Oncocytic variant of secretory carcinoma:
Expanding the morphological spectrum of secretory carcinoma in salivary gland

Dr. M.N. Hau[1], Dr. Chris Lai[2], Dr. J.K.C. Chan[1], Dr. W Cheuk[1].
1: Department of Pathology, Queen Elizabeth Hospital. 2: Department of Pathology, Hong Kong Baptist Hospital

Introduction

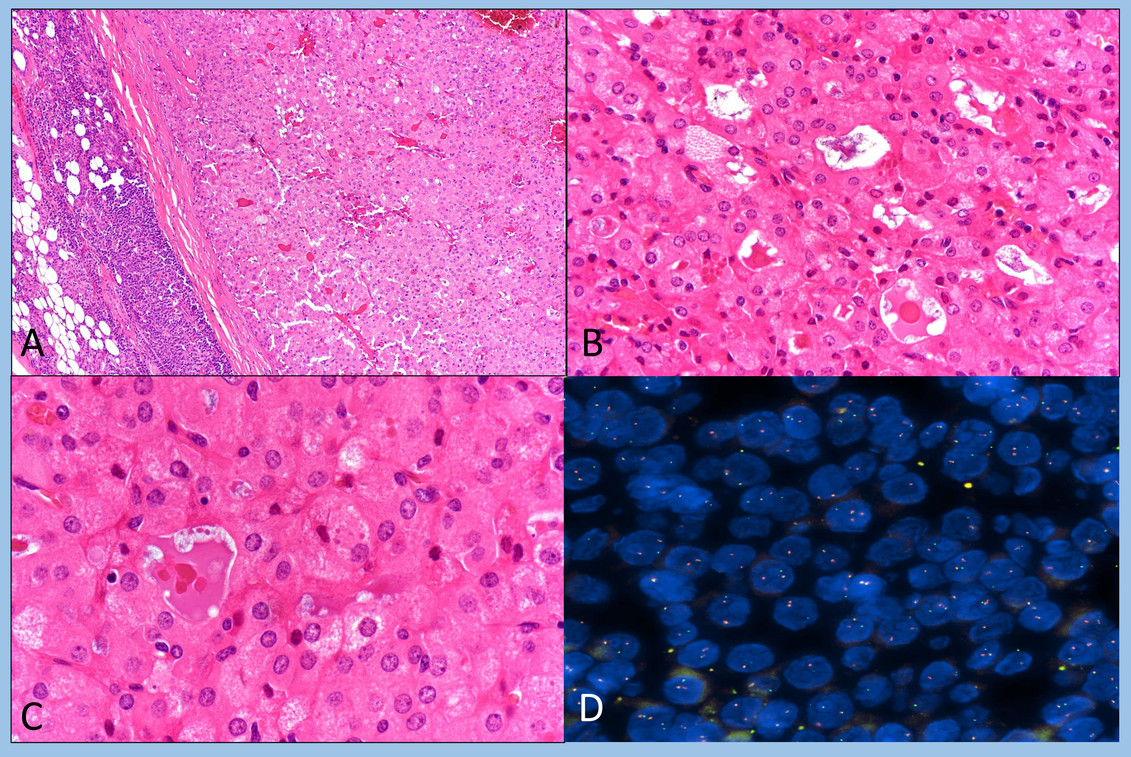
Secretory carcinoma, formerly called mammary analogue secretory carcinoma of the salivary gland, is a low grade carcinoma first described by Skalova et al in 2010. Histologically the tumor shares identical morphology with secretory carcinoma of the breast and harbors the same pathognomonic ETV6-NTRK3 translocation. Recently, variant translocation partners of ETV6 with RET, MET, MAML3, and ALK have been described. Morphologically, the tumor comprises microcystic nests, papillary cystic structures and sheets of cells with granular eosinophilic or multivacuolated cytoplasm, very similar to the so-called pauci-granular variant of acinic cell carcinoma. We describe herein the first case of a molecular-proven secretory carcinoma with oncocytic cytology, expanding the morphologic spectrum of this tumor.

