Molecular Signalling Pathway in Sinonasal Polyposis- The Role of MAPK/JNK, P13K/mTOR and LC3 pathways in the Pathogenesis of Sino-Nasal Polyposis

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Nasal polyps are benign masses arising from the mucous membranes of the nose and paranasal sinuses. Despite the significant morbidity of this recurrent disease the underlying central mechanisms regarding the pathogenesis of sinonasal polyposis are complex and poorly understood.

Presumably the morphological characteristics of nasal polyposis include epithelial hyperplasia, metaplasia, inflammatory cells infiltration, stromal fibrosis and edema. Eosinophils are the most common inflammatory cells. Increased collagen synthesis due to inhibition of apoptosis of eosinophils has been researched as a contributing factor in polyposis. Apoptosis and delayed cellular apoptosis are researched as contributory factors. Consequently effective apoptotic pathways can potentially prevent the formation of nasal polyposis.

Autophagy has been identified as a highly specific process to mitigate various types of cellular stress. Here the cytoplasmic contents are sequestered, transported by autophagosomes to lysosomes and degraded. Mitogen activated protein kinases (MAPKs) play an important role in the regulation of processes like cell proliferation, differentiation and apoptosis. MAPKs consists of c-jun NH2 terminal kinases (JNKs), p38 MAPKs and stress activated MAPKs which infers that a low MAPK/JNK activity supress apoptosis. On the contrary the phosphatidyl inositol 3-kinase/mammalian target of rapamycin P13K/mTOR signal transduction pathway, a signalling molecule for protein synthesis and cell survival is activated and inhibits autophagy, implying a high P13K/mTOR activity suppress autophagy. Light chain 3 (LC3-2) interacts with the mTOR pathway and increases directly proportional to the number of autophagosomes.

The inference of the Brazillian research study demonstrated that decreased expression of P38/MAPK, JNK and LC3 pathways and increased expression of P13K and mTOR pathways may have related to down regulation of apoptosis and autophagy in nasal polyposis. MAPKs is the major intracellular, oxidative stress -sensitive signal transduction pathway. Therefore , the expression of MAPK may be one of the key determinants of apoptosis in nasal polyposis. The terminal deoxynucleotidetransferase-mediated dUTP nick end labelling (TUNEL) assay was done to assess the distribution of apoptosis. Apoptotic index as the percentage of TUNEL positive cells with positive brown immunostaining was determined.

The results showed that increased expression of antiapoptotic molecules decreased expression of proapoptotic and autophagic molecules in nasal polyposis and especially the absence of apoptosis

in eosinophil cells in nasal polyposis maybe the contributing factor for the development of polyps.

Eosinophils have cytotoxic functions such as releasing major basic protein, eosinophilic peroxidase, the eosinophilic cationic protein that causes tissue damage and eosinophilia increases the likelihood of recurrent disease.

Apoptosis, eosniphilia and hyperproliferation are the major cellular processes in nasal polyposis and these proteins may take part and play some important role in the further understanding of the disease process and newer treatment protocols.

END NOTE

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