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ELUCIDATE APOPTOSIS PATHWAY AND CELL CYCLES IN CARDIAC MYXOMA

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BACKGROUND/AIMS: Cardiac myxoma, the most common primary tumor of the heart, has variable clinical presentations and a variable immunohistochemical profile. The existence of apoptosis in the cardiac myxoma has been demonstrated. This investigation will elucidate further the pathways of apoptosis and cell cycle in the cardiac myxomas.

METHODS: This study included a cultured cardiac myxoma cell line, and 20 patients with cardiac myxoma were treated with surgical excision of the lesion. Apoptosis signal transduction, Fas, Fas-ligand (FasL), tumor necrosis factor-α (TNF-α), Bcl-2, *survivin*, caspase-3, and terminal deoxynucleotidyl transferase nick-end labeling (TUNEL) assay; and cell cycle proteins, Ki-67 (MIB-1), p16, p53, and p63, were studied by both immunohistochemical and Western blot analysis.

RESULTS: The patient population comprised of 12 (60%) women and 8 (40%) men. The mean age of participants was 46 years, with an age range of 32 to 64 years. All cases were sporadic myxomas rather than familial myxoma. The clinical presentations included: absence of symptoms (26%), dyspnea (44%), stroke (9%), chest pain (9%), and fever (11%). All lesions were located in the left atrium. The myxoma did not differ with location or clinical event in terms of pathological scores, such as inflammation, cellularity, hyaline change, calcification and thrombosis. Apoptosis documented by TUNEL (70.9±17.6%) and caspase-3 (66.5±32.5%) final common pathway in cardiac myxoma is characterized by extrinsic Fas/Fas-L (positive stained 70.9±19.2%; 26.0±17.2% each) dependent pathway, but not intrinsic TNF-α or Bcl-2 dependent pathway. On the other hand, *survivin*, which suppresses apoptosis and regulates cell division, is strongly expressed in the cytoplasm (65.5±19.4%) to effect cell proliferation (Ki-67; 10.1±8.9%) and cell death (p63; 49.5±29.1%). Western Blot analysis (Fas/Fas-L, TNF-α, p16, p53 p63 and *caspase-3*) of the cultured cardiac myxoma cells validated the immunochemical results.

DISCUSSION/CONCLUSION: Cardiac myxomas enter both extrinsic dependent (Fas/FasL) and anti-apoptosis (*survivin)* pathways to control cell cycles with changes of Ki-67, p16, p53 and p6.

Key Words: Apoptosis, Cardiac myxoma, Cell cycle