(N)Tracking the clinical and pathologic features of an anomalous case of secretory breast carcinoma

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Secretory carcinoma (SC) is a very rare type of invasive breast carcinoma (IBC) composed of cells with cytoplasmic vacuoles and extracellular secretions. Its hallmark genetic alteration is a translocation causing ETV6-NTRK3 gene fusion and production of a chimeric tyrosine kinase. Most SCs are triple-negative with low Ki-67. Among IBCs, SC carries a favourable prognosis [1]. We report the case of a 60-year-old woman seeking medical attention for a lump in her left breast. Mammography and ultrasonography confirmed the presence of a mass, which was diagnosed on core biopsy as IBC of no special type (NST) with cribriform morphology. ER was positive in 35% of cells, PR was negative and HER2 was not overexpressed. Ki-67 was 30%. At surgery, the tumour measured 4 cm and was classified as SC. ER was weakly positive in 5% of cells (ER-low IBC), PR and HER2 were negative, Ki-67 was 23%. CT scan raised suspicion of nodal mediastinal metastases, and the patient was treated with epirubicin and cyclophosphamide followed by paclitaxel. Restaging was negative and both breast radiotherapy and anastrazole were started. Two years later, CT scan identified two lung metastases, treated with metastasectomy and confirmed to be SC (Fig.1A). ER was positive in 25% of cells (Fig.1B), PR and HER2 were negative, Ki-67 was 30%. Real Time PCR successfully detected NTRK3 alteration (Fig.1C) and, in accordance with the current guidelines, therapy with entrectinib, an NTRK inhibitor, was initiated.

This case reflects how challenging it can be to deal with rare entities, especially when the presentation is atypical. Diagnosis of SC was not initially formulated because of the unusual "luminal B" hormonal phenotype. After surgery, choice of adjuvant therapy was complicated by the lack of experience with rare IBC types and by the uncertainty around management of "ER-low" IBCs. Unusually for SC, our patient developed metastases, raising the issue of appropriateness of surgery in the oligometastatic setting. Lastly, as metastatic SC is eligible for treatment with NTRK inhibitors after confirmation of NTRK rearrangement [1], the pathology unit had to elect and validate an appropriate molecular technique. This case highlights the importance of a multidisciplinary approach and of constant updates in knowledge and methods.

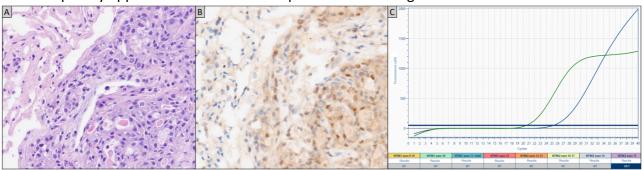


Figure caption

Fig.1 (A; H&E; 20x) Secretory breast carcinoma, metastatic to the lung. The tumour presents a prevalently microcystic growth pattern, with evidence of extracellular secretions. The tumour cells have eosinophilic, granular cytoplasm and mild to moderate nuclear atypia. (B; immunohistochemistry; 20x) Immunohistochemistry for estrogen receptors is focally positive. (C) Qualitative detection by One-Step RealTime-PCR of NTRK3 exon15 fusion in an RNA sample isolated from tumour tissue. The blue and green sigmoidal fluorescence curves represent the amplification reactions of the sample and of the endogenous control respectively.

References

1. Pareja F, Weigelt B, Reis-Filho JS. Problematic breast tumors reassessed in light of novel molecular data. Mod Pathol. 2021;34(Suppl 1):38-47. doi:10.1038/s41379-020-00693-7