Case Report

Mammary analogue secretory carcinoma presenting as a cystic parotid mass

Karisma Gupta[a], Hafiz S. Patwa, MD[b], Angela G. Niehaus, MD[c], Gileno O.F. Filho, MD[b], Christopher M. Lack, MD, PhD[a],*

[a] *Department of Radiology, Wake Forest School of Medicine, Medical Center Blvd, Winston-Salem, NC 27157, USA*
[b] *Department of Otolaryngology, Wake Forest School of Medicine, Medical Center Blvd, Winston-Salem, NC 27157, USA*
[c] *Department of Pathology, Wake Forest School of Medicine, Medical Center Blvd, Winston-Salem, NC 27157, USA*

ABSTRACT

We present a case of a 63-year-old male with an 8-year history of a left-sided cystic facial mass which recurred despite multiple drainage procedures. Imaging findings showed a cystic mass in the left parotid gland and it was surgically resected. Pathology confirmed it to represent a mammary analogue secretory carcinoma, a relatively newly described entity. This case illustrates that mammary analogue secretory carcinoma can masquerade as a cyst within the parotid gland.

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Introduction

Parotid gland masses frequently present as clinical and radiographic challenges. Around 80% of the masses in the parotid gland are benign, but low-grade and high-grade tumors represent a significant proportion of masses. [1,2] Clinically, benign parotid masses usually present as a slow growing and painless mass without associated facial nerve deficits or lymphadenopathy. Symptoms suggesting a malignant parotid mass include a rapidly enlarging mass, facial nerve deficits, or metastatic lymphadenopathy. Unfortunately, there can be a considerable overlap in symptoms, leading to further investigations in order to establish a more definitive diagnosis.

Imaging of parotid masses is often nonspecific. The most common etiologies of benign parotid masses include

pleomorphic adenomas and Warthin tumors. [2] Previous studies have tried to characterize imaging appearances to assist in establishing a specific diagnosis, but a significant overlap between the different pathologies exists. [3] Thus, imaging is often used to delineate the extent of the mass, surrounding anatomy, and guide fine needle aspirations or surgical excision. Imaging can also evaluate for enlarged or necrotic lymph nodes suggestive of metastatic lymphadenopathy.

Here we report a case of a recently described entity known as mammary analogue secretory carcinoma (MASC). This is a tumor of the salivary gland that bears some resemblance to breast secretory carcinoma. [4] Clinically, MASC follows an indolent course in most patients and is associated with a favorable prognosis.

Case report

Clinical presentation

A 63-year-old African-American male presented to our clinic with an 8-year history of left sided facial mass with associated tenderness, hypesthesia, muffled hearing, and restricted jaw movement. The mass was initially pea-sized but had started to grow over the past 5 years. During that time, he reported receiving 4-5 outpatient drainage procedures of the mass that produced "motor oil" fluid, only to experience regrowth of the cystic mass over time. After the most recent drainage, it regrew over a 2-week course to a "grapefruit-sized" mass, prompting him to present to our otolaryngology clinic for further evaluation and treatment.

On examination, he was found a large cystic nontender mass overlying, and likely involving, the left parotid gland. The mass grossly measured about 10 cm in diameter, causing some soft tissue expansion and displacing the left ear lobule posteriorly and superiorly. Facial nerve appeared to be grossly intact and symmetric. There was no palpable anterior cervical lymphadenopathy. In-office ultrasonography was performed, showing a cystic mass that contained turbulent material. Given its cystic nature, differential diagnosis at time of examination included a first branchial cleft cyst, lymphatic malformations, Warthin tumors, or a necrotic lymph node. Decision was made to obtain an Magnetic resonance imaging (MRI) of the neck to better delineate the mass, including its margins, relationship with adjacent deep lobe of the parotid gland, and assess for potential facial nerve involvement.

Imaging

MRI of the neck was performed before and after intravenous administration of gadolinium-based contrast. Imaging showed a 6.2 cm T1 and T2 hyperintense mass lesion centered in the superficial portion of the left parotid gland. There were several nodular soft tissue areas along the wall of the cyst which were thought to arise from the left parotid gland and protruding into the cyst. No ductal enlargement was seen within the parotid or along the course of the parotid duct. No abnormal surrounding soft tissue signal was seen

to suggest significant inflammation or cellulitis. No connection with the external auditory canal was identified to suggest a first branchial cleft cyst (Fig. 1). Overall, imaging findings were most suggestive of a large cystic mass in the superficial portion of the left parotid gland. Differential considerations included an atypical appearance of the most common neoplasms of the parotid gland including pleomorphic adenoma and Warthin tumor as well as cystic non-neoplastic etiologies such as a sialocele or possibly an atypical first branchial cleft cyst.

