A Systematic Review Including an additional Pediatric Case Report: Pediatric Cases of Mammary Analogue Secretory Carcinoma

Amanda L. Ngouajio BS1, Sarah M. Drejet MD1, D. Ryan Phillips MD, MS1, Don-John Summerlin DMD, MS2, John P. Dahl, MD, PhD, MBA1 *

1Department of Otolaryngology Head and Neck Surgery, Indiana University School of Medicine, Indianapolis, IN USA

2Department of Pathology and Laboratory Medicine, Indiana University School of Medicine, Indianapolis, Indiana USA

Conflict of Interest: none

Financial disclosure: none to report

*Corresponding Author: John P. Dahl, MD, PhD, MBA, Department of Otolaryngology-Head and Neck Surgery, Indiana University School of Medicine, Fesler Hall, 1130 W. Michigan Street, Suite 400, Indianapolis, IN  46202-5209, 317.278.1258, 317.274.8285(fax), jpdahl@iu.edu

This is the author’s manuscript of the article published in final edited form as:

ABSTRACT

Importance
Mammary Analogue Secretory Carcinoma (MASC) is a newly characterized salivary gland carcinoma resembling secretory carcinoma of the breast. Prior to being described, MASC was most commonly misdiagnosed as Acinic Cell Carcinoma. Though MASC is predominantly an adult neoplasm, cases have been reported in the pediatric population. Reporting and summarizing of known cases is imperative to understand the prognosis and clinical behavior of MASC.

Objective
(1) Report a rare case of pediatric MASC
(2) Review and consolidate the existing literature on MASC in the pediatric population

Evidence Review
Web of Science, Medline, EMBASE, and The Cochrane Library were searched for studies that included pediatric cases of MASC. Data on clinical presentation, diagnosis and management, and pathology were collected from all pediatric cases.

Findings –

Case Report
14 year old with left-sided parotid mass diagnosed as MASC based on histology and immunohistochemistry. He was managed surgically with left superficial parotidectomy with selective neck dissection.

Literature review
The majority of MASC cases have been identified via retrospective reclassification of previously misclassified salivary gland tumors. Of all the pediatric cases (N=11) of MASC, the female-to-male ratio is 1:1.2 with an age range of 10-17 years old. The most common clinical presentation was a slowly growing, fixed, and painless mass of the parotid gland, often detected incidentally on physical examination. Common pathological features include eosinophilic vacuolated cytoplasm within cystic, tubular, and/or papillary architecture. Immunohistochemistry showed positivity for S100, mammaglobin, cytokeratin 19, and vimentin. The diagnosis was confirmed by the detection of the characteristic ETV6-NTRK6 fusion gene via fluorescent in-situ hybridization (FISH). Only 4 cases discussed treatment. Each of these underwent successful surgical resection alone with or without lymph node dissection.

Conclusions and Relevance
Since the first case of MASC in the pediatric population was described in 2011, only 12 cases, including this one, have been described in the literature. With this paucity of information, much remains unknown regarding this new pathologic diagnosis. The collection of clinical outcomes data of children with MASC is needed to better understand the behavior of this malignancy as well as determine optimal treatment regimens.
Key Words
Mammary analog secretory carcinoma; mammary analogue secretory carcinoma; MASC; pediatric
1. INTRODUCTION

Mammary Analogue Secretory Carcinoma (MASC) of the salivary glands is a recently described pathologic entity of unknown incidence that resembles secretory carcinoma of the breast. Both tumors share the balanced translocation t(12;15) (p13;q25) forming the $ETV6$-$NTRK6$ fusion gene which encodes a chimeric tyrosine kinase. Prior to its description, MASC was most likely identified as salivary acinic cell carcinoma (AcICC), mucoepidermoid carcinoma (MEC), cystadenocarcinoma, or other salivary gland tumors; each shares overlapping histological and immunohistochemical features. With detection of the translocation by fluorescent in-situ hybridization (FISH), the current gold standard for diagnosis, many cases previously diagnosed as aforementioned salivary gland tumors have been retrospectively reclassified as MASC.

