LETTER TO THE EDITOR

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Multinucleated cells in parotid Warthin tumor: a potential diagnostic pitfall?

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Sir,

Cell atypia may be one of the potential pitfalls in the preoperative frozen section diagnosis of Warthin tumor [1]. The two main tumor-types, which have to be ruled out, are squamous cell carcinoma and mucoepidermoid carcinoma.

We would like to point out a potential pitfall, of possible interest in the differential diagnosis with carcinomas, that of multinucleated epithelial cells.

We had the occasion to identify multinucleated tumor cells both basally and luminally located in a Warthin tumor (Figure 1). Interestingly, we have identified in this case, CK5/6-, P63-, Bcl2- and HBME1-positive M-phase cells, both metaphasic and telophasic (binucleated) (Figure 2). These observations strongly suggest cytokinesis abnormalities in the tumor epithelial cells leading to the identification of a binucleated, telophase cell morphotype, possibly resulting in a multinucleated morphotype after several divisions. To mention would be that the quinoxaline derivative XK469 suppresses cytokinesis in MCF10A and 1c1c7 cells, 28% of cells being binucleated cells in treated the human normal mammary cell line MCF10A cultures and, 35% being multinucleated in treated murine hepatoma 1c1c7 cultures [2]. Interestingly, the contents of Bcl-2 "plummets" after XK469 treatment. The presence of several Bcl-2 positive binucleated cells in the epithelial Warthin tumor cells we have studied, was, however, consistent with the report of Bcl-2 overexpression blocking the dynamin induced caspase-mediated apoptosis after a cytokinesis failure [3].

In conclusion, multinucleated epithelial cells may occur in parotid Warthin tumors and may represent a diagnostic pitfall on intraoperative frozen section examination. The histogenesis of such cells is incompletely elucidated, interferences of noxes, including of drug-type, with the Bcl-2 anti-apoptosis pathway being possibly involved.

References

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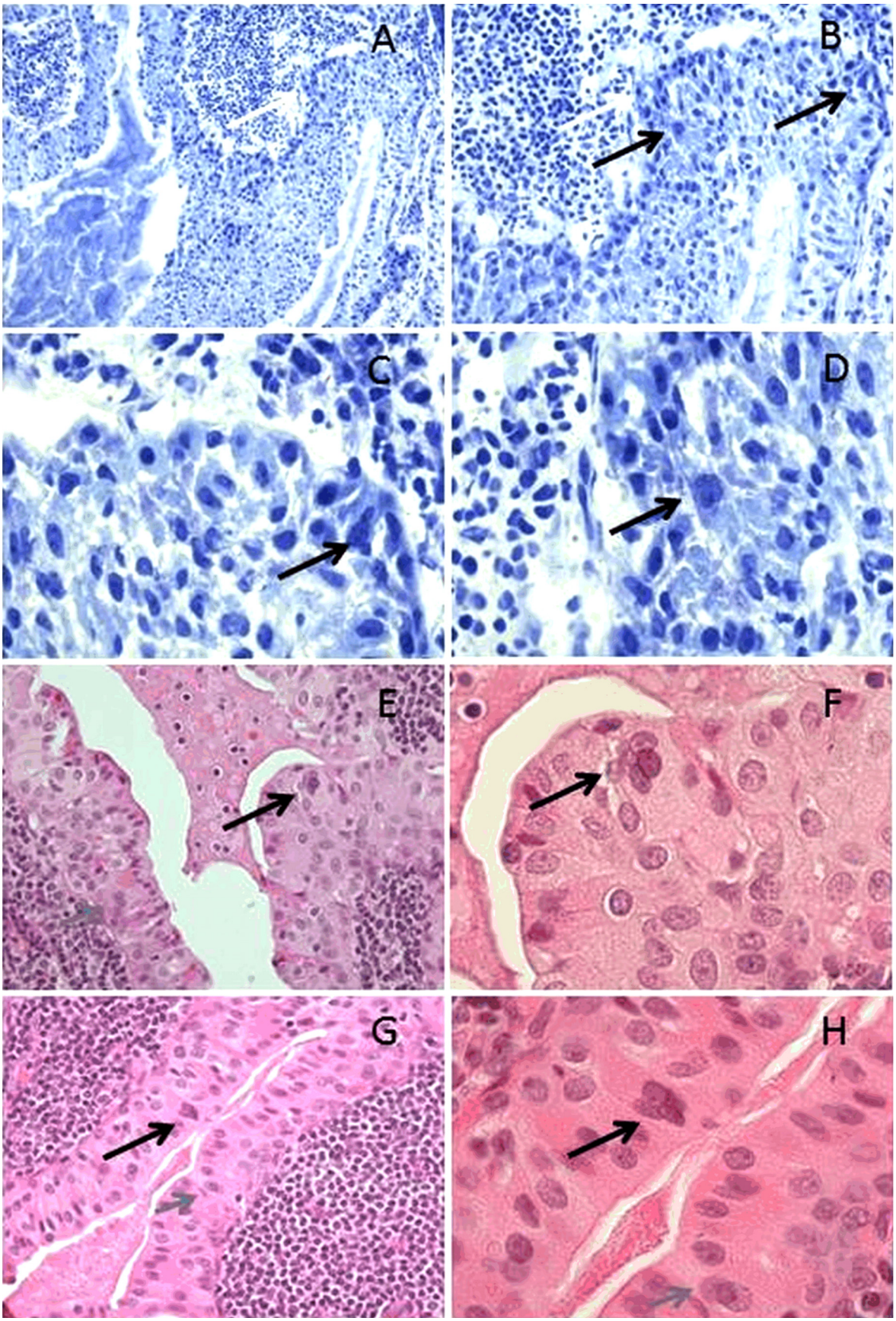

Figure 1 – ***Toluidine blue staining performed on the frozen section examination (FSE) tissue section showed epithelial foci at direct contact to lymphoid tissue. Several epithelial cells showed nuclear atypia difficult to differentiate from multinucleation (A–D): white arrow for epithelial foci, black arrow for atypical/multinucleated cells. After formalin-fixation, on the Hematoxylin–Eosin (HE)-stained section of the FSE block, these cells were not found. Rare multi-nucleated cells were identified in the other tissue specimens of the same tumor (E–H): black arrow for multinucleated cells, grey arrow for binucleated cells). Original magnification: ×200 (A); ×400 (B, E and G); ×1000 (C, D, F and H).***

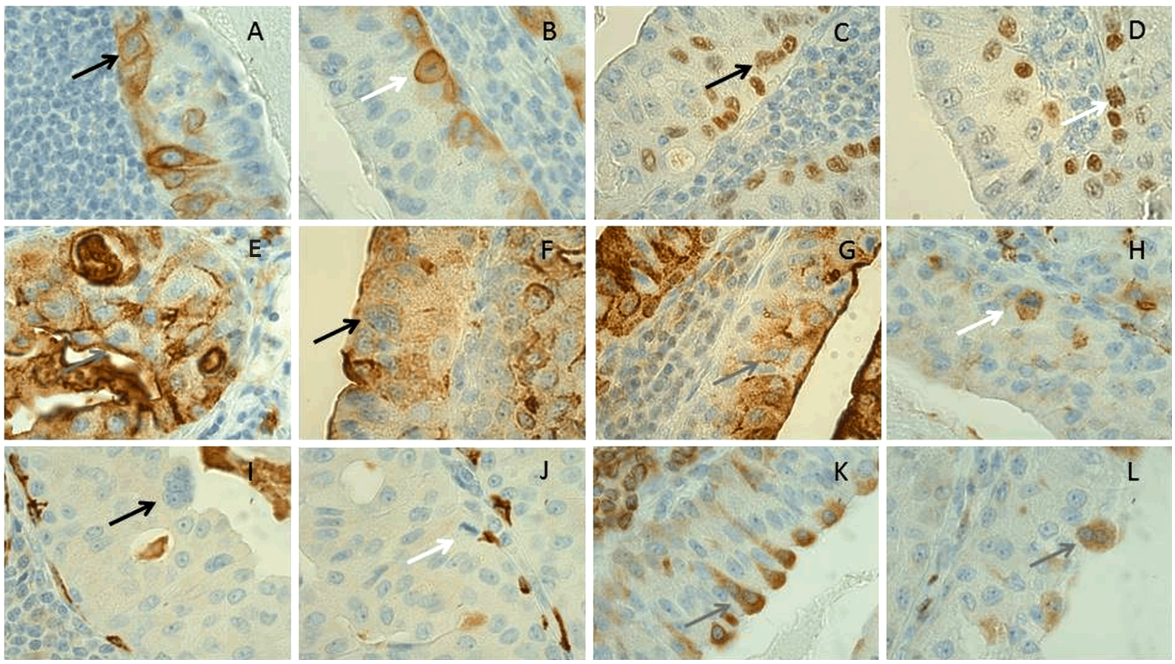

Figure 2 – ***Cytokeratin 5/6 (A), P63 (C), HBME1 (E–G) and Bcl2 (K and L) were positive in bi- or multinucleated cells (black arrow for multinucleated cells, grey arrow for binucleated cells). Cytokeratin 5/6 (B), P63 (D) and HBME1 (H) positive mitotic cells were also seen (white arrows for mitotic cells). WT1 was negative both in multinucleated cells and basal mitotic cells (I and J): black arrow for multinucleated cells, white arrow for mitotic cell). To note would be that serial and multistep sectioning was not helpful in identifying varied protein expression in a same cell. Original magnification, ×1000 (A–L).***