Management options and surgical description

Given the size of the mass, cosmetic deformity, and history of prior recurrences, surgical treatment was deemed to be the appropriate management option for curative reasons and definite diagnosis. The patient subsequently underwent excision of left facial mass including left superficial parotidectomy and excision of facial skin. The subsequent defect was reconstructed with a cervicofacial rotational flap. Consistent with exam findings and imaging, the mass was found to be very superficial beneath the skin, extending down to the superficial lobe of the parotid. The superficial lobe, along with the mass, was gently dissected off the facial nerve (Fig. 2). An approximately 2.5 cm left level 2 lymph node was identified during surgery and was sent for pathologic examination.

Macroscopic and histopathological findings

The left superficial parotid gland was submitted for pathological evaluation. The specimen grossly consisted of an $8.7 \times 7.5 \times 6.7$ cm fragment of skin with underlying soft tissue and was serially sectioned to reveal an $8.5 \times 7.5 \times 5.6$ cm cyst containing dark red hemorrhagic fluid with no appreciable solid component. The internal fluid was not sent for specific laboratory analysis.

Sections show an unremarkable parotid gland adjacent to a low-grade salivary gland neoplasm. The neoplastic cells have vesicular nuclei with small nucleoli with abundant pale to eosinophilic secretions. The neoplasm is characterized by large nests of cells showing a nodular pattern of growth and invasion with a tubular to follicular pattern. Minimal mitotic figures are identified (1 mitotic figure/10 high power field). No tumor necrosis is appreciated. The left level 2 lymph node was normal in appearance.

A panel of immunohistochemical stains was performed and revealed the neoplastic cells were positive for cytokeratin AE1/AE3, cytokeratin 7, epithelial membrane antigen (EMA), and S-100 with patchy positivity for cytokeratin 5/6. The tumor was negative for SOX-10 and gross cystic disease fluid protein 15 (GCDFP-15), smooth muscle myosin (SMM), smooth muscle actin (SMA), cyclin D1, p63, and C-kit.