There are currently four pediatric case reports in the current literature dating back to 2011 describing patients with MASC. Recent case reports and studies have made efforts to describe the unique cytopathological and clinical characteristics as a means to accurately differentiate and diagnose MASC. Some key features identified include:

- Slow growing, fixed, and painless nodule, often detected incidentally on physical examination.
- Eosinophilic vacuolated cytoplasm within cystic, tubular, and/or papillary architecture.
- Secretions that stain positive for periodic acid Schiff (PAS) and are diastase-resistant.
- Low-grade, pale nuclei, and rare mitotic figures.
- Positive staining for S-100, mammaglobin, vimentin, cytokeratin.
The purpose of this study is to report a rare case of pediatric MASC as well as to review and consolidate the existing literature involving this new salivary gland malignancy within the pediatric population.

2. METHODS

The institutional review board (IRB) reviewed the included case report and it was determined that no further approval was required. Photo consent was obtained and all patient information was handled in a manner consistent with the Health Insurance Portability and Accountability Act (HIPAA).

We reviewed the clinical records of one child with MASC treated at our tertiary care pediatric hospital. Data collected included basic demographic information, clinical notes, pathology, laboratory and radiologic reports relevant to this study. The patient’s medical history including: past medical history, surgical history, and social history were retrieved from the electronic medical record.

A literature review was performed to identify all documented cases of patients with MASC in the pediatric population. A medical librarian was enlisted to employ the search strategy included in eFigure 1 (Supplement 1). Web of Science, Medline, EMBASE, and The Cochrane Library were queried and the resultant articles screened by four independent reviewers. Only studies that included pediatric cases of MASC were included. Clinical presentation, diagnosis and management, and pathology were collected for each documented case.
3. RESULTS

3.1 Clinical Presentation – Case Report

A 14-year-old otherwise healthy male presented with a history of a left-sided facial mass that had been increasing in size for several months. The lesion was painless and without associated symptoms. Physical exam revealed a 3 cm firm, immobile mass in the patient's left parotid gland with no overlying skin changes. Facial movement and symmetry were intact bilaterally. A computed tomography (CT) scan (Figure 1) and positron emission tomography (PET) were obtained which demonstrated a cystic, peripherally enhancing mass centered in the left parotid gland measuring 2.6 cm x 2.1 cm. The left cervical lymph nodes, predominantly level 2, were non-pathologically enlarged and mildly hypermetabolic.

An ultrasound-guided fine-needle aspirate (FNA) and core biopsy were performed and found to have cytologic features consistent with MASC. Following review by the multidisciplinary head and neck tumor board, the decision was made to proceed with left superficial parotidectomy with facial nerve (FN) dissection and left neck level II lymph node dissection. The surgery and post-operative course were uncomplicated. The tumor board recommended no further therapy and the patient is currently under routine surveillance. Furthermore, the patient is disease free at 14 months post-operatively.

3.1.1 Assessment and Diagnosis

The surgical pathology of the left superficial parotidectomy and left level II neck dissection specimens prominently demonstrated a well demarcated but unencapsulated, yellow-tan to red-brown, diffusely degenerative mass that has overall dimensions of 2.8 x 2.5 x 2 cm. The mass was focally cystic containing red-brown hemorrhagic fluid and demonstrated a
papillary cystic architecture.

Abundant granular and eosinophilic vacuolated cytoplasm within the cells, which were arranged in solid, tubular, and microcystic patterns with eosinophilic secretions. Perineural invasion (PNI) and lymphovascular invasion (LVI) were not identified. Left neck level 2 lymph node dissection showed no evidence of malignancy in 0 of the 17 lymph nodes (LN) identified. On immunohistochemistry evaluation the tumor cells were positive for S100 and mammaglobin, as demonstrated in Figure 2. A mucicarmine stain was negative. PAS stain highlighted some pink secretion within the lumen and was diastase resistant. Fluorescence in situ hybridization (FISH), performed courtesy of the University of Pittsburgh Medical Center, was positive for the ETV6-NTRK6 fusion gene (Figure 3).

The constellation of these findings was consistent with the diagnosis of mammary analogue secretory carcinoma (MASC) of the parotid gland.

