Apoptosis, Autophagy, and Anesthesia; Correlation of the Three "A"s

Apoptosis is termed from an ancient Greek word that means falling off, and it is used from 1972 to address a morphologically distinct form of programmed and energy-dependent cell death (1, 2).

During development and aging apoptosis occurs as a normal phenomenon to maintain hemostasis and control cell population (2). Apart from physiologic apoptosis which counterpart to mitosis, pathologic apoptosis can occur which results in different clinical scenarios like cancer, autoimmune lymphoproliferative syndrome, Parkinson's Disease, Alzheimer's Disease, etc. This pathology could result from excessive apoptosis or on the other hand insufficient apoptosis (3).

Autophagy is also a Greek word meaning self-devouring or self-eating (4, 5). It is a cellular degradation and recycling process which can be categorized into three primary types:

1. Macroautophagy
2. Micro autophagy
3. Chaperone-Mediated Autophagy (CMA), which is fully discussed in this issue by Zandi et al. (6)

Autophagy is responsible for the clearance and degradation of abnormal proteins, organelles and removing infectious agents from the cell. Excessive or insufficient autophagy could result in cell death therefore dysregulated autophagy would result in numerous diseases like diabetes mellitus, neurodegenerative disorders, infectious disease, and cancer (5, 7).

Eisenberg-Lerner et al. described a cross-talk between autophagy and apoptosis and called them "life and death partners" (8). In this point of view, autophagy has a paradox effect as it may lead the cell to death or survival. Therefore, this connection between autophagy and apoptosis is complex and yet to be thoroughly defined. This definition and understanding could be a basis for future treatments of numerous diseases like cancer.

Anesthesia is a state of controlled, temporary loss of sensation induced by pharmacologic coma to provide patient comfort and optimized condition for surgical or procedural intervention (5, 9). Numerous agents are used during general or regional anesthesia and all of them are potentially considered to affect autophagy and apoptosis (3, 5, 9-14). GABA agonists and NMDA antagonist are accused as a trigger for neuronal apoptosis. Propofol, Sodium thiopental, and Benzodiazepins acts as GABA agonist which are used frequently in daily routine of an anesthesiologist and other options like Ketamin or N_2O are are NMDA antagonist therefore there would be limited choice for these agents (9). On the other hand regional block and neuraxial block also have impacts on regulation of apoptosis and autophagy (3, 14).

This massive data supports the correlation between these three A's (Apoptosis, Autophagy, and Anesthesia) could be interpreted as a way to choose the best anesthetic agents for patients as individualized medicine proposed. Though it may be plausible to consider a significant distance from basic researches related to "anesthesia-related apoptosis and anesthesia-related autophagy" to practical conclusions and clinical applications in our daily practice, things change so fast.

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