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Secretory Carcinoma of Salivary Glands

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Abstract

Secretory Carcinoma (SC) is a type of cancer recently identified in the salivary glands. Before its discovery, it was often classified as either Acinic Cell Carcinoma or adenocarcinoma. SC has distinct histopathological and immunohistochemical characteristics similar to breast secretory carcinoma. A unique t(12;15) (p13;q25) translocation resulting in the ETV6-NTRK3 gene fusion is also observed in SC and has not been found in other salivary gland cancer. This translocation is considered the definitive diagnostic standard, although some cases without the translocation have been reported. SC typically shows a lobulated growth pattern and is composed of microcystic, tubular, and solid structures with abundant eosinophilic homogenous or bubbly secretion. SC is generally considered a low-grade malignancy and is unlikely to metastasise. This article provides a comprehensive overview of secretory carcinoma of the salivary glands.

Keywords: Mammary Analogue Secretory Carcinoma, Salivary Glands, Parotid Gland

Introduction

Secretory Carcinoma is a rare type of malignant tumour found in the salivary gland. It was first described by Skalova et al. in 2010.[1] Initially, it was named mammary analogue secretory carcinoma (MASC) because it resembled secretory carcinoma (SC) of the breast. Later, the latest WHO classification replaced MASC with secretory carcinoma. A fusion gene ETV6-NTRK3, resulting from the translocation t (12;15) (p13; q25), is associated with this tumour. Before the definition of Secretory Carcinoma, many cases were mistakenly diagnosed as Acinic cell carcinoma.[2] Some specific immunohistochemical features such as positive

Mammaglobin, S-100, and Vimentin stains are related to this tumour.[3]

Clinical Features and Pathogenesis

According to reports, MASC accounts for up to 4.5% of malignant salivary gland tumour cases.[4]

Adults diagnosed with SC have a mean age of 47. SC is slightly more prevalent in men than women, unlike acinic cell carcinoma. [5]The most frequent location of origin is the parotid gland, while the oral cavity (including the soft palate, oral mucosa, and lips), the submandibular glands, and the accessory parotid glands follow in frequency. [6,7] It has been described that a case of secretory carcinoma (SC) occurred in the ethmoidal sinus. [8]

In the case of secretory carcinoma (SC), a unique t (12;15) (p13;q25) chromosomal translocation has been identified. This translocation leads to the fusion of the ETV6 gene on chromosome 12 with the NTRK3 gene on chromosome 15, resulting in the formation of a chimeric tyrosine kinase protein. This protein plays a crucial role in the development and progression of the tumour. It's important to note that this specific translocation has not been observed in any other type of salivary gland tumour.[7, 9]However, it is important to note that not all cases of SC's have this particular translocation.[10] ETV6-RET translocation and ETV6-MET fusion have also been reported as molecular alterations associated with SC in some specific cases.[11, 12]

Histopathological Features

SC is characterized by a cell proliferation that is located within fibrous septa and has a well-defined appearance. These septa may or may not display hyalinization and they contribute to the lesion's lobular appearance. The growth pattern of SC is primarily secretory and can take on various forms such as microcystic, tubular, solid, macrocystic, or papillary. It is common to observe a papillary cystic pattern in SC cases, whereas acinic cell carcinomas tend to display a solid pattern. [13]The mucicarmine and PAS (pre- and post-diastase digestion) positive eosinophilic secretion is abundant and homogeneous in nature, which is a characteristic feature. In some cases, there may be a fibrosclerotic stroma present, with isolated cell islands usually found in the centre of the lesion.

SC always displays a positive immunohistochemical profile, which is usually intense and diffuse. This profile typically includes the presence of mamma globin, S-100 protein, and vimentin. [19]- The tumour tends to express different proteins, such as pancytokeratin, CK7, CK8, EMA, STAT5a, and GCDFP15, but in a variable manner. The tumour usually tests negative for DOG-1 and calponin, SMA, CK5/6, and p63, which are basal and myoepithelial cell markers.DOG-1 is a useful protein to improve the specificity of mammaglobin in SC diagnosis, as it is selectively present in serous acinar cells and intercalated ductal cell membranes. A combination of S-100, mammaglobin, vimentin, and adipophilin positivity, along with DOG-1 negativity, is suggestive of SC. [14, 15]

Differential diagnosis of SC can be arrived at by considering acinic cell carcinoma, intraductal carcinoma (low-grade cribriform cystadenocarcinoma), and low-grade mucoepidermoid carcinoma. Among these, acinic cell carcinoma holds the greatest significance.

Treatment

The treatment strategy for SC varies depending on the stage of the disease upon diagnosis, as well as the molecular and histological characteristics of the tumor. Low-grade SC can be treated with complete surgical resection, which is the preferred method of treatment. However, in some cases, recurrence can occur. For larger tumors or those with perineural invasion or

positive margins, locoregional radiation therapy may be an option. Whether lymph node dissection is necessary will depend on the individual case.

When dealing with cases of SC with high-grade transformation, it is recommended to completely remove the affected gland and follow up with adjuvant radiotherapy. Furthermore, as this type of neoplasm tends to spread to the cervical lymph nodes, it is advisable to perform lymph node dissection to ensure optimal management of these patients. [16]

Entrectinib, which is a Tropomyosin receptor kinase (TRK) inhibitor, has been found to be effective in treating NTRK fusion-positive tumours, including secretory carcinoma. This medication's role in treating such tumours has been explained.[17]

The potential use of Larotrectinib as a treatment for NRTK fusion-positive tumours was also studied. Larotrectinib is another TRK inhibitor. [18]

Janik et al. reported in their meta-analysis that the recurrence rate is 19.9%.[19]

Conclusion

Secretory carcinoma is a type of malignant tumour recently identified to affect the salivary gland, primarily the parotid gland, though fewer cases are reported in the submandibular gland, lip, and oral cavity. This type of cancer is typically characterized as low-grade, with a comparatively low rate of regional and distant spread. Consequently, not all cases warrant elective neck dissection. In addition, the prognosis for secretory carcinoma is generally favourable, with a low recurrence rate and low disease-related mortality.

References

1. Skálová A, Vanecek T, Sima R, et al. Mammary analogue secretory carcinoma of salivary glands, containing the ETV6-NTRK3 fusion gene: a hitherto undescribed salivary gland tumor entity. Am J SurgPathol. 2010;34(5):599-608.
2. Terada T, Kawata R, Noro K, et al. Clinical characteristics of acinic cell carcinoma and secretory carcinoma of the parotid gland. Eur Arch Otorhinolaryngol. 2019;276(12):3461-3466
3. Bishop JA, Yonescu R, Batista D, Begum S, Eisele DW, Westra WH. Utility of mammaglobin immunohistochemistry as a proxy marker for the ETV6-NTRK3 translocation in the diagnosis of salivary mammary analogue secretory carcinoma. Hum Pathol. 2013;44(10):1982-1988.
4. Mammary Analogue Secretory Carcinoma (MASC) of the salivary gland: A new tumor entity. Biomol Biomed. 2016;16(3):237-238.
5. Skálová A, Gnepp DR, Lewis JS Jr, et al. Newly Described Entities in Salivary Gland Pathology. Am J SurgPathol. 2017;41(8): e33-e47.
6. T.M.Stevens, A.O.Kovalovsky, C.Velosaetal. Mammary analog secretory carcinoma, low-grade salivary duct carcinoma and mimickers: a comparative study. Mod Pathol.2016; 28 (8):1084–1100.
7. H. Majewska, A. Sk´alov´a, D. Stodulski et al. Mammary analogue secretory carcinoma of salivary glands: a new entity associated with ETV6 gene rearrangement. VirchowsArchiv. 2015; 466(3): 245–254.
8. Lurquin E, Jorissen M, Debiec-Rychter M, Hermans R, Hauben E. Mammary analogue secretory carcinoma of the sinus ethmoidalis. Histopathology. 2015; 67(5):749-751.
9. H. T. Chi, B. T. Ly, Y. Kano, A. Tojo, T. Watanabe, and Y. Sato. ETV6–NTRK3 as a therapeutic target of small molecule inhibitor PKC412. Biochemical

and Biophysical Research Communications.2012; 429(1-2):87–92.

10. A. Sk´alov´a, T. Vanecek, R. H. Simpson et al. Mammary analogue secretory carcinoma of salivary glands. Am J SurgPathol. 2016; 40(1):3–13.
11. Skalova A, Vanecek T, Martinek P, et al. Molecular Profiling of Mammary Analog Secretory Carcinoma Revealed a Subset of TumorsHarboring a Novel ETV6-RET Translocation: Report of 10 Cases. Am J SurgPathol. 2018; 42(2):234-246.
12. L.M.Rooper, T.Karantanos, Y.Ning, J.A.Bishop, S.W.Gordon, and H.Kang. Salivary secretory carcinoma with a novel ETV6 MET fusion. Am J SurgPathol. 2018;42(8):1121–1126.
13. Hsieh MS, Chou YH, Yeh SJ, Chang YL. The papillary-cystic pattern is characteristic in mammary analogue secretory carcinomas but is rarely observed in acinic cell carcinomas of the salivary gland. Virchows Arch. 2015;467(2):145-153.
14. J.A.Bishop, R.Yonescu, D.Batista, S.Begum, D.W.Eisele, and W.H.Westra. Utility of mammaglobin immunohistochemistry as a proxy marker for the ETV6-NTRK3 translocation in the diagnosis of salivary mammary analogue secretory carcinoma. Hum. Pathol. 2013;44(10):1982–1988.
15. N. Said-Al-Naief, R.Carlos, G.H.Vance, C.Miller, and P. C. Edwards. Combined DOG1 and mammaglobin immuno histochemistry is comparable to ETV6-breakapart analysis for differentiating between papillary cystic variants of acinic cell carcinoma and mammary analogue secretory carcinoma. Int. J. Surg. Pathol. 2016;25(2): 127–140.
16. B. A. Khalele and D. W.Eisele. Systematic review of mammary analog secretory carcinoma of salivary glands at 7 years after description. Head & Neck. 2017; 39(6):1243–1248.
17. Doebele RC, Drilon A, Paz-Ares L, et al. Entrectinib in patients with advanced or metastatic NTRK fusion-positive solid tumours: integrated analysis of three phase 1-2 trials [published correction appears in Lancet Oncol. 2020 ;21(2): e70] [published correction appears in Lancet Oncol. 2020 Jul;21(7): e341]
18. Drilon A, Laetsch TW, Kummar S, et al. Efficacy of Larotrectinib in TRK Fusion-Positive Cancers in Adults and Children. N Engl J Med. 2018;378(8):731-739.
19. Janik S, Faisal M, Marijic B, et al. Prognostic factors in mammary analogue secretory carcinomas of the parotid gland: systematic review and meta-analysis. Head Neck. 2022;44(3):792-804