Case Report

Mammary analogue secretory carcinoma of the parotid: An arduous maze to solve

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ABSTRACT

Mammary analogue secretory carcinoma (MASC) is an unusual and rare salivary gland malignancy that recapitulates the genetic and microscopic features of secretory carcinoma of the breast (SCB) which is an equally rare entity. MASC and SCB express S-100 protein, vimentin, mammaglobin, and harbor a t (12; 15) (p13; q25) translocation which leads to ETV6-NTRK3 fusion product. The morphology of MASC is not specific and can overlap with many salivary gland tumors. S100 and mammaglobin's strong positivity confirm the diagnosis of MASC. The morphology along with immunohistochemical findings provides important clues for diagnosis. Recent advances in molecular pathology help in investigating both differential diagnosis and prognosis in salivary gland oncology. Molecular testing is recommended to arrive at a diagnosis of MASC. We report a case of MASC of the parotid gland in a 47-year-old male patient with his immunohistochemical profile.

Key words: ETV6-NTRK3 fusion, Mammary analogue secretory carcinoma, Secretory carcinoma of breast

Mammary analogue secretory carcinoma (MASC) of the parotid was first described in 2010 [1]. It is a rare low-grade salivary gland neoplasm that shares the same morphology and genetic rearrangement (ETV6-NTRK3) of secretory carcinoma of the breast (SCB) [2]. MASC more commonly affects adult males and it has to be differentiated from other salivary gland tumors that mimic MASC. MASC has been most commonly reported in the parotid gland (70%), other less common sites include the submandibular salivary gland, base of the tongue, soft palate, lip, and buccal mucosa [3]. MASC shows consistent histological features such as microcystic and/or papillary architecture, with the individual cells showing uniform bland nuclei, abundant pink cytoplasm, and extracellular secretory material but these features are not specific [4]. The most common mimickers of MASC with overlapping features include acinic cell carcinoma (AciCC), adenocarcinoma not otherwise specified (NOS), mucoepidermoid carcinoma (MEC), and low-grade cribriform cystadenocarcinoma [4]. S100 protein, cytokeratin 7 and 18, vimentin, and mammaglobin expression are very useful diagnostic clues for the diagnosis [5].

Here, we report a case of MASC of the parotid gland in an adult male with their immunohistochemical profile.

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CASE REPORT

A 47-year-old male presented with swelling in the left parotid region for 5 years which was progressively increasing in size. He first noticed a swelling of size 2 × 2 cm near the left jaw.

On examination, there was a mobile and non-tender mass in the left parotid region measuring 4 × 4 cm. There were no enlarged lymph nodes in the neck. The oral cavity, ear, nose, and VII cranial nerve were normal. The patient did not have any other significant comorbidities or constitutional manifestations.

Magnetic resonance imaging showed a left parotid mass in the superficial lobe. A fine needle aspiration cytology (FNAC) was done; the smears were highly cellular and composed of poorly cohesive clusters and sheets of epithelial cells with abundant well-defined cytoplasm and regular ovoid nuclei with bland finely granular chromatin. The background showed few plasmacytoid-like cells (Fig. 1). Hence, two differential diagnoses of pleomorphic adenoma (PA) and basal call adenoma were kept. An excision biopsy was suggested for confirmation.

Superficial parotidectomy was done. Grossly, the specimen was 6 × 5 × 3 cm in size and was globular, nodular, and weighing 36 g. The external surface was unremarkable. The cut surface revealed a well-circumscribed, pale-brown, and firm lesion measuring 4 × 3 cm. Microscopic examination showed a fibrous

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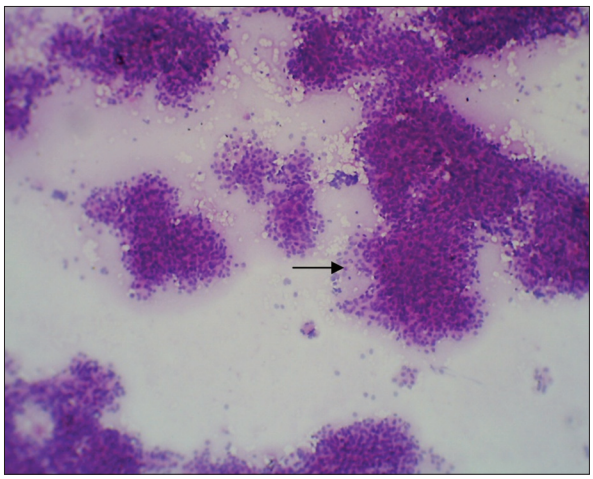

Figure 1: Cytology picture showing dyscohesive sheets of tumor cells with ovoid nucleus, fine granular chromatin and abundant eosinophilic cytoplasm (Hematoxylin and Eosin stain, 10×)

encapsulated neoplasm composed of cells arranged in sheets. The cells had indistinct cell borders with abundant eosinophilic cytoplasm; round to oval, and vesicular nuclei. Few areas showed polygonal cells arranged around vascular spaces containing abundant clear cytoplasm with centrally placed hyperchromatic nuclei and mitosis was 0–1/10HPF. Areas of necrosis were also seen (Fig. 2). With the above histological features, the possible differential diagnosis of AciCC, MEC, and myoepithelioma was given. Level II lymph nodes showed reactive features.