3.2 Review of Literature

The initial database query and resulted in a total of 35 articles as demonstrated in the prisma flow diagram in eFigure 1 (Supplement 1). Four independent reviewers screened the full text articles for pediatric cases of MASC and 11 articles were deemed relevant to this study. One paper was excluded because the pediatric case could not be distinguished from the adult cases reported. The 10 remaining papers included a total of 4 pediatric case reports, 19-21,28 5 retrospective reviews 8,9,12,17,18 and 1 editorial letter 6 of pediatric MASC, evaluating or reporting a total of 11 pediatric patients, which are displayed in Table 1. Based on the Oxford Center for Evidence-based Medicine for rating of individual studies, 5 papers were rated 5 consistent with “Opinion of respected authorities; case report” and the remaining 5 papers consistent with a
score of 4 consistent with “Case Series with or without intervention.” The majority of documented cases of pediatric MASC were derived from retrospective review of institutional archives of other salivary gland diagnoses with limited detail on the clinical presentation or medical and surgical management. Of the 7 cases extracted from studies re-reviewing pathology archives, previous diagnoses included 3 patients\textsuperscript{6,12,18} with AciCC, 1 with MEC, 1 with pleomorphic adenoma\textsuperscript{9}, 1 case with MASC\textsuperscript{17} and 1 patient was not specified\textsuperscript{8}.

### 3.2.1 Clinical Presentation

The 11 pediatric patients ranged in age of 10-17 years with a median age of 15 years, and a female-to-male ratio of 1:1.2. The mean size of the tumor, reported in 10 of 11 patients, was 2.41 cm (range 1.0-3.8 cm)\textsuperscript{6,8,9,12,18-21,28}. The most common clinical presentation, in the 4 case reports, was a slowly enlarging, fixed, and painless mass, often detected incidentally on physical examination. Of 11 pediatric patients included in this analysis, 9 of the tumors were located in the parotid gland\textsuperscript{9,12,17,18,19-21,28}, one was reported in the submandibular gland\textsuperscript{8} and one in the upper lip\textsuperscript{6}.

### 3.2.2 Assessment and Diagnosis

Work-up described in the 4 case reports included combinations of magnetic resonance imaging (MRI), computerized tomography (CT) and/or FNA; 2 cases utilized MRI\textsuperscript{19,21}, one utilized CT imaging\textsuperscript{28}, and one utilized both CT imaging and MRI\textsuperscript{20}. MRI findings were described as: well-circumscribed lesion with internal T2 hyper-intensity and intermediate T1 signal with a dependent fluid\textsuperscript{19}, mildly enhancing preauricular subcutaneous soft tissue mass\textsuperscript{20}, and a heterogeneously enhancing tumor at the superficial parotid lobe\textsuperscript{21}. CT scan findings were
described as a 2 x 2 cm fluid collection with rim enhancement in the anterior left parotid\textsuperscript{20}. FNA was utilized in two cases\textsuperscript{19,20}. One of which was non-diagnostic\textsuperscript{19} and the other was suggestive of salivary neoplasm\textsuperscript{20}.

All 4 case reports and 6 re-review cases reported histology and immunohistochemical staining results, individual findings reported in Table 1. The tumors were grossly described as a yellow-brown to tan, well-demarcated, unencapsulated cystic mass\textsuperscript{19-21,28}. Common histologic features comprise of a well-circumscribed mass with eosinophilic vacuolated cytoplasm within cystic, tubular, and/or papillary architecture, bland and low-grade nuclei, and rare mitotic figures. The panel of immunohistochemical stains reported varied among all studies with S100 being the only marker tested in all patients. S100 was positive in all 11 cases. Positive staining for vimentin (n=4), cytokeratin 19 (n=3), and mammaglobin (n=2) has also been described in all cases that utilized these stains. FISH was used to detect the \textit{ETV6-NTRK3} fusion gene for final confirmation of MASC in 11 of the patients; all were positive apart from one case\textsuperscript{17}, which was confirmed by histological features and immunohistochemical staining. Currently, molecular confirmation is considered the gold standard for the diagnosis of MASC. However, it has been postulated that the morphologic features together with supporting immunohistochemistry are sufficient for a diagnosis of MASC\textsuperscript{10,16-18}.

### 3.2.3 Treatment

All cases of MASC were surgically resected. Surgical intervention and adjuvant therapy was discussed only in the 4 case reports\textsuperscript{19-21,28}. Two cases described superficial parotidectomy with FN dissection\textsuperscript{19,20}, one of which required sacrifice of the FN\textsuperscript{20}, one case described a total parotidectomy with preservation of the FN and right selective neck dissection with exploration of
preauricular, level I, and level II lymph nodes\textsuperscript{28}, and one case simply reported a “tumor excision”\textsuperscript{21}. In all cases, post-operative radiation therapy was not deemed necessary.