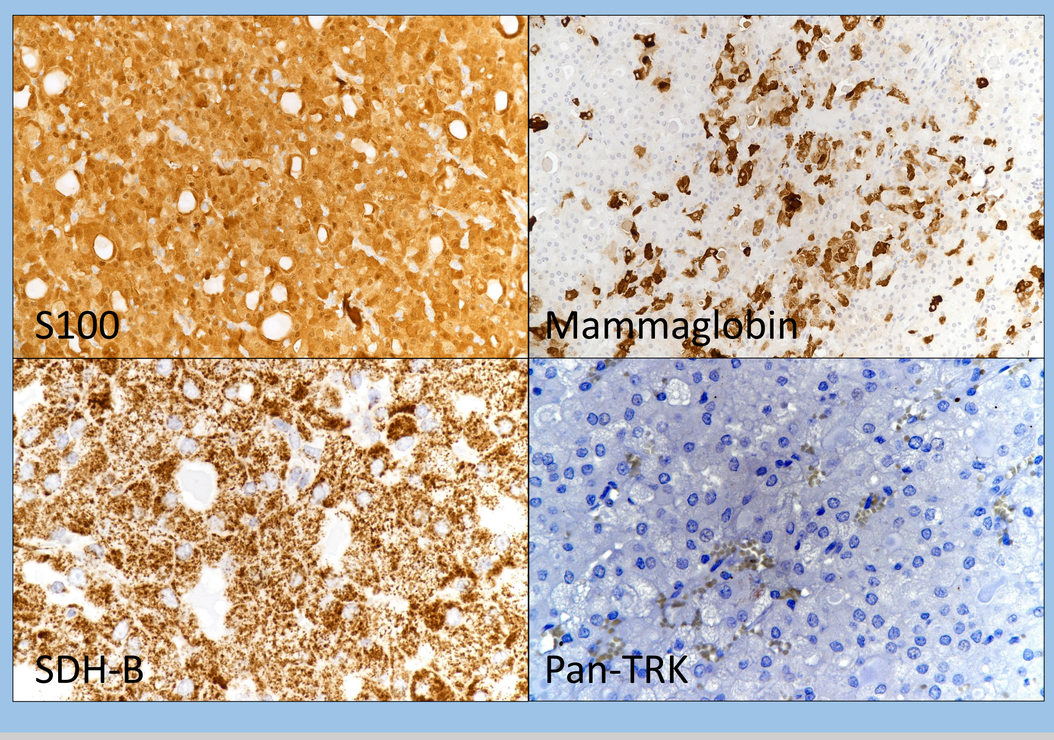
Case report

The patient was a previously healthy 46-year-old female who presented with a 3-cm progressive mass in the left parotid gland. Superficial parotidectomy was performed with adjuvant radiotherapy due to close excision margin. The patient was well with no evidence of disease at 5 years follow-up.

Pathological findings:

Grossly the tumor was circumscribed and bounded by a thin fibrous capsule with focal protuberance. Histological examination showed a circumscribed tumor comprising polygonal cells forming packets and rounded glands with myxohyaline secretion in the lumen and occasional broad papillae (Figures A, B). Throughout the lesion, the tumor cells possessed abundant granular eosinophilic cytoplasm, round to oval nuclei with fine chromatin and distinct nucleoli, imparting a prominent oncocytic appearance (Figure C). Mitotic figures were not seen. On immunostaining, the tumor cells expressed S100, MUC4, mammaglobin (patchy), and STAT5 (weak), and was negative for DOG1 (acinar cell marker). Basal cells were absent as evidenced by negative staining for CK5/6 and p63. Ki67 proliferative index was about 10%. Immunostaining for SDH-B highlighted the intracytoplasmic granules in the tumor cells. Immunostainings for pan-TRK and ALK were both negative. FISH for ETV6 using Vysis break-apart probes (Abbott, USA) showed ETV6 translocation (Figure D).





Discussion

We describe an oncocytic salivary gland tumor characterized by circumscribed border, nests and broad papillae that are composed of polygonal cells with abundant eosinophilic granular cytoplasm. The morphologic features raise the possibilities of oncocytic neoplasm, which was in fact the initial referral diagnosis. Oncocytoma is composed of nests and trabeculae of oncyocytic cells with interspersed basal cells which can be highlighted by high molecular weight cytokeratin or p63/p40. Oncocytic variant of mucoepidermoid carcinoma can be exclusively composed of oncocytic cells, but it shows extensive staining for p63/p40. Tumor such as Warthin tumor, pleomorphic adenoma and basal cell adenoma may show focal oncocytic changes, but careful assessment of other more characteristic areas can solve the diagnostic problem. Oncocytic variant of secretory carcinoma, on the other hand, is negative for p63/p40. Extensive positivity for S100, mammaglobin and STAT5a further aid the diagnosis of secretory carcinoma. Demonstration of characteristic ETV6-NTRK3 gene fusion provides a definitive confirmation of the diagnosis.

A few morphological variants have been described in the literature, including macrocystic variant and lipid-rich variants. Intraductal component of MASC has also been reported in association with low-grade mucinous adenocarcinoma.

Apart from the characteristic ETV6-NTRK3 gene fusion, a number of alternative fusions have been recently identified, including ETV6-RET, ETV6-MET, as well as CTNNA1-ALK fusion. A case of dual-fusion ETV6-NTRK3 and ETV6-MAML3 shows dual-morphology, including a more classical component as well as a second component with cribriform and papillary structures lined by pseudostratified cuboidal-to-columnar cells.

Oncocytic variant of secretory carcinoma is a previously undescribed morphological variant. The intracytoplasmic eosinophilic granules in our case are highlighted by SDH-B immunostaining, suggesting that the granules are mitochondria in nature. Unfortunately, there is lack of suitable material for ultrastructural examination. The presence of ETV6 breat-apart by FISH and the negative immunostaining for Pan-TRK raises the possibility of ETV6 translocation with an alternative partner.

Conclusion

We describe the first case of a molecular-proven secretory carcinoma with oncocytic cytology, expanding the morphologic spectrum of this tumor.