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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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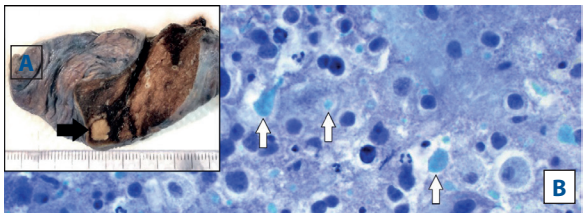

Figure 1. Macroscopy, showing a beige lung nodule (black arrow) (**A**). Intraoperative touch imprint cytology (toluidine blue, 60x), showing epithelioid neoplastic cells and scattered densely stained globular intracytoplasmic inclusions (white arrows) (**B**)

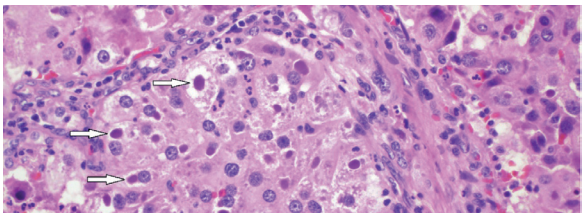

Figure 2. Histology (hematoxylin and eosin, 40x) confirmed the presence of intracytoplasmic autophagic eosinophilic inclusions (white arrows)

A 67-year-old man presented with a lung nodule, suspected metastatic as he underwent nephrectomy 4 years earlier for an unclassified renal cell carcinoma (RCC). Such nodule was sent for an intraoperative microscopic evaluation (fig. 1A) and cytology was consistent with a metastasis. The intriguing feature was the intracytoplasmic hyaline globules (IHG) (fig. 1B), confirmed on histology (fig. 2), suspected to be phagolysosomes from aberrant autophagy. Immunohistochemistry allowed both the diagnosis of metastasis from TFE3-rearranged RCC (RCC+, CD10+, Vimentin+, PAX8+, TFE3+; TTF1–, Napsin–) and the IHG autophagic nature (LC3B+, p62+, ATG5+, PD-L1+). Microphthalmia transcription factor (MiT) family translocation RCC (tRCC) is a very rare RCC, and is characterized by translocations involving TFE3 or TFEB, 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 to incorporate and fragment autologous structures to obtain elements essential for cellular life itself; autophagy is also crucial in cells process of antigen presentation. However, autophagy impairment plays a role in cancer progression, particularly in: immune evasion; conversion of metastatic cells to stem cells resulting chemo-resistant; motility of metastatic cells [1, 2]. To date, the molecular relationship between autophagy and PD-L1 expression in cancer is not clear.

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