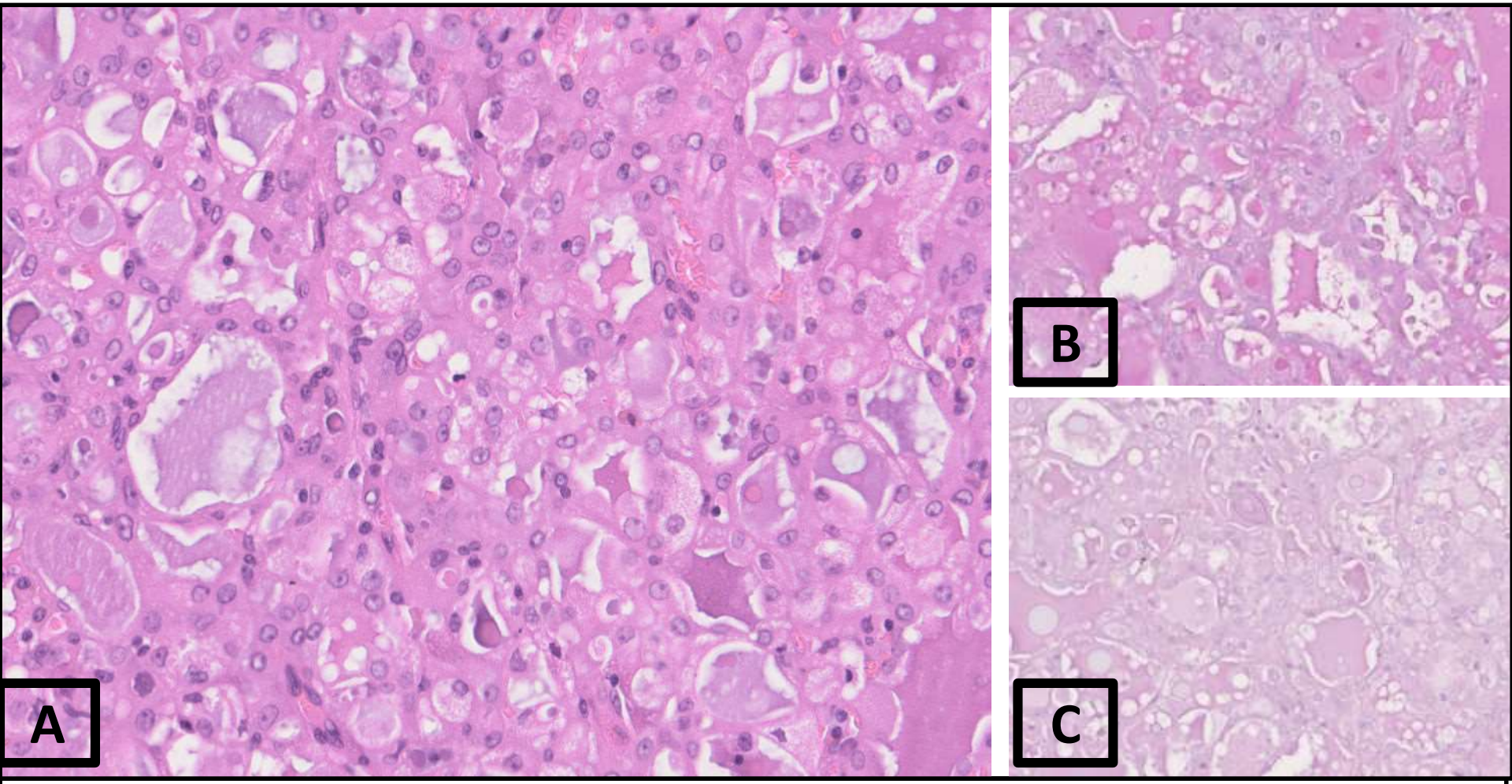




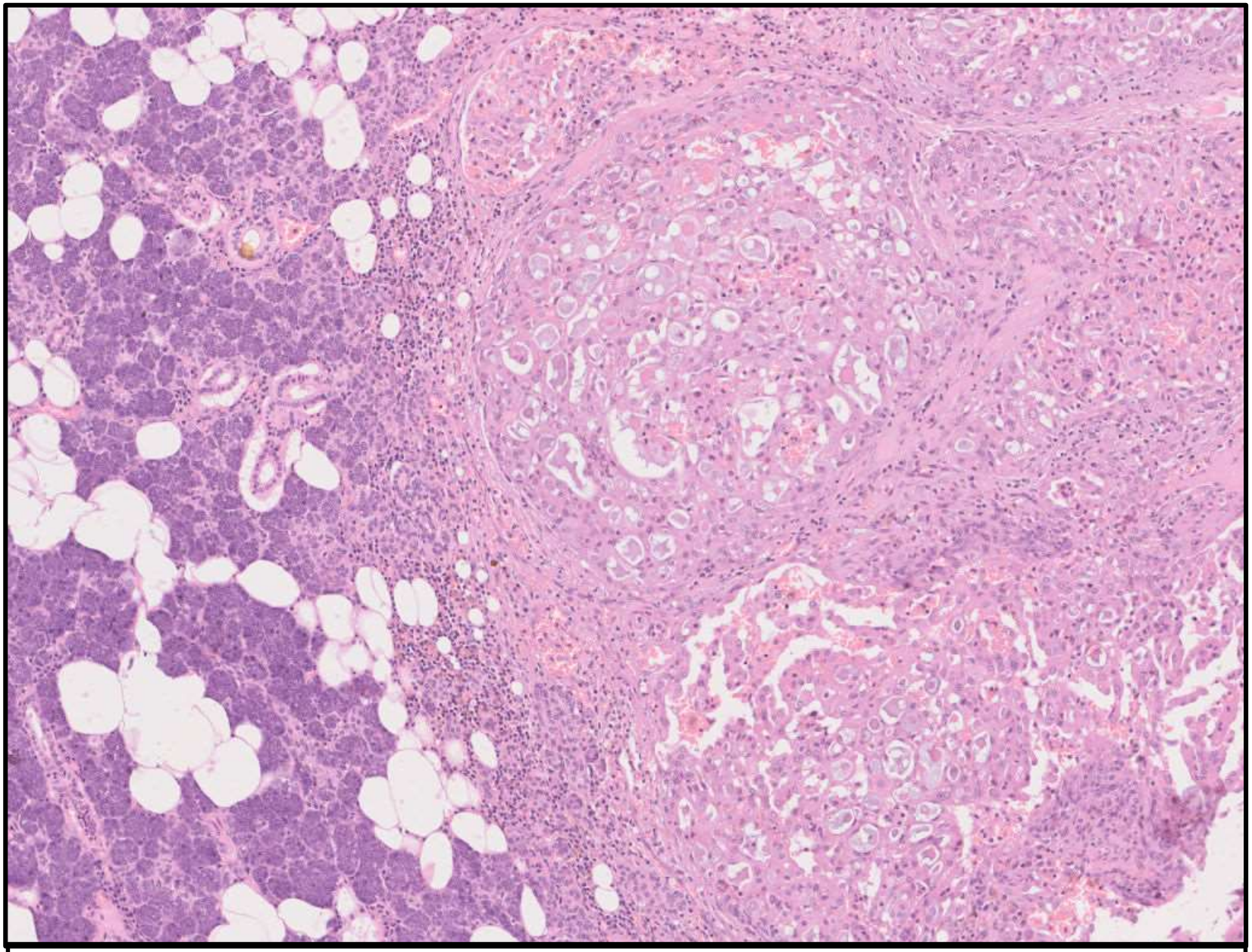
Gross images: A. Parotid gland measuring 5 x 5 x 2CM; B. Well circumscribed grey brown nodule measuring 0.7 x 0.6 x 0.4cm with solid and cystic areas