Additional immunohistochemical stains were performed at a reference laboratory and reportedly the tumor cells were patchy positive for mammaglobin with DOG1 stain exhibiting focal weak luminal reactivity. The immunohistochemical staining pattern was not entirely specific for a definitive diagnosis; thus, molecular analysis was performed. Florescent in-situ hybridization for t(12;15)(p12;q25) translocation, which
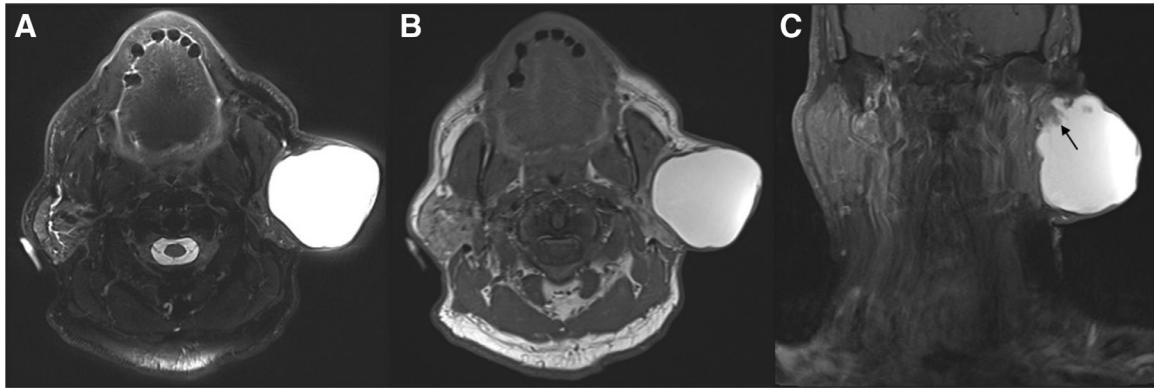
Fig. 1 – MRI of the face and neck with and without contrast. (A) Axial T2 fat-saturated sequence. There is a 6.2 cm hyperintense mass arising from the superficial portion of the left parotid gland. (B) Axial T1 noncontrast sequence. The mass is intrinsically T1 hyperintense suggesting proteinaceous material or hemorrhage. (C) Coronal T1 fat-saturated sequence with contrast. Small amount of soft tissue nodularity is noted along the margins of the mass (arrows) which is contiguous with the parotid gland. No significant enhancement is noted of the wall of the lesion or the nodularity.
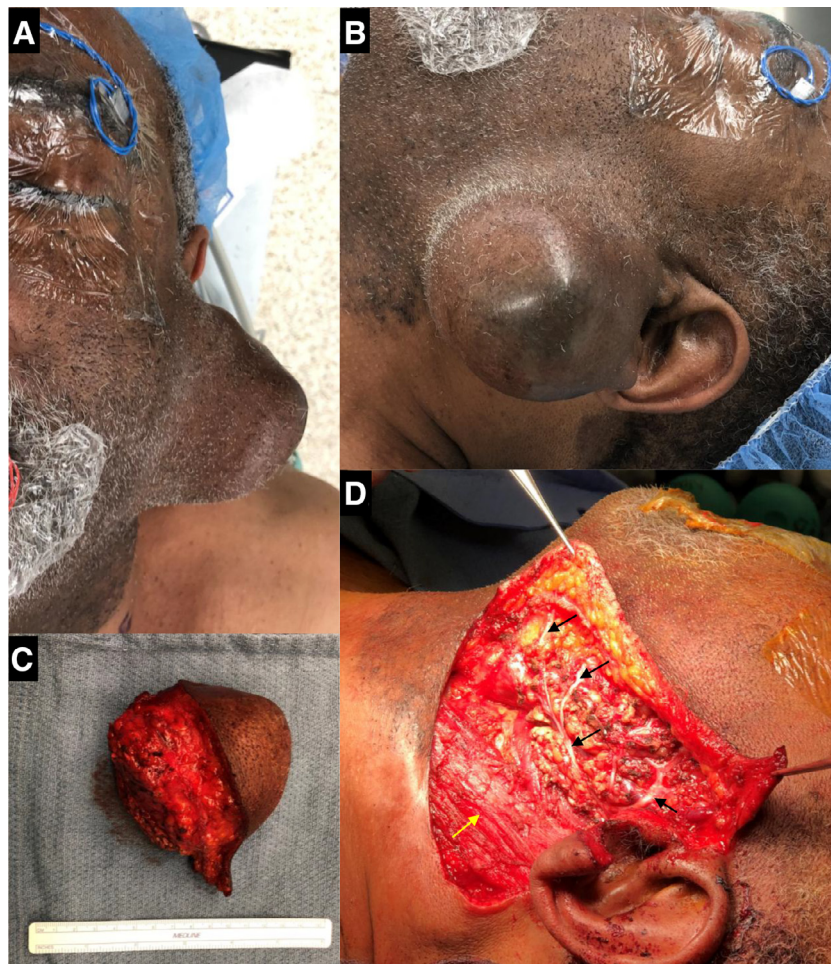