### 3.2.4 Prognosis

Long-term disease specific outcomes are limited due to disease incidence and reporting as well as the relatively new identification of MASC as a distinct pathology. One study reports a patient with six recurrences in a 15-year period\textsuperscript{9}. No evidence of disease was reported in 5 patients\textsuperscript{9,12,18,21,28}, however duration of follow-up ranging from 8 months to 10 years, was only reported in 3 patients\textsuperscript{12,21,28}.

### 4. DISCUSSION

The \textit{ETV6-NTRK3} fusion gene is a result of the balanced translocation t(12;15)(p13;q25); the fusion gene encodes for a chimeric tyrosine kinase.\textsuperscript{1} MASC is a predominantly adult neoplasm, diagnosed at a median age of 45, and with a predilection for the parotid gland.\textsuperscript{4,5} Many of the published cases of MASC are re-reviewed salivary tumors found retrospectively to harbor the t(12;15)(p13;q25) translocation. In the largest of these reviews, which analyze both adult and pediatric patients, tumors previously diagnosed as other salivary gland tumors were found to represent MASC\textsuperscript{4,12,23,30}. Of 546 total cases of salivary gland carcinomas re-reviewed in these studies, 34 (6.2\%) were found to be MASC. Of those that reported information on previous diagnosis\textsuperscript{4,12,30} (n=21): 15 were Acinic, 2 MEC, 2 Adenocarcinoma, 1 Cystadenocarcinoma, and 1 Salivary duct carcinoma.

The MASC diagnosis is exceedingly rare in the pediatric population with 11 cases reported in the literature. There is a slight male predilection with a female-to-male ratio of 1:1.2,
age range from 10 to 17 years old with a median of 15 years old. The typical clinical course is a slowly growing, painless mass most commonly of the parotid gland, detected incidentally on physical examination, which is consistent with what is known from the adult literature. Only 4 studies commented on initial work-up, imaging, medical and surgical management. Our case report of an adolescent male with a slow growing asymptomatic parotid mass, was similar in presentation and demographic to those in existing literature. He was also managed in a comparable fashion with the addition of a selective neck dissection due to the hypermetabolic lymph nodes seen on imaging. Though only one study reports a case of disease recurrence, and 5 cases are reported with no evidence of disease, reporting of follow-up duration is limited to 3 patients, leaving very little data on outcomes of MASC in the pediatric population.

There is insufficient data on patient outcomes to base clinical management. Optimal management is therefore currently unknown but given that MASC was likely previously treated as AciCC, managing MASC like AciCC is logical until more data is obtained on MASC. Additional research and long-term follow-up are necessary to determine the prognosis and clinical behavior of MASC in the pediatric population. Overall, MASC seems to have survival outcomes comparable to AciCC in the adult population. The reported 5-year survival for AciCC being 90%, but 10- and 20-year survivals are 83% and 67%, respectively. Data on disease outcomes in large cohorts of AciCC patients are well known, but complicated by the probable inclusion of a sub-group of patients with a diagnosis of MASC.

As awareness of this recently described malignancy increases and more cases are identified, our knowledge about this rare neoplasm should improve. Going forward, MASC should be included within the differential diagnosis of clinicians treating salivary gland tumors in adult and pediatric populations.
5. CONCLUSION

Much is still unknown about MASC, clinicians must become aware of this when considering salivary gland neoplasm. Reporting of clinical data, particularly clinical course, medical and surgical management, and long-term follow-up are greatly needed in order to guide clinical practice.

ACKNOWLEDGMENTS

We would like to extend our sincere thanks to Dr. Simon Chiosea of the Department of Pathology at University of Pittsburgh Medical Center for performing fluorescence in situ hybridization enabling the confirmation of our diagnosis.

AUTHOR CONTRIBUTIONS

Authors Ngouajio, Drejet, Phillips and Dahl had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Drejet and Dahl

Acquisition, analysis, or interpretation of data: Ngouajio, Drejet, Phillips

Drafting of the manuscript: All Authors

Critical revision of the manuscript for important intellectual content: All Authors.