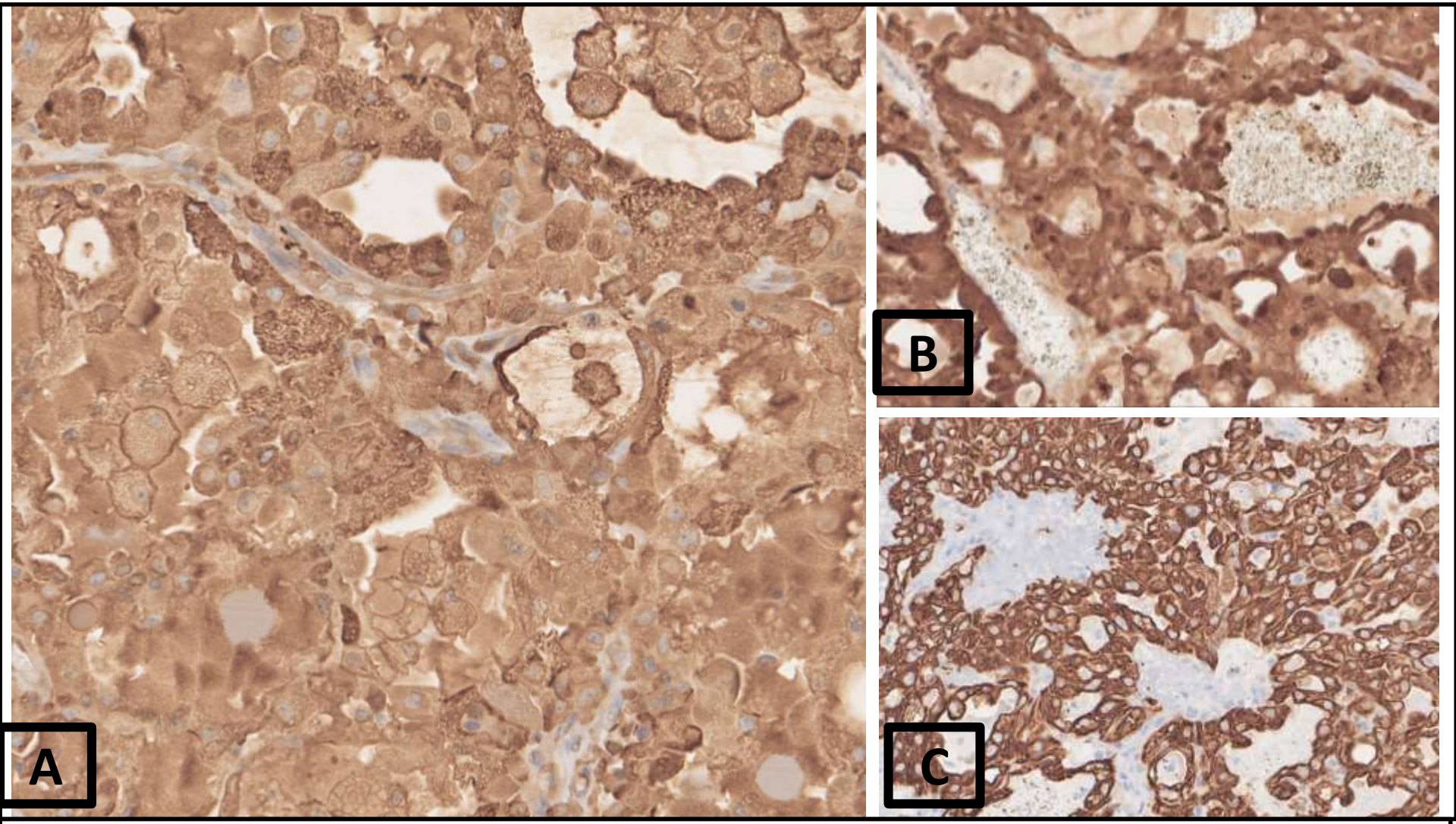
MICROSCOPY: Circumscribed lobulated tumor exhibiting microcystic, follicular and solid growth pattern with luminal secretions (X2,H&E)



A. Tumor cells have eosinophilic granular cytoplasm, round nuclei bland chromatin, and tiny nucleoli. (x20, H&E); B. PAS positive intraluminal secretions (X20, PAS Stain): C. Mucin negative intraluminal secretions (X20 Mucicarmine stain)



Tumor focally merging with the salivary gland parenchyma. No infiltrative edges. (X4,H&E)



