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Title: Secretory carcinoma of the salivary gland: TRK immunohistochemistry as a diagnostic and surrogate marker for NTRK screening

Body: Background: Secretory carcinoma of the salivary gland (SCSG) is a rare malignancy, characterised usually by an ETV6::NTRK3 fusion. Molecular testing for identification of this fusion is expensive and not widely available.

Aim: To determine whether PAN-TRK immunohistochemistry (IHC) could be used as a screening tool for NTRK3 fusions in secretory carcinomas of the salivary gland.

Materials and methods: 10 SCSGs diagnosed between 2017 and 2024 were identified and Pan-Trk immunohistochemistry was performed on each.

NTRK3 gene fusion status was determined using a variety of available testing platforms.

Results: 10 cases of SCSG were identified in the parotid and submandibular glands, buccal mucosa, lip and soft palate.

Positive Pan-Trk IHC staining was seen in 9 of the 10 cases.

In 6 of these, Pan-Trk IHC correlated with positive identification of NTRK3 fusion.

In 3 of the Pan-TrK positive cases, Fluorescent in situ Hybridisation (FISH) for ETV6 rearrangement was performed, therefore no knowledge of the fusion partner.

Of note, in the single case where Pan-Trk IHC was negative, a RET fusion partner (not NTRK3) was identified. Given the recent reports of effectiveness of entrectinib (TRK inhibitor) in treating solid tumours with NTRK fusions, identification of NTRK fusions may be more important.

Conclusion: Preliminary data shows that Pan-Trk IHC correlates with the presence of an NTRK3 fusion in SCSG, and shows promise as a putative screening test for NTRK3 fusion

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