Statistical analysis: Ngouajio, Drejet
FUNDING

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
Table 1. Cases of MASC in pediatric patients reported in the literature

<table>
<thead>
<tr>
<th>Study Year</th>
<th>Age/Sex</th>
<th>Location</th>
<th>Size (cm)</th>
<th>Histology</th>
<th>IHC</th>
<th>Previous Diagnosis</th>
<th>Outcome/Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>RETROSPECTIVE REVIEWS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jung, 2013/2015</td>
<td>17 / F</td>
<td>Parotid</td>
<td>1.0</td>
<td>Papillary-cystic pattern with micropapillary features predominated</td>
<td>(+) S-100</td>
<td>MEC</td>
<td>Recurred x 6/15 years</td>
</tr>
<tr>
<td></td>
<td>17 / M</td>
<td>Parotid</td>
<td>1.5</td>
<td>Predominant microcystic pattern with or without solid nesting</td>
<td>(+) S-100</td>
<td>PA</td>
<td>NED, follow up not reported</td>
</tr>
<tr>
<td>Ito, 2015</td>
<td>10 / M</td>
<td>SMG</td>
<td></td>
<td>Lobulated growth structure divided by thin fibrous septa with microcystic, tubular, solid, and papillary. Secretions present in the cystic lumens were colloid-like and eosinophilic.</td>
<td>(+) S-100</td>
<td>Not Specified</td>
<td>Not Reported</td>
</tr>
<tr>
<td>Majewska, 2015</td>
<td>17 / M</td>
<td>Parotid</td>
<td>4.0</td>
<td>Macrocystic growth pattern</td>
<td>(+) S-100</td>
<td>AciCC</td>
<td>NED/10 years</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Zymogen Poor</td>
<td>(+) MBG</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(+) CK7, CK8</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(+) STAT5a</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(+) Vimentin</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(-) p63</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(-) DOG-1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shah*, 2015</td>
<td>16 / F</td>
<td>Right Parotid</td>
<td></td>
<td>Cystic lesions filled with friable tumor with a thick fibrous cyst wall; tumor nests often focally extended through the cyst wall. Microcystic and solid patterns</td>
<td>(+) S100</td>
<td>MASC</td>
<td>Unknown</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(+) MGB</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(+) CK</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(-) SMA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urano, 2015</td>
<td>14 / F</td>
<td>Parotid</td>
<td>2.8</td>
<td>Microcystic primary, solid secondary, vacuolated, oncocytic</td>
<td>(+) S-100</td>
<td>AciCC</td>
<td>NED</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>No zymogen granules</td>
<td>(+) CK19</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(+) Vimentin</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(+) LMWCK</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>(-) DOG-1</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

EDITORIAL LETTER

Griffith, 2011 | 15 / M | Upper Lip | 1.0 | PAS-D demonstrated scant zymogen granules | (+) S-100 | AciCC | Not Reported |
<table>
<thead>
<tr>
<th>Study Year</th>
<th>Age/Sex</th>
<th>Location</th>
<th>Size (cm)</th>
<th>Histology</th>
<th>IHC</th>
<th>Diagnosis</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rastatter 2011</td>
<td>14 / F</td>
<td>Right Parotid</td>
<td>3.0</td>
<td>Papillary formations and several microscopic cystic spaces that are filled with pale eosinophilic. Abundant eosinophilic cytoplasm and prominent nucleoli. There were moderately abundant pale, eosinophilic, bubbly secretions throughout the tumor. • PAS with pale staining • One periparotid lymph node was positive for metastatic carcinoma. • Low mitotic activity • No significant areas of necrosis • No PNI or LVI</td>
<td>(+) S-100</td>
<td>Original</td>
<td>NED, 12 months post-operatively</td>
</tr>
<tr>
<td>Hwang 2013</td>
<td>13 / M</td>
<td>Left Parotid</td>
<td>2.1</td>
<td>Microcysts, tubular structures, solid nest, papillary architecture, with secretions within the cyst lumen Tumor cells with pale nuclei and centrally located nucleoli. Cytoplasm was pale eosinophilic to vacuolated. • Low mitotic activity • PAS, PAS-D showed mucin focally within the cells • No zymogen granules • No PNI</td>
<td>(+) S-100 (+) CK 19 (+) Vimentin (-) CK5/6 (-) p63 (-) CEA, (-) alpha 1-antichymotrypsin</td>
<td>Original</td>
<td>NED on post-operative PET, Follow up: 8 months</td>
</tr>
<tr>
<td>Woo 2014</td>
<td>14 / M setting of 2/2 radiation</td>
<td>Left Parotid</td>
<td>2.0</td>
<td>Monotonous with granular and vacuolated amphophilic cytoplasm. Confluent nests and solid sheets. Medium-sized pleomorphic cells with abundant vacuolated eosinophilic cytoplasm and prominent nucleoli. Abundant extracellular mucin production within luminal structures (+) mucicarmine stain • PAS, PAS-D showed no evidence of true zymogen granule formation</td>
<td>(+) S-100 (+) Vimentin (+) EGFR (-) p63 (-) DOG-1</td>
<td>Original</td>
<td>Not Reported</td>
</tr>
<tr>
<td>Study Year</td>
<td>Age/Sex</td>
<td>Location</td>
<td>Size (cm)</td>
<td>Histology</td>
<td>IHC</td>
<td>Previous Diagnosis</td>
<td>Outcome/ Follow up</td>
</tr>
<tr>
<td>------------</td>
<td>---------</td>
<td>----------</td>
<td>-----------</td>
<td>---------------------------------------------------------------------------</td>
<td>-----</td>
<td>-------------------</td>
<td>-------------------</td>
</tr>
<tr>
<td>Quattlebaum 2015</td>
<td>15 / F Left Parotid</td>
<td>3.0</td>
<td>Within the lumen of the cyst were focal areas of neoplastic epithelial proliferation composed of uniform polygonal epithelial cells, some forming duct structures filled with bright eosinophilic seromucinous material and some forming papillary structures.</td>
<td>(+) S-100 (+) CK 19</td>
<td>Original</td>
<td>Not Reported</td>
<td></td>
</tr>
<tr>
<td>Our Case</td>
<td>14 / M Left Parotid</td>
<td>2.8</td>
<td>Papillary cystic architecture comprised of cells with abundant granular and vacuolated cytoplasm and eccentrically located nuclei. Arranged in solid, tubular and microcystic patterns with somewhat abundant eosinophilic secretions. Focal Atypia, Low mitotic activity, (-) mucicarmine stain, PAS, PAS-D poorly highlighted some pink secretion within the lumen. No zymogen granules. No PNI or LVI identified</td>
<td>(+) S-100 (+) GATA-3 (+) MGB (-) DOG-1 (-) BRST-2</td>
<td>Original</td>
<td>NED, follow up 4 months</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: BRST, breast-2.  CEA, carcinoembryonic antigen.  CK, cytokeratin.  DOG, discovered on GIST (Gastrointestinal Stomal Tumor). EGFR, epidermal growth factor receptor. ER, estrogen receptor.  LVI, lymphovascular invasion.  MGB, mammaglobin.  PAS, PAS-D, periodic acid-schiff diastase.  PNI, perineural invasion. PR, progesterone receptor

*tested negative for ETV6-NTRK3 fusion gene
References:


Figure Legend:

**Figure 1.** Axial computerized tomography scan. The asterisk identifies the mass in the left parotid gland.

**Figure 2.** (a) Hematoxylin and Eosin, x200. (b) s100 Immunohistochemical stain, x200. S100 stain revealing cytoplasmic and nuclear staining, (c) Mammaglobin Immunohistochemical stain, x200. Mammaglobin positivity within MASC.

**Figure 3.** Fluorescence in situ hybridization (FISH) — positive for the *ETV6-NTRK6* fusion gene

e**Figure 1 in the supplement:** Prisma Flow Diagram
Supplementary Online Content


eFigure 1. Prisma Flow Diagram

This supplementary material has been provided by the authors to give readers additional information about their work.
**eFigure 1.** Prisma Flow Diagram

- **Identification**
  - Records identified through database searching (n = 35)
  - Additional records identified through reference review (n = 1)

- **Screening**
  - Records screened (n = 36)
  - Records excluded (n = 25)

- **Eligibility**
  - Full-text articles assessed for eligibility (n = 11)
  - Full-text articles excluded -- no individual data available (n = 1)

- **Included**
  - Studies included in final analysis (n = 10)