Mammary analogue secretory carcinoma - A case report

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Abstract

Introduction: Mammary analogue secretory carcinoma (MASC) is a recently described salivary gland tumor that harbors the recurrent ETV6-NTRK3 translocation.(1) With this paper we report a rare case of MASC of the parotid salivary gland due to its rarity and a review of this disorder.

Case Report: A62yr old Male presented with a recurrent solitary swelling in his left parotid region. A CT of head & neck revealed a 5x4 cm well circumscribed radio opacity in the left parotid gland. The patient presented with no symptoms and had no co morbidities. A sample of the lesion was obtained for histopathological study, which yielded a definitive diagnosis of oncocytoma .He was operated for the same with wide surgical excision and reconstruction with PMMC flap and close monitoring and regular follow up care was done.

Discussion: According to the 2005 WHO Classification of Head and Neck Tumors, the groups of malignant epithelial salivary gland tumors contain many heterogeneous entities. The histomorphological classification of these tumors is complex, and their clinical behavior is not completely elucidated, partly because they are rare. Some entities, such as adenocarcinoma/cystadenocarcinoma NOS, might encompass subtypes still to be discovered by molecular analysis. Careful histomorphological examination of cases that did not entirely fulfill the criteria of one given entity in conjunction with a typical pattern of expression of immunohistochemically markers enabled Skalova et al to define mammary secretory analogue carcinoma (MASC) as a new entity.

Keywords: Mammary analogue secretory carcinoma, MASC, Salivary gland, ETV6-NTRK3 fusion, Translocation t (12;15).

Introduction

Mammary analogue secretory carcinoma (MASC) is a recently described salivary gland neoplasm, characterized by its striking morphologic and molecular similarities to secretory carcinoma of the breast which predominantly arises in the parotid gland. These tumors represent locally invasive malignancies with micro cystic architecture, low-grade nuclei, and granular pink vacuolated cytoplasm. They display strong vimentin and S100 positivity and harbor an identical t fusion results in a constitutively active chimeric tyrosine kinase and probable activation of the Ras-MAP kinase mitogenic pathway and the phosphatidyl inositol-3-kinase-AKT pathway and has transforming activity, not only in epithelial but also in mesenchymal and blood cell lineages. Earlier, the ETV6-NTRK3 translocation has been described in infantile fibro sarcoma,(3) congenital mesoblastic nephroma and acute myelogenous leukemia.(4) ETV6 is genetically unstable and fuses not only with *NTRK3* but also with other genes such as ABL1, EGFR3, PAX5, SYK and JAK2 in leukemia, myelodysplastic syndromes and sarcomas.(4,5) These features help exclude the most important differential diagnostic considerations, namely, acinic cell carcinoma (AciCC) and low-grade cystadenocarcinoma, not otherwise specified.

MASC predominantly affects men and normally does not behave in an aggressive way. The parotid gland is the most common affected gland by MASC.(2) We present a case of MASC occurring in a 62-year-old male, manifested as an asymptomatic mass in the left pre-auricular region. This article reports and gives reviews of this rare lesion and the treatment protocol followed.

Case Report

A 62-year-old male patient with complaint of a solitary swelling in the left middle 3 rd. of his face since 3 years with no relevant medical history reported to our unit .He noticed this mass of approximately 1x1 cm on the left angle of his jaw 3yrs ago for which he visited a Dental school where a incisional biopsy was done and was diagnosed as Warthin's tumor following which he underwent superficial parotidectomy and was relieved of his condition. 6 months later he noted a recurrence of swelling which on physical examination revealed a 5 × 6 cm, firm, fixed, non-tender mass on the left pre-auricular region. Facial nerve function was preserved. FNAB was done which was suggestive of oncocytoma/adenocarcinoma. No palpable lymphadenopathy was present on the neck region. A head and neck CT showed 5x5cm ovoid radio opaque lesion, of the left parotid gland and was reported as a probable pleomorphic adenoma.