Immunohistochemistry (IHC) was suggested for confirmation. A panel of IHC parameters was done, among them, Pancytokeratin, S-100 protein, Vimentin, and Cytokeratin 7 were positive (Fig. 3). The negative markers include Calponin, smooth muscle actin (SMA), Anti-p63, CD117, Anti-human gross cystic disease fluid protein-15, epithelial membrane antigen (EMA), and carcinoembryonic antigen. Periodic acid-schiff (PAS) special stain was done and the tumor cells were negative.

Hence, the final diagnosis was given as MASC of the salivary gland. The patient was referred to a higher center for medical oncologist follow-up and management but was lost to follow-up.

DISCUSSION

SCB, a rare, low-grade, and slow-growing mammary ductal carcinoma, is seen in adolescent women. These tumors are also known as juvenile breast cancer [1,2]. SCB and MASC of the salivary glands share the same histology and molecular alterations [1,4]. Microscopic features of MASC include circumscribed and well-encapsulated nodules that have bland-appearing neoplastic cells arranged in tubular, microcystic, papillary, and solid patterns. Tumor cells have vesicular nuclei with eosinophilic and vacuolated cytoplasm. The tubular and microcystic spaces show abundant intraluminal colloid-like secretions. Multiple immunohistochemical markers stain positive for MASC includes high molecular weight keratin, Vimentin, S100 protein, CK–7, 8, 18, and 19 (cytokeratin). Ki67 staining shows a low proliferation index in these tumors [2].

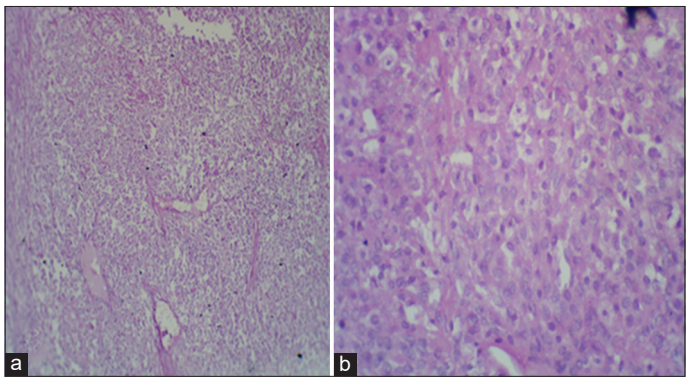

Figure 2: (a) Photomicrograph showing tumor cells arranged in sheets (Hematoxylin and Eosin stain, ×10); (b) Photomicrograph showing tumor cells with round to oval, vesicular nucleus, and abundant eosinophilic cytoplasm (Hematoxylin and Eosin stain, ×40)

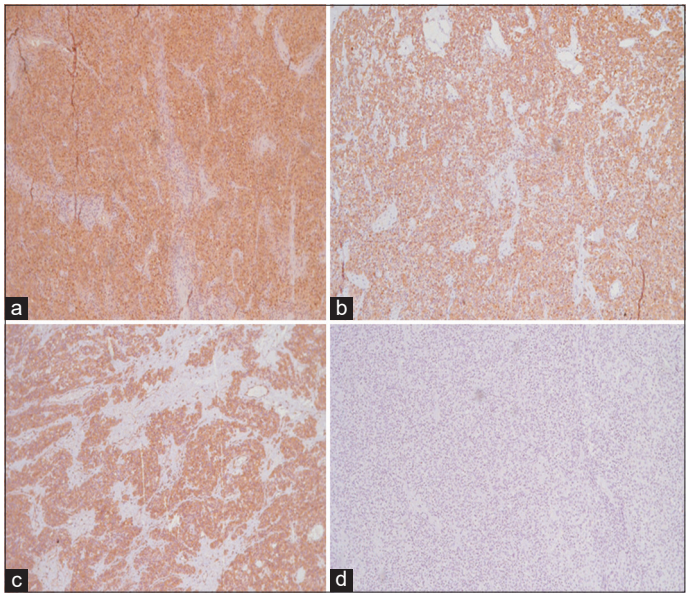

Figure 3: (a) Photomicrograph of tumor cells showing strong and diffuse positivity for S 100 protein (S100p immunohistochemical stain, ×10); (b) Photomicrograph showing Cytokeratin 7 positive tumor cells (cytokeratin 7 immunohistochemical stain, ×10); (c) Photomicrograph of tumor cells showing strong positivity for Vimentin (vimentin immunohistochemical stain, ×10×); (d) Photomicrograph of tumor cells showing negative for anti-human gross cystic disease fluid protein (GCDFP) (GCDFP immunohistochemical stain, ×10)