Fig. 2 – (A) Frontal view of the left parotid mass. (B) Left lateral view of the parotid mass. (C) Encapsulated parotid mass after excision with overlying skin. (D) Left parotid bed after surgical resection of mass with intact upper and lower divisions of facial nerve (black arrows) and sternocleidomastoid muscle (yellow arrow).
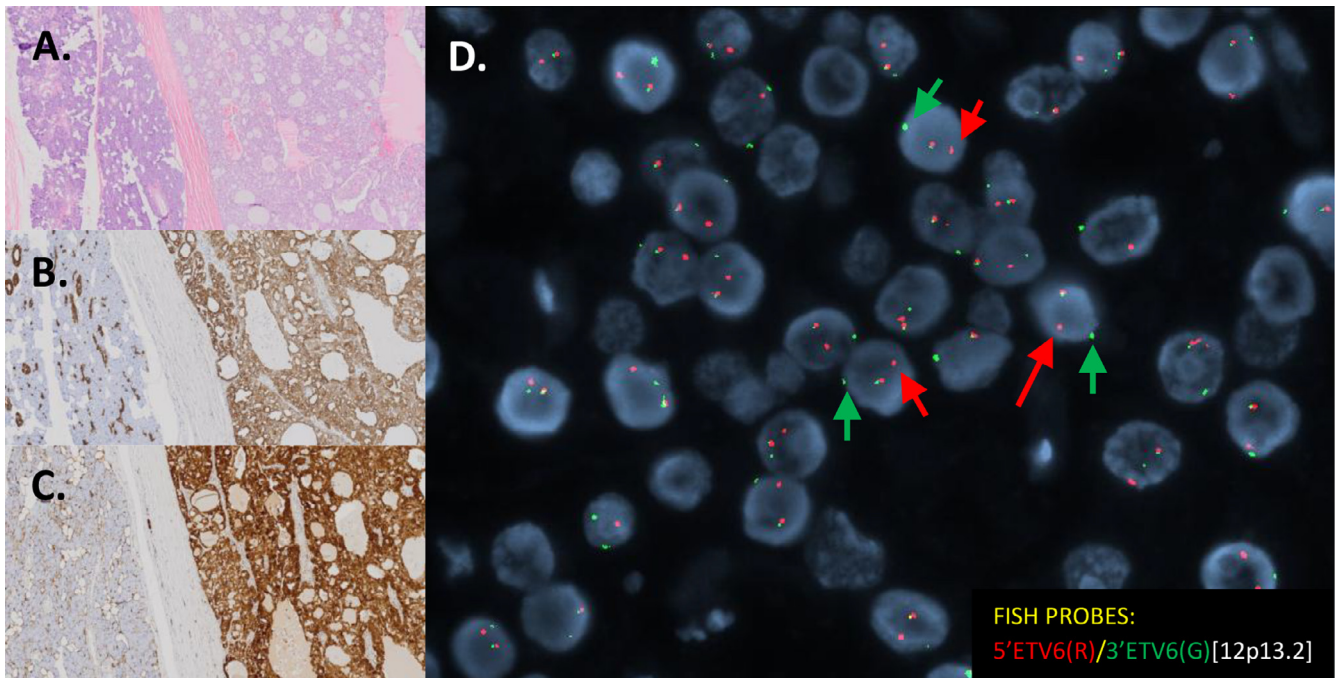
Fig. 3 – (A) Low power view demonstrates normal parotid gland (left) composed of serous acini, ductal epithelial cells with admixed adipose tissue adjacent to a low-grade salivary neoplasm (MASC, right) with a follicular growth pattern and abundant pale to eosinophilic (colloid-like) secretions (hematoxylin-eosin, original magnification ×2). (B) Immunohistochemistry (IHC) for MASC (right-neoplasm): Cytokeratin AE1/AE3 IHC shows strong diffuse cytoplasmic staining as compared to the parotid gland (left-normal), highlights ductal epithelial cells (original magnification ×4). (C) IHC for MASC (right-neoplasm): S100 protein shows strong diffuse cytoplasmic staining as compared to the parotid gland (left-normal) where S100 protein has immunoreactivity for myoepithelial cells (original magnification ×4). (D) Fluorescent in-situ hybridization (FISH) break-apart for ETV6: showing separation of the red and green signals (as highlighted by the arrows) indicating a break in the gene sequence and confirming the diagnosis of MASC. Analysis, interpretation, and image rendered by Mayo Clinic Genomics Laboratory, courtesy of Drs. Patricia T. Griepp and William R. Sukov.

results in the ETV6-NTRK3 gene fusion, was performed. Result was positive, confirming the diagnosis of mammary secretory carcinoma (Fig. 3).

Immediate postoperative period was complicated by left marginal mandibular nerve weakness and a hematoma under the local advancement flap, requiring bedside drainage and irrigation, placement of Penrose drain and application of pressure dressing. From there, the patient progressed well, and he was discharged home. However, he returned to our emergency department 3 days later with recurrence of a hematoma, requiring wider drainage, antibiotic treatment, and daily irrigation with Dakin's solution. Local wound care was then performed with iodoform gauze packing with eventual secondary intention healing of the wound over the course of 2 months. The patient did not have any signs or symptoms of metastatic disease but was subsequently lost to follow-up despite multiple attempts of re-establishing care.

Discussion

Most parotid tumors are slow-growing and painless masses, but some may present with symptoms such as fast growth, focal pain, facial nerve palsy, otalgia, ulceration, and cervical adenopathy, which raise a red flag and increase suspicion of malignancy [5]. MRI and CT can be used to potentially differentiate between benign and malignant lesions using findings such as ill-defined margins, extra-glandular infiltrative growth into surrounding tissue, and signal intensity [3]. However, none of these characteristics are highly specific for malignancy.