IHC: A. The tumor cells and secretions are diffuse strong positive for Mammoglobin; B. S-100 stains both the cytoplasm and nuclei of tumor cells; C. Membrane positivity seen with CK7 (X20)

FINAL DIAGNOSIS

MAMMARY ANALOGUE SECRETORY CARCINOMA

DISCUSSION

- Mammary analogue secretory carcinoma (MASC) - **a newly defined entity**

- Secretory carcinoma was first documented in salivary glands in 2010 by Skalov *et al*. in a series of 16 cases

- These are rare tumors with **an incidence of 3 per 1,00,000**

- MASC has similar histopathology and IHC features to Secretory carcinoma of breast because of origin from the same embryonic ectoderm exhibiting same ductulo-acinar architecture, hence named so

- Mostly located in the parotid region as a painless swelling; can appear in any location of the head and neck region

- All age groups are affected, including children and young adults

- Considered to be a low-grade malignancy; however, high-grade transformation and aggressive clinical behavior has been described

- **Characterized by a specific rearrangement of the *ETV6* gene locus- *ETV6-NTRK3* gene fusion with translocation t(12;15) (p13;q25)**

- **CYTOLOGY:** papillary structures, extracellular and intracellular secretory material, vacuolated cytoplasm, tumor cells with low-grade nuclear atypia.

- Cytology is a diagnostic pitfall .

- Differentials on cytology include acinic cell carcinoma, mucoepidermoid carcinoma or adenocarcinoma

- Misinterpretation of the background secretions as mucin and vacuolated cytoplasm as mucinophages can lead to an inaccurate diagnosis of mucoepidermoid carcinoma as was noted in our case.

- **GROSS:** Poorly circumscribed solid white tan nodules

- **MICROSCOPY:**
  - Invasive growth with multiple nodules in fibrotic stroma
  - Complex architecture with microcystic / cribriform, solid, trabecular, tubular and papillary growth patterns
  - Polygonal eosinophilic cells with vacuolated cytoplasm
  - Intraluminar (sometimes intracytoplasmic) colloid-like mucin secretions

- **SPECIAL STAINS:** PAS and PASD for secretions

- **IMMUNOHISTOCHEMISTRY:** Mammaglobin, GATA3, and Low Ki67 (1 - 7%)

- **MOLECULAR TESTING:**

  -FISH (on paraffin sections) to detect chromosome translocation **t(12;15)(p12;q25)**

  -RT-PCR or NGS (RNA template) to detect **ETV6-NTRK3 gene fusion**

DIFFERENTIAL DIAGNOSIS

- Acinic cell carcinoma, Mucoepidermoid carcinoma and Adenocarcinoma-NOS
- Acinic cell carcinoma- contains blue-purple cytoplasmic zymogen granules, a sign of serous acinar differentiation
- Mucin production and occasional differentiation into serous cells may point towards MEC. However, MASC does not contain the combination of goblet-type mucous cells, intermediate and squamoid/epidermoid cells characteristic of MEC

	SECRETORY CARCINOMA	ACINIC CELL CARCINOMA	MUCOEPIDERMOID CARCINOMA
POSITIVE STAINING OF TUMOR CELLS	S-100 Mammoglobin	Amylase S-100 DOG-1	P63 Cytokeratins
NEGATIVE STAINING OF TUMOR CELLS	P63	P63	S100
GENETICS	ETV6-NTRK3	None	CRTC1-MAML2; CRT3-MAML2

- **TREATMENT:**
  - Surgical excision, usually total thyroidectomy with lymph node dissection
  - Does not respond to RAI
  - **ETV6-NTRK3 is a "druggable" fusion**
  - Trk inhibitors are currently used for MASC patients in clinical trials

CONCLUSION

- Mammary analogue secretory carcinoma is a rare salivary gland tumour which was often diagnosed as acinic cell carcinoma, mucoepidermoid carcinoma or adenocarcinoma in the past

- Can often be misdiagnosed on fine needle aspiration cytology

- Histopathology with the aid of appropriate immunohistochemistry and molecular testing can help in the correct diagnosis and appropriate treatment of this low grade carcinoma

THANK YOU!