MASC was previously misclassified as adenocarcinoma NOS or AciCC. MASC is one of the salivary gland tumors with a breast tumor analogue, including AciCC, MEC, and PA [3].

FNAC in MASC reveals hypercellular smears composed of neoplastic cells arranged in sheets, papillary pattern, and dyscohesive clusters of various sizes. The tumor cells have round to oval and minimally atypical nuclei with or without nucleoli and abundant vacuolated or bubbly cytoplasm. The background is cystic or granular with no matrix material or any stromal tissue. However, these features are not pathognomonic of MASC [1-6].

Macroscopically, MASCs are well-circumscribed and rubbery tumors showing tan-white to grey cut surface and may show cystic areas with yellow fluid [2,4]. Microscopically, these are low-grade tumors with solid, microcystic, glandular, and papillary patterns. The tumor cells show round to oval

vesicular nuclei with fine granular chromatin, centrally placed nucleoli, and eosinophilic or vacuolated cytoplasm along with intraluminal secretions [6]. Some of the tumors may show capsular or neural invasion and adjacent glandular invasion. However, these microscopic features are also not very specific for MASC. Molecular studies are the mainstay for accurate diagnosis [6,7].

The intraluminal secretions seen in MASC show positivity for Mucicarmine and PAS, in our case, a PAS stain was done and was found to be negative. MASC shows diffuse and strong immunoreactivity for S100 protein, Cytokeratin 7 and 18, STAT5a, vimentin and mammaglobin, GCDFP, and EMA also stain positive but stain negative for SMA and calponin. MASCs are negative for estrogen and progesterone receptors [5,7].

Molecular methods give a precise diagnosis and aid in treatment decisions in various fields, more importantly in head-and-neck lesions. Salivary gland tumors are interesting and pose diagnostic difficulties due to their controversial and overlapping morphological features [4,8]. MASC harbors a balanced translocation t (12, 15) (p13; q25) leading to the formation of ETV6–NTRK3 fusion product which encodes tyrosine kinase. Documentation of this translocation is of utmost diagnostic importance in MASC, but most laboratories do not have molecular testing [5,7]. IHC analysis may help in arriving at a diagnosis of MASC among the diverse group of salivary gland neoplasms.

After the first publication and reporting of MASC, many institutes took up retrograde analysis of the salivary gland tumor cases reported and reanalyzed the cases of AciCC, Adenocarcinoma NOS, and MEC which were found to be MASC [8]. MASCs are differentiated from AciCC through immunohistochemical studies. The tumor cells in AciCC are negative for S-100p and mammaglobin but characteristically show strong cytoplasmic staining of DOG1. They do not harbor the ETV6-NTRK3 fusion gene. MASC can be differentiated from MEC by their diffuse nuclear expression of p63 but negative staining for S-100p [1,7,9]. Adenocarcinoma NOS is a diagnosis of exclusion as it is a poorly defined/unclassifiable salivary gland carcinoma; hence, documentation of ETV6-NTRK3 translocation is essential for MASC. Low-grade/high-grade salivary duct carcinomas also should be ruled out by molecular studies and demonstrating the genetic fusion product [1,4,5,10].

Even though MASC is low-grade tumors, they have an aggressive clinical course but the prognosis is generally favorable. High-grade transformation can occur rarely with regional lymph node/distant metastasis. Some cases even show local recurrence. Treatment of MASC includes local radiation therapy following the excision of the tumor [1,9].

CONCLUSION

MASC of the salivary gland is a rare and low-grade salivary gland tumor showing overlapping cytological and microscopic features of other salivary gland tumors and also histological and genetic rearrangement as that of SCB. Microscopic examination reveals tumor cells in microcystic, tubular, solid, or papillary architecture with round to oval vesicular nuclei and abundant eosinophilic. Molecular testing with a demonstration of the ETV6-NTRK3 fusion product is diagnostic of MASC. Since these tumors are rare, further clinical and pathological research studies have to be done to understand the diagnosis, course, and prognosis of this new entity.

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