The most common malignant etiologies include mucoepidermoid carcinoma, adenoid cystic carcinoma, acinic cell carcinoma, and carcinoma ex-pleomorphic adenoma. [2] Systemic disease such as lymphoma and metastatic disease, especially from adjacent cutaneous malignancies should also be considered. Purely cystic masses would suggest either a cystic Warthin tumor, cystic metastatic disease from squamous cell carcinoma, sialocele, or cysts associated with HIV or Sjögren syndrome. Our case demonstrates that the relatively new entity of MASC should also be included in the differential diagnosis for cystic parotid masses masquerading as a recurrent cyst.

MASC was first described by Skalova and others in 2010 [4]. It has a preference for male patients (8:2) [6] with a mean age of presentation at 47 years of age [7]. It classically presents as a painless, nontender mass that increases in size

over time [4]. The majority of MASC arise from the parotid gland (70%), while other locations include the submandibular gland, soft palate, buccal mucosa, base of tongue, and lips [6,8].

MASC is characterized by its histologic and genetic similarities to secretory carcinoma of the breast and can be difficult to distinguish from acinic cell carcinoma. Histologically, MASC has a circumscribed lobulated growth pattern composed of uniform neoplastic epithelial cells with either cystic, tubular, solid, or papillary architecture. These tumor cells contain low-grade vesicular nuclei and abundant eosinophilic homogenous secretory material [9]. The histological appearance can resemble that of acinic cell carcinoma. In fact, a large proportion of tumors diagnosed as acinic cell carcinoma may in fact be MASCs [7]. Internal hemorrhage has recently been suggested as a finding that can distinguish MASC from acinic cell carcinoma. [10] This may explain why our case demonstrated increased T1 signal within the lesion and repetitive drainages yielded "motor oil" fluid - both compatible with older blood products.

Immunohistochemically, MASCs are often positive for S-100 protein, epidermal growth factor eceptor, and vimentin while negative for estrogen receptor, progesterone receptor, and HER2. MASC has a recurrent balanced chromosomal translocation t(12;15) (p13;q25) ETV6-NTRK3, a fusion gene that encodes for a chimeric tyrosine kinase known to play a role in the oncogenic transformation of epithelial cells in mammary glands [11]. Both MASC and SC of the breast share the t(12;15)(p13;q25) translocation which results in the fusion of the ETV6-NTRK3 gene. MASC and SC of the breast also share positive S100 protein, EMA, and vimentin, while being triple negative for ER, PR, and Her2. [12] Current definitive diagnoses guidelines require testing of the t(12;15)(p12;q25) translocation, however negative test for the ETV6-NTRK3 gene does not rule out diagnosis of MASC. [12] The diagnosis can be done with the presence of positive immunohistochemical studies of STAT5a, mammaglobin, and S-100[4].

MASC is currently treated as a low-grade carcinoma with an overall favorable prognosis, however some have been reported to have the potential for regional and distant metastases [8]. Some sources report a moderate risk for local recurrence (15%), a moderate risk of lymph node metastases (20%), and a low risk for distant metastases (5%) [4,13–15]. There have been reports of high-grade transformations of MASC that have resulted in aggressive tumors with a higher rate of dissemination and death [13]. Of the 91 reported cases of MASC, only 4 cases reported death from the disease; however, survivability data was poor due to minimal follow-up [16]. Current treatment guidelines of MASC are not well-defined due to low rate of literature reports, but historically have not been treated any differently to other low-grade malignant salivary gland cancers [16]. Treatments have included neck dissections with or without postoperative radiotherapy and adjuvant chemotherapy.

Conclusion

Clinical and radiological findings of parotid gland masses are nonspecific and require a wide differential diagnosis, including both benign or malignant processes. MASC is a low-grade malignant salivary gland tumor with characteristic morphology and immunohistochemical profile. The differential diagnosis by histology includes, but is not limited to, acinic cell carcinoma and polymorphous low-grade adenocarcinoma. MASC, however, has a unique and a distinctive molecular translocation t(12;15)(p13;q25) resulting in ETV6-NTRK3 fusion product. Our case demonstrates that the relative newly described MASC should be included in the differential diagnosis of cystic parotid gland tumors.

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