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Case Report of a Secretory Carcinoma of the Salivary Gland: Clinical Management Following High-Grade Transformation

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Abstract : Secretory carcinoma (SC) is a rare type of salivary gland cancer. It was first realized as a distinct type of malignancy in 2010and wasinitially termed “mammary analogue secretory carcinoma” because of similarities with secretory breast cancer. The name was later changed to SC. Most SCs originate in parotid glands, and most harbour a rare gene mutation: ETV6-NTRK3. This mutation is rare in common cancers and common in rare cancers; it is present in most secretory carcinomas. Disease outcomes for SC are usually described as favourable as many cases of SC are lowgrade (LG), and cancer growth is slow. In early stages, localized therapy is usually indicated (surgery and/or radiation). Despitea favourable prognosis, a sub-set of casescan be much more aggressive.These cases tend to be of high-grade(HG).HG casesare associated with a poorer prognosis.Management of such cases can be challenging due to limited evidence for effective systemic therapy options. This case report describes the clinical management of a 46-year-oldmale patient with a unique case of SC. He was initially diagnosed with a low/intermediate grade carcinoma of the left parotid gland in 2009; he was treated with surgery and adjuvant radiation. Surgical pathology favoured primary salivary adenocarcinoma, and 2 lymph nodes were positive for malignancy. SC was not yet realized as a distinct type of cancerat the time of diagnosis, and the pathology reportvalidated this gap by stating that the specimen lacked features of the defined types of salivary carcinoma.Slow-growing pulmonary nodules were identified in 2017. In 2020, approximately 11 years after the initial diagnosis, the patient presented with malignant pleural effusion. Pathology from a pleural biopsy was consistent with metastatic poorly differentiated cancer of likely parotid origin, likely mammary analogue secretory carcinoma. The specimen was sent for Next Generation Sequencing (NGS); ETV6-NTRK3 gene fusion was confirmed, and systemic therapy was initiated.One cycle ofcarboplatin/paclitaxel was given in June 2020. He was switched to Larotrectinib (NTRK inhibitor (NTRKi)) later that month. Larotrectinib continued for approximately 9 months, with discontinuation in March 2021 due to disease progression. A second-generation NTRKi (Selitrectinib) was accessed and prescribedthrough a single patient study. Selitrectinib was well tolerated. The patient experienced a complete radiological response within~4 months. Disease progression occurred once again in October 2021. Progression was slow, and Selitrectinib continuedwhile the medical team performed a thorough search for additional treatment options. In January 2022, a liver lesion biopsy was performed, and NGS showed an NTRKG623R solvent-front resistance mutation. Various treatment pathways were considered. The patient pursuedanother investigational NTRKi through a clinical trial, and Selitrectinib was discontinued in July 2022. Excellent performance status was maintained throughout the entire course of treatment.It can be concluded that NTRK inhibitors provided satisfactory treatment efficacy and tolerance for this patient with high-grade transformation and NTRK gene fusion cancer. In the future, more clinical research is needed on systemic treatment options for high-grade transformations in NTRK gene fusion SCs.

Keywords : secretory carcinoma, high-grade transformations, NTRK gene fusion, NTRK inhibitor
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