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Autophagy in cancer cytopathology: a case of intraoperative touch imprint of lung metastasis from TFE3-rearranged renal cell carcinoma

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A 67-year-old man presented with a lung nodule, suspected metastatic as he underwent nephrectomy 4 years earlier for a histologically unclassified renal tumor: such nodule was sent for a quick intraoperative microscopic evaluation (fig. 1A). Cytology, obtained by touch imprint, showed a pattern more consistent with a metastasis. The intriguing feature was the presence of intracytoplasmic hyaline globules (fig. 1B), confirmed on histology (fig. 2), suspected to be phagolysosomes from aberrant autophagy.

Immunohistochemistry allowed both the diagnosis of metastasis from TFE3-rearranged renal cell carcinoma (RCC+, CD10+, Vimentin+, PAX8+, TFE3+; TTF1-, Napsin-, p40-) and the autophagic nature of intracytoplasmic globules (LC3B+, p62+, ATG5+, PD-L1+).

Among renal cell carcinomas, Microphthalmia transcription factor (MiT) family translocation renal cell carcinoma (trCC) represents one of the rarest, and is characterized by chromosomal translocations involving transcription factor E3 (TFE3) or EB (TFEB) (on chromosomal loci Xp11.2 and 6p21, respectively), the former being the more aggressive. Recent studies identify autophagy as a molecular player in trCC [1]. Autophagy is the physiological mechanism of human cells – usually activated in stress situations – to incorporate and fragment autologous structures to obtain elements essential for cellular life itself; autophagy is also crucial in the cell process of antigen presentation. However, impairment of this mechanism plays an important role also in cancer progression, particularly in: immune evasion (incorrect antigen presentation leads to non-recognition of the cancer cell by the immune system); conversion of metastatic cells to stem cells resulting chemo-resistant (usually CD44+ cells that for their new condition of stemness are not recognized by the action of anti-tumor drugs); motility of metastatic cells [1, 2]. To date, the molecular relationship between autophagy and PD-L1 expression in cancer cells remains not entirely clear.

Conflict of interest: none declared

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References

1. Qu Y, Wu X, Anwaier A et al. Proteogenomic characterization of MiT family translocation renal cell carcinoma. *Nat Commun.* 2022 Dec 5;13(1):7494. doi: 10.1038/s41467-022-34460-w.
2. Smith AG, Macleod KF. Autophagy, cancer stem cells and drug resistance. *J Pathol.* 2019 Apr;247(5):708-718. doi: 10.1002/path.5222.

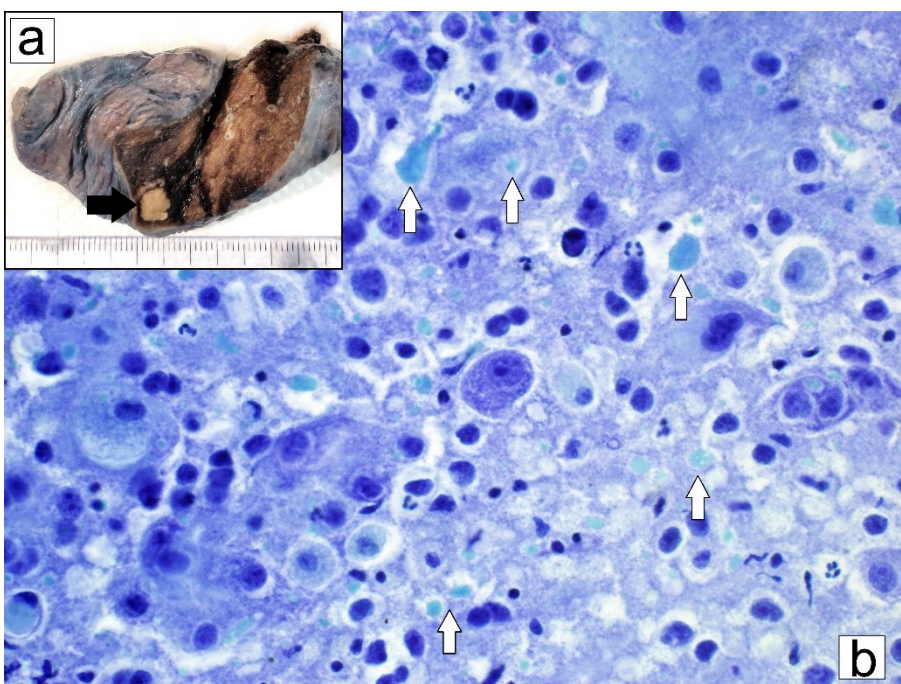


Figure 1. Macroscopy, showing a 1-cm, beige lung nodule with irregular contours (black arrow) (A). Microscopy of intraoperative cytology (touch imprint, toluidine blue stain, 60x), showing epithelioid cells with large granular cytoplasm, irregular and atypical nuclei, sometimes binucleated and prominent nucleoli. Scattered globular intracytoplasmic inclusions of various sizes, densely stained, were also noted (white arrows) (B)

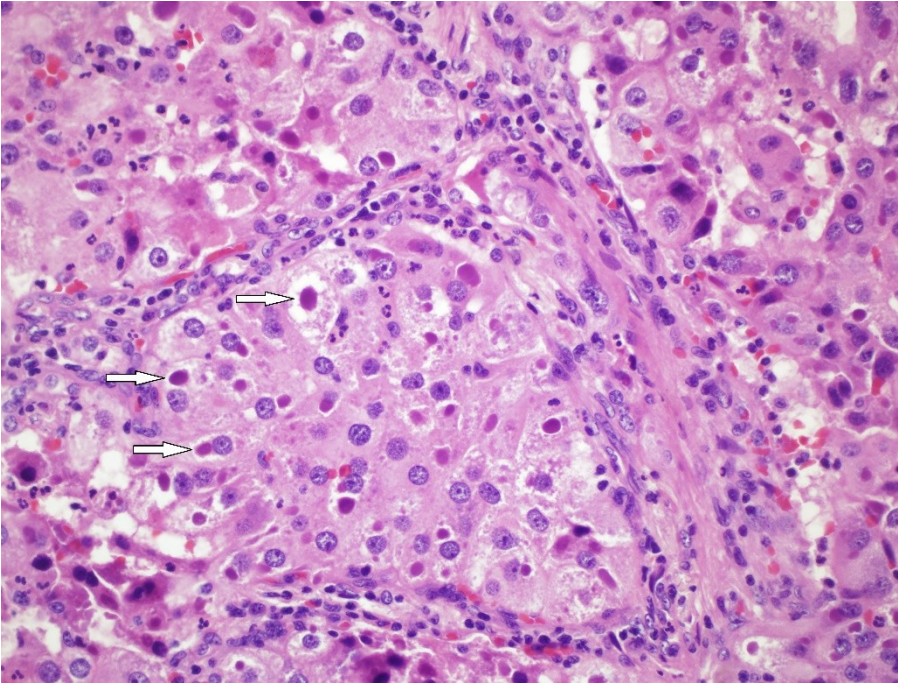


Figure 2. Histology (hematoxylin and eosin stain, 40x) confirmed the presence of those intracytoplasmic autophagic inclusions that were intensely eosinophilic (white arrows)