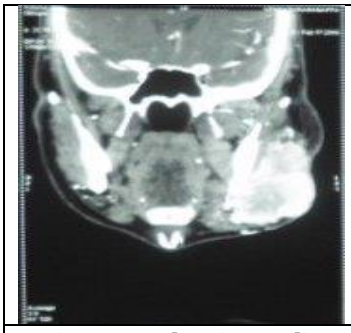

Fig. I: CT showing radio

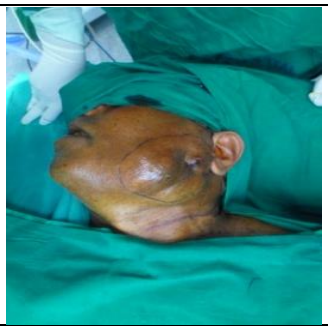

Fig. II: wide local

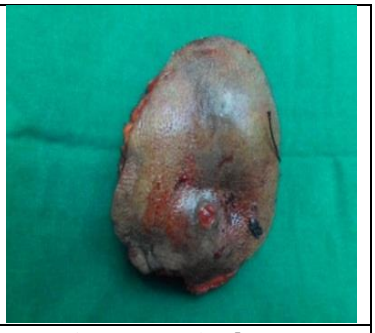

Fig. III: Excised mass opaque mass in parotid excision of lesion

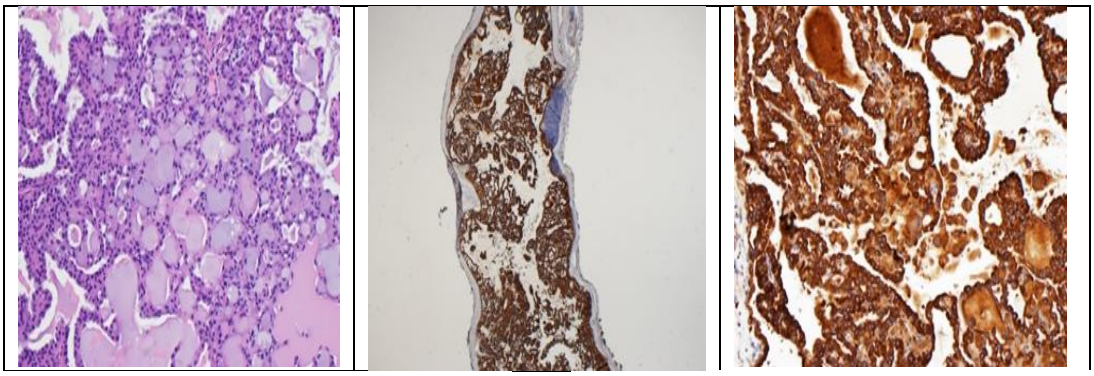

Fig. IV: Microscopic picture of the pathologic slide confirmed with IHC

Post-surgery the patient presented with facial nerve palsy. With close monitoring and follow up the wound healed satisfactorily with no breakdown or Frey's syndrome. There was no evidence of persistence or recurrence of disease, 6 months post-surgery.

Discussion

Salivary gland tumors account for 3% of head and neck lesions and approximately 80% of these occur in the parotid gland. The majority of parotid gland tumors are located in the superficial lobe and some investigations have reported that 2–4% of parotid tumors originate from the deep lobe. A total of 80–90% of these are benign, mixed tumors and the others are adenoid cystic, mucoepidermoid, acinic cell carcinomas and lipomas. MASCs are newly described, can occur in a wide age range, favor males, and can be misinterpreted as ACC or adenocarcinoma not otherwise specified by routine microscopy.

With limited experience about its prognosis, the patients with this tumor have a slightly aggressive clinical course than the patient with acinic cell carcinoma .Mostly adults are affected ranging from 13-77 years of age with male: female ratio is 1.4:1 we state the gender preferences of MASC from nine case series published between 2010and 2014. It is commonly found in parotid and submandibular glands.

Table 1: Characteristics of patients with MASC diagnosis in nine case series.

Cash Series Author	Publish Year	Number of Cases	Male	Female	Mean age	Age range
Skalova et al[1]	2010	16	9	7	46	21-75
Connor et al.[4]	2012	7	6	1	40	14-77
Chiosea et al.[17]	2012	10	8	2	45.5	NA
Bishop et al.[2,15]	2013	5	3	2	52	21-78
Griffith et al.[14]	2013	6	3	3	43.7	27-66
Bishop et al.[2,15]	2013	11	4	7	56	20-86
Skalova e al.[5]	2014	3	3	0	63	55-73
Majewska et al.[3]	2014	7	5	2	51.4	17-73
Serrano-Arevalo et al.[18]	2014	4	1	3	50.5	28-83

NA indicates not available.

MASC mimimics and can be easily misinterpreted as ACC. ACC is characterized by the presence of large, serous, acinar cells with cytoplasmic PAS positive zymogen like granules that are absent in MASC.[6] MASC is histologically characterized by the proliferation of uniform eosinophilic cells with a vacuolated cytoplasm, growing within a micro cystic, macro cystic, and papillary architecture .Even though the similar growth rate is between MASC and ACC, MASC is more likely to metastasize to the regional lymph nodes. It should thus be considered as a more aggressive tumor compared with the regular low grade ACC.

MASC usually presents as a painless, non-tender mass that increases in size over time.[10] The majority of MASC arising from the parotid gland account for two thirds of the reported cases[7,8] Table 2 presents the location, size, and lymph node involvement of MASC in eight case series. Bishop found that the mean age for presentation of MASC is 47 years (Table 2), in contrast with SC of the breast that usually occurs in younger patients.[9] MASC is considered as a low-grade carcinoma with a favorable prognosis according to Skálová et al it has moderate risk for local recurrence (15%),lymph node metastases (20%), and a low risk for distant metastases (5%).

Table 2: Size, Location & Lymph node involvement of MASC in eight case Series

Case series author	Number of cases	Size (cm)		Location					
		Mean	Range	Parotid gland	Subman-dibular	Minor salivary glands in the buccal mucosa	Lips	Palate	Lymph node involment at time of diagnosis
Skalova et al.[1,5]	16	2.1	0.7-5.5	13	0	1	1	1	0
Connor et al.[4]	7	1.8	0.5-0.3	2	1	3	1	0	0
Bishop et al.[2,15]	5	1.9	0.8-4.0	4	1	0	0	0	NA
Griffith et al.[14]	6	1.72	1.0-2.5	4	1	1	0	0	1
Bishop et al.[2,15]	11	0.9	0.3-2.0	0	2	1	4	4	0
Skalova et al.[1,5]	3	3.6	3.0-4.0	3	0	0	0	0	1
Majewska et al.[3]	7	2.8	2.0-4.0	6	0	0	0	1	3
Serrano-Arevalo et al.[18]	4	2.6	0.5-7.5	1	1	2	0	0	1

The definite diagnosis of MASC is done by confirming the translocation t (12;15) (p13;q25), which results in the ETV6-NTRK3 gene fusion. However, a negative test for ETV6-NTRK3 gene fusion does not rule out the diagnosis of MASC, it can also be done with the presence of positive immunohistochemical studies for STAT5, mammoglobin, and S-100 protein.[6] The treatment of choice in high-grade transformation MASC, should be radical surgery with neck dissection in addition to adjuvant radiotherapy. In the future, the inhibitions of ETV6-NTRK3may become a therapeutic target for patients with risk of MASC.

Conclusion

MASC is considered a low-grade carcinoma with a favorable prognosis. Therefore, treatment should mimic the management of other low-grade malignant salivary gland neoplasms. When high-grade transformation occurs, a more aggressive multidisciplinary management should be undertaken because of its poor prognosis. The inhibition of ETV6-NTRK3 gene fusion could be used as a treatment modality in